Judging Your Genome:
Adducing Genetic Evidence to Support or Refute Causation in Australian and American Toxic Tort Litigation

By Sara Golru

A thesis submitted in fulfillment of the requirements for the degree of

Doctor of Philosophy

Faculty of Law

The University of Sydney

September 2022

Abstract

Proof of causation in toxic tort litigation has been plagued by issues of causal indeterminacy. The traditional deterministic causation model creates a potentially insurmountable obstacle for plaintiffs who must prove not only that they were exposed to a toxic substance but also that the relevant exposure caused their illness. Toxic tort plaintiffs are often unable to prove causation due to unknown or uncertain biological mechanisms of exposure and disease. Some academics and legal practitioners are increasingly embracing genetic information as a potential solution to this problem. However, others are exercising great caution and scepticism, arguing that genetic information poses similar or even more obstacles than other forms of scientific and medical evidence. This thesis investigates the interpretations and applications of genetic evidence in supporting or refuting causation in toxic tort claims. It answers the following question, '*Does genetic information alleviate or exacerbate the causal uncertainty in toxic torts?'* In order to answer this question, the thesis provides an original contribution to knowledge, by critically examining Australian and United States ('US') case law and literature focusing on genetic evidence in toxic torts. A comprehensive analysis of the case law and literature is vital to inform best practice for the future by identifying the past, present and predicted impact and challenges of genetic evidence.

The comparative case law analysis has ultimately demonstrated that issues of causal uncertainty affect both Australian and US toxic tort cases. However, US toxic tort litigants have exhibited a greater proclivity towards introducing genetic evidence to explore the issue of causation, with varying degrees of success. This reveals that genetic markers can provide valuable evidence of causation, or alternative causation, in addition to traditional forms of evidence such as epidemiological and/or toxicological studies. However, this thesis ultimately maintains that there is no single scientific method that can conclusively prove toxic tort causation. Despite the optimism of some scholars and practitioners, genetic evidence is presently by no means a solution to the problem of causal indeterminacy. Yet, if used properly, this evidence could shed light on causation, especially when viewed alongside all the other available evidence. Litigants, lawyers and courts should be aware of the limitations of this evidence and avoid overselling it as a solution to the causal indeterminacy problem.

Incorporation of genetic markers in scientific research and clinical practice, let alone trial and evidence, is still in its early stages. There is still much variability in scientific interpretations

of these markers, and there is limited usefulness where the markers are not sufficiently valid, sensitive or specific. Inconsistencies in the case law suggest there is substantial judicial disagreement, stemming from broader scientific disagreement, regarding the utility and validity of genetic markers. Tensions in the case law do not necessarily signal a need for doctrinal reform, rather they highlight that courts require greater guidance in assessing genetic information. A different approach to causation would do little to remedy the *scientific* indeterminacy at the heart of toxic tort cases. Even if courts were to abandon the counterfactual inquiry and adopt a different approach to factual causation, the courts would still have to grapple with understanding the scientific evidence in order to reach a conclusion as to causal contribution.

Without further guidance on the utility of such markers, this evidence will only further confuse and mislead the judge or jury. This could exacerbate the problem of causal indeterminacy, leading to inconsistent case outcomes and posing further obstacles to meritorious claims. This thesis therefore concludes that there is a strong need for practice-oriented instruments designed to assist courts, legal professionals and litigants in considering the strengths and weaknesses of genetic markers as a means of proving or disproving causation. As articulated throughout the thesis, a Reference Guide would help to ensure that the probative value of genetic evidence is properly weighed against any potential harms. The proposed guide would mimic the structure and contents of Chapters 4-7 of this thesis, containing a comprehensive survey of the case law and literature, and a detailed explanation and analysis of both the legal and scientific issues pertaining to genetic evidence. The original reference guide proposed in this thesis would ultimately promote a better understanding of how to assess the validity and utility of different types of genetic evidence in order to ensure that courts/litigants avoid misusing the evidence.

The findings outlined in this thesis are not unique to toxic torts. In fact, they are relevant to a wide variety of legal areas where health-related genetic evidence is likely to be used including employment law, criminal law, family law and insurance claims (such as workers' compensation or life insurance). This thesis focuses on toxic torts but also analyses personal injury cases more broadly (including medical negligence claims and workers' compensation claims). The original practice-oriented instrument proposed in the thesis therefore extends beyond toxic torts and can be applied in many areas of the law where health-related genetic evidence is used as a method to support or refute causation.

Acknowledgments

I am extremely grateful to all those who guided and supported me throughout this PhD journey.

I am most thankful to Professor Cameron Stewart and Dr Gemma Turton for their patient and encouraging supervision. I am indebted to them for their significant support, kindness, and guidance throughout my research, their invaluable feedback and their facilitation of numerous teaching, research and scholarship opportunities. I extend my gratitude to Professor Terry Carney for his very helpful insights and detailed feedback which was pivotal in helping to shape this thesis. I am thankful to the Hon Justice Elisabeth Peden and Professor Peter Cashman for kindly providing references for my PhD application. I am most grateful to the University of Sydney Law School for the invaluable teaching/research opportunities and scholarships that I have received throughout my candidature. This research is supported by an Australian Government Research Training Program (RTP) Fees Offset Scholarship, Postgraduate Research Scholarship in Law and Genetics, Postgraduate Research Support Scheme and Walter Reid Memorial Fund.

I have also been fortunate to publish and present papers on parts of this thesis. I would like to express my thanks to Associate Professor Yane Svetviev for the opportunity to present parts of this thesis at the Sydney Law School Research Seminar Series. I am grateful to all of the participants at that seminar for a helpful discussion, with special thanks to Dr Belinda Reeve, Professor Roger Magnusson and Professor David Hamer for their insightful comments and suggestions on that occasion. I am very appreciative of Professor Elise Bant and Henry Cooney at University of Western Australia Law Review for publishing parts of this thesis in their Special Edition on Causation, and graciously inviting me to present at the 2022 Causation Conference. It was an immense honour to present my research at the Causation Conference on the 'Law, Science and Causation' Panel alongside the Hon Justice Jonathan Beach and The Hon Robert French AC. I extend my thanks to the Journal of Civil Litigation and Practice, and the Torts Law Journal, for publishing parts of this thesis. I am also beholden to the University of New South Wales Law Journal for publishing my research on regulating the use of genetic information in life insurance.

Sincere thanks to all of my friends and colleagues who have offered invaluable encouragement and advice throughout this PhD. Finally, and most importantly, I am indebted to my family for their unwavering love, patience, motivation, and support in everything I do. I dedicate this thesis to them.

Declaration of Originality

This is to certify that to the best of my knowledge, the content of this thesis is entirely my own work and that any material written by others has been acknowledged in the text.

The thesis has not been submitted for a degree or any other purposes at The University of Sydney or at any other university or institution.

I certify that the intellectual content of this thesis is the product of my own work and all the assistance received in preparing this thesis and sources have been acknowledged. No human ethics approval was required or obtained for this thesis.

Sara Golru

Authorship Attribution Statement

This thesis contains material published in *University of Western Australia Law Review,* and later presented at the 2022 Causation Conference, sponsored by Herbert Smith Freehills, the Australian Academy of Law and The University of Western Australia Law School. This is chapter 1.1, 1.3, 1.5, 4.1.3-4.1.6, most of 4.6, all of Chapter 5 and most of the abstract. I am the sole author of this paper and was the sole presenter on my paper at this conference.

Golru, Sara, 'The Challenge of Proving Toxic Tort Causation: Genetic Markers as the Solution?' (2022) 49 *University of Western Australia Law Review* 186

Golru, Sara, 'The Challenge of Proving Toxic Tort Causation: Genetic Markers as the Solution?', Presented at the 2022 Causation Conference, sponsored by Herbert Smith Freehills, the Australian Academy of Law and The University of Western Australia Law School on 9 September 2022

This thesis also contains material published in the *Torts Law Journal.* This is chapter 3. I am the sole author of this paper.

Golru, Sara, 'The Extrapolation Dilemma: Toxicological Evidence and Toxic Torts' (2022) 27(3) *Torts Law Journal* 210

This thesis also contains material presented in the University of Sydney Law School Research Seminar Series, and later published in the Journal of Civil Litigation and Practice. This is all of chapter 7 and parts of 8.3.2. I am the sole author of this paper and was the sole presenter at this seminar.

Golru, Sara, 'Court-Ordered Genetic Testing: The Defendant's Right to Examine the Plaintiff's Genome?' (2022) 10(4) *Journal of Civil Litigation and Practice* 171

Golru, Sara, 'Court-Ordered Genetic Testing in Toxic Torts', Presented at the Sydney Law School Research Seminar Series on 10 November 2021

This thesis also includes citations to a publication, of which I am sole author, in *UNSW Law Journal Forum.* The citations are included in chapters 1.7, 7.3.1, and 8.3.2.

Golru, Sara, 'Regulating the Use of Genetic Information in the Life Insurance Industry' (2020) 7 *UNSW Law Journal Forum* 1

Table of Contents

1. Chapter One: Introduction

This thesis investigates the role of genetic evidence in overcoming the issue of causal uncertainty associated with toxic torts.[1] This research thematically analyses Australian and US case law where genetic evidence is adduced to support or refute causation in toxic tort cases. The rationale behind this study is to reveal the influence of genetic evidence on judicial decision-making and the outcome of toxic tort cases by investigating how lawyers are using genetic evidence, how courts are treating such evidence, and to what extent this method of proving exposure and effect advances toxic tort claims. Comprehensive case law analysis is vital to improving our understanding of genetic evidence, which is at a fairly early stage of development. Such analysis allows researchers to identify the impact and challenges of genetic evidence in order to inform best practice for the future. This thesis finds that notable misinterpretation and misuse of this evidence by litigants/lawyers/courts has resulted in inconsistencies in the case law. Accordingly, the thesis concludes that a reference guide is needed to inform the use of genetic evidence by the courts. Such a guide would help to promote consistency and fairness across judgments and across jurisdictions. It is argued that the content and structure of Chapters 4 to 7 of this thesis would form the basis of such a guide.

This chapter identifies the research problem, describes the purpose of the research and outlines the research questions. It also provides background information about the topic, and explains the methodology and structure of the thesis.

1.1. Statement of the Problem

Proof of causation in toxic tort litigation has been plagued by issues of causal indeterminacy. The traditional deterministic causation model creates a potentially insurmountable obstacle for plaintiffs who must prove not only that they were exposed to a toxic substance but also that the relevant exposure caused their illness. Toxic tort plaintiffs are often unable to prove causation due to unknown or uncertain biological mechanisms of exposure and disease. Some academics

[1] The term ‘toxic tort’ broadly encompasses situations where plaintiffs suffer harm as a result of exposure to a substance, such as chemicals, radiation or prescribed medicines. Accordingly, toxic tort claims can result from either environmental exposures or consumer products, including, for example, occupational injuries such as dust diseases, product injuries such as illnesses from tobacco, chronic adverse drug reactions and environmental diseases caused by fertilisers, inhalation of respirable carcinogens and radiation. For a more detailed definition, see Part 1.2 of this chapter.

and legal practitioners are increasingly embracing genetic information as a potential solution to this problem.[2] However, others are exercising great caution and scepticism, arguing that genetic information poses similar or even more obstacles than other forms of scientific and medical evidence.[3]

1.2. Defining Toxic Torts

In order to define toxic torts, it is important to first briefly explain what constitutes a tort. Tort law provides the body of rules that determines who will be responsible where a person or entity suffers personal injury, property damage, or other forms of economic, reputational, or emotional harms at the hands of another person or entity where there is no contract governing their respective rights with finality.[4] In effect, torts provide protection from another's wrongful conduct by compensating injured parties, usually through an award of damages covering economic and non-economic losses. A number of actions fall under the scope of tort law, including: assault, false imprisonment, battery, trespass, nuisance, intimidation, defamation, deceit and negligence.

The term 'toxic tort' is not so easily defined. It appears to have first been coined in a 1977 publication of the Association of Trial Lawyers of America where the authors noted:

> An action for personal injuries arising out of exposure to pollutants is a remedy long overlooked by lawyers. Part of the reason for the failure of the bar to appreciate the right to sue for environmental wrongs is that the area has not, at least until now, had a name of its own by which it could be identified. We propose to refer to it as an action for toxic torts. [5]

[2] See, eg, Susan Brice and Whitney Christian, 'The Use of Genetic Evidence to Defend Against Toxic Tort Claims—Part I' (2017) 29(9) *Intellectual Property & Technology Law Journal* 3; Gary Marchant, 'Genetic Data in Toxic Tort Litigation' (2016) 45(2) *The Brief* 22; Gary Marchant, 'Genetic susceptibility and biomarkers in toxic injury litigation' (2000) 41(1) *Jurimetrics* 67; Jamie Grodsky, 'Genomics and Toxic Torts: Dismantling the Risk-Injury Divide' (2007) 59(6) *Stanford Law Review* 1671; Albert Lin, 'Beyond Tort: Compensating Victims of Environmental Toxic Injury' (2005) 78 *Southern California Law Review* 1439; Allison Hite, 'Who's to Blame: How Genetic Information Will Lead to More Accurate Decisions in Toxic Tort Litigation' (2012) 63(4) *South Carolina Law Review* 1031.

[3] See, eg, Steve Gold, 'When Certainty Dissolves into Probability – A Legal Vision of Toxic Causation for the Post-Genomic Era' (2013) 70(1) *Washington & Lee Law Review* 237; Steve Gold, 'The More We Know, the Less Intelligent We Are – How Genomic Information Should, and Should Not, Change Toxic Tort Causation Doctrine' (2010) 34(2) *Harvard Environmental Law Review* 369; Susan Poulter, 'Genetic Testing in Toxic Injury Litigation - The Path to Scientific Certainty or Blind Alley?' (2001) 41(2) *Jurimetrics* 211; David Adelman, 'The False Promise of the Genomics Revolution for Environmental Law' (2005) 29 *Harvard Environmental Law Review* 117; Jennifer Champagne, 'Genetic Testing and Testimony in Toxic Tort Litigation' (2011) 13(1) *North Carolina Journal of Law & Technology* 1.

[4] Michael Green, *Bendectin and Birth Defects: The Challenges of Mass Toxic Substances Litigation* (University of Pennsylvania Press, 1996) 4.

[5] Paul Rheingold and N Jacobson, 'The Toxic Tort Cause of Action: Law and Procedure' in Paul Rheingold, Norman Landau and Michael Canavan (eds), *Toxic Torts: Tort Actions for Cancer and Lung Disease due to Environmental Pollution* (The Association of Trial Lawyers of America, 1977).

This definition seems to confine toxic torts to 'environmental wrongs' causing personal injury as a result of exposure to 'pollutants'. The term toxic tort has since been significantly broadened to encompass not only pollutants causing personal injury but also any toxic substance causing injury or damage 'to persons, to property, or to the environment due to the toxicity of a product, a substance, or a process'.[6]

An expansive dictionary definition of toxic torts describes these torts as 'A legal claim for damages due to injury or other harm resulting from exposure to environmental toxin(s) or adverse toxic effects of a pharmaceutical preparation'.[7] Accordingly, contemporary literature broadly describes 'toxic substances' to include asbestos, tobacco, nuclear material and prescribed medicines.[8] In essence, the definition of toxic torts has 'become a catch-all phrase loosely applied to any potential lawsuit involving a substance unfamiliar to the lay public which is suspected of causing some insidious disease process or which is thought to be potentially carcinogenic'.[9]

These broad definitions have resulted in significant ambiguity concerning whether toxic torts are a type of product liability or their own subset of law distinctly different from all other forms of traditional torts.[10] Any analysis of toxic torts is inherently complicated due to the absence of a coherent and unified definition across the unpredictable American federal system, which allows each state to develop its own legal principles.[11] Although it is beyond the scope of this thesis, it should be briefly noted that a precise definition may not be warranted, as 'toxic torts is not a term of art, but is, rather, one of convenience'.[12]

For the purpose of this thesis, the term 'toxic tort' will be used to denote a tort involving personal injury caused by exposure to toxic substances. Consistent with contemporary literature, the term 'toxic substance' is broadly interpreted to include both environmental exposures and consumer products.[13] The term 'substance' also encompasses emanations from toxic substances, such as radiation.[14] Accordingly, this definition of toxic torts includes, for

[6] Stuart Madden, *Toxic Torts Deskbook* (Taylor & Francis, 1992) 2.
[7] Miquel Porta and John Last, *Oxford Dictionary of Public Health* (Oxford University Press, 2nd ed, 2018).
[8] Brice and Christian (n 2) 3.
[9] Lawrence Cetrulo, *Toxic Torts Litigation Guide* (Thomson-West, 1st ed 2002) § 1.2.
[10] Anthony Roisman, Martha Judy and Daniel Stein, 'Preserving Justice – Defending Toxic Tort Litigation' (2004) 15(1) *Fordham Environmental Law Review* 191, 194-195.
[11] Ibid 197.
[12] Cetrulo (n 9).
[13] See, eg, Porta and Last (n 7); Brice and Christian (n 2).
[14] Elizabeth Adeney, 'The Challenge of Medical Uncertainty: Factual Causation in Anglo-Australian Toxic Tort Litigation' (1993) 19(1) *Monash University Law Review* 23, 23.

example, occupational injuries such as dust diseases, product injuries such as illnesses from tobacco, chronic adverse drug reactions and environmental diseases caused by fertilisers, inhalation of respirable carcinogens and radiation.[15]

In a typical toxic tort case, plaintiffs will sue under one or more fairly traditional causes of action: negligence, nuisance, trespass, strict liability and breach of statutory duty.[16] Some plaintiffs may rely on more novel theories relating to breach of warranty, failure to warn and design defect, but these claims are far less common.[17] The most commonly pled cause of action in toxic tort cases is negligence.[18] Subsequently, the focus of this thesis is on the tort of negligence so it is beyond the scope of this work to address tort law or private law more generally. Broadly speaking, negligence claims involve conduct which 'falls below the standard established by law for the protection of others against unreasonable risk of harm'.[19] In toxic tort cases where negligence is alleged, the plaintiff must satisfy the traditional negligence elements on the balance of probabilities in Australian law or by a preponderance of the evidence under US law.[20] In brief, these elements are 1) duty of care 2) breach of duty; 3) causation; and 4) damage. This thesis will confine its focus to causation, because this traditional tort element is greatly complicated by certain unique features of toxic torts.

1.3. **Introducing the Toxic Tort Causation Problem**

In order to better understand the causal indeterminacy problem in toxic torts, it is important to first briefly consider proof of causation in the tort of negligence. Both Australian and US courts adopt similar principles of tort law in their adjudication of causation. Plaintiffs in these jurisdictions must prove both factual causation (also known as *sine qua non,* cause-in-fact or actual cause) and legal causation (also known as scope of liability, proximate cause or remoteness). This thesis focuses solely on the test/s for factual causation.

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[15] Jane Stapleton, 'Compensating Victims of Disease' (1985) 5(2) *Oxford Journal of Legal Studies* 248, 248. As the term 'toxic tort' was not yet widely adopted at the time Stapleton's article was written, Stapleton refers to these torts as 'actual or apparently non-traumatic injuries' including personal injury arising from 'asbestos, thalidomide, diethylstilbestrol (DES), agent orange, etc.'. Despite the difference in terminology, Stapleton is undoubtedly referring to claims now covered under the contemporary definition of toxic torts.
[16] Roisman et al (n 10) 197-198; Madden (n 6) 21.
[17] Roisman et al (n 10) 197-198.
[18] Ibid.
[19] The American Law Institute, *Restatement of the Law (Second), Torts* (The American Law Institute, 1965) § 202.
[20] See, eg, *Civil Liability Act 2002* (NSW) s 5E; The American Law Institute, *Restatement of the Law (Third), Torts: Liability for Physical and Emotional Harm* (The American Law Institute, 2010) § 28, Comment *(a) ('Third Restatement')*.

The 'but-for' test presently dominates judicial approaches to factual causation in both Australian and US law.[21] This test stipulates that an act is a factual cause of an outcome if the outcome would *not* have occurred in the absence of the act. In other words, factual causation is established where the plaintiff's injury would *not* have occurred 'but for' the defendant's conduct. The defendant's conduct need only be *a* cause of the harm, not the sole cause.[22] US common-law suggests that a factual cause can also be described as a 'necessary condition' for the outcome.[23] Under Australian law, the common law but-for test has been embedded in state legislation stipulating that the defendant's negligence must be a 'necessary condition' of the occurrence of the plaintiff's harm.[24] As noted by the High Court of Australia in *Wallace v Kam,* 'The determination of factual causation in accordance with [statute] involves nothing more or less than the application of a "but for" test of causation'.[25]

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[21] See, eg, *Strong v Woolworths* (2012) 246 CLR 182 [18] (French CJ, Gummow, Crennan and Bell JJ) ('*Strong*'); *Adeels Palace Pty Ltd v Moubarak* (2009) 239 CLR 420 [55] (French CJ, Gummow, Hayne, Heydon and Crennan JJ); *Third Restatement* (n 20) § 26.

[22] *Third Restatement* (n 20) § 26, Comment *(b)*; *Strong* (n 21) [20]-[28].

[23] *Third Restatement* (n 20) § 26, Comments *(b)* and *(c)*. The American 'substantial factor' test was established to address cases of multiple *sufficient* causes, where each cause is independently and equally sufficient to cause the harm. In these cases of so-called 'overdetermined harm', factual causation was established because the defendant's conduct was a 'substantial factor' in causing the plaintiff's harm, even though the harm would have occurred 'but for' the defendant's conduct, see, eg, *Third Restatement* (n 20) § 27; *Summers v Tice* (1948) 33 Cal.2d 80; *Anderson v Minneapolis, St.Paul & Sault Ste. Marie. Ry. Co.* (1920) 179 NW 45. Despite the adoption of the substantial factor test in prior *Restatement*s, the black letter law enshrined in the *Third Restatement* no longer supports the test and has established a new 'sufficient-to-have-caused' test, see *Third Restatement* (n 20) §§ 26, Reporter's Note on Comment *(j)*, 27, Reporter's Note on Comment *(b)*. Although *Restatements* are not binding authority, they are highly persuasive because the American Law Institute effectively 'restates' existing common law into a series of rules. In cases of multiple sufficient causes, the *Third Restatement* has reformulated the test so that there is no evaluative discretion pertaining to the substantiality of the harm. Where there are two or more acts, each cause is a factual cause of the harm, without any evaluative exception, if each cause would have been sufficient to cause the harm under the 'but for' test in the absence of the other acts, ibid § 27. Therefore, it appears that the 'but for' test has regained its position of primacy in US cases of multiple sufficient causes.

[24] See, eg, *Civil Liability Act 2002* (NSW) s 5D(1); *Civil Law (Wrongs) Act 2002* (ACT) s 45(1); *Civil Liability Act 2003* (Qld) s 11(1); *Civil Liability Act 1936* (SA) s 34(1); *Civil Liability Act 2002* (Tas) s 13(1); *Wrongs Act 1958* (Vic) s 51(1); *Civil Liability Act 2002* (WA) s 5C(1). State legislation provides some limited judicial guidance for 'exceptional' or 'appropriate' cases involving multiple potential causes, see, eg, *Civil Liability Act 2002* (NSW) s 5D(2); *Civil Law (Wrongs) Act 2002* (ACT) s 45(2); *Civil Liability Act 2003* (Qld) s 11(2); *Civil Liability Act 1936* (SA) s 34(2); *Civil Liability Act 2002* (Tas) s 13(2); *Wrongs Act 1958* (Vic) s 51(2); *Civil Liability Act 2002* (WA) s 5C(2). For more information on the application of the 'material contribution' test in 'exceptional' cases, see, eg, *Review of the Law of Negligence* (Final Report, September 2002) 109-110 ('*Ipp Report*'); *King v Western Sydney Local Health Network* [2013] NSWCA 162 [155]; *Woolworths v Strong* [2010] NSWCA 282 [29], [47]-[49]; *Amaca v Booth* (2011) 246 CLR 37, 51-2 [37]; *Amaca v Ellis* [2010] HCA 5 [65], [68]; *Adeels Palace Pty Ltd v Moubarak* (2009) 239 CLR 420 [57]. Australian civil liability legislation generally excludes dust-related diseases from their scope. For example, both dust diseases and worker's compensation are excluded under the *Civil Liability Act 2002* (NSW) s 3B(1)(b), (f) and (g); For state legislation governing dust diseases and workers compensation, see, eg, *Dust Diseases Tribunal Act 1989* (NSW) and *Workers Compensation Act 1987* (NSW).

[25] *Wallace v Kam* (2013) 250 CLR 375 [16] (French CJ, Crennan, Kiefel, Gageler and Keane JJ) ('*Wallace*'). Following the pivotal case of *March v E & MH Stramare Pty Ltd* (1991) 171 CLR 506, the but-for test was qualified by reference to common sense principles, see *March* (n 15) 522 (Deane J); For more on the origins of the 'common sense' test, see HLA Hart and Tony Honoré (n 12); *Fitzgerald v Penn* (1954) 91 CLR 268, 277 (Dixon CJ, Fullagar and Kitto JJ). However, the civil liability legislation adopted since the *Ipp Report* (n 24)

Toxic tort plaintiffs are typically required to establish two types of factual causation: (1) general causation to show that a toxic substance is *capable* of causing the alleged harm in at least *some* of the population; and (2) specific causation to demonstrate that exposure to that substance in fact caused that *particular* plaintiff's harm.[26] Although the nomenclature of 'general' and 'individual' or 'specific' causation stems from US jurisprudence and has not been widely adopted in Australia, Australian courts do implicitly rely upon this two-step process of causal determination in toxic tort cases.[27] As noted by Professor Steve Gold, these concepts of general and specific causation 'lurk, as a philosophical matter, in almost any causal inquiry, but their express invocation is virtually unique to toxic torts'.[28]

In some instances, distinct forms of evidence about general causation and specific causation are either unavailable (as with exposures so rare that group-based, epidemiologic data cannot

clearly distinguishes a factual and normative stage of the causal requirement (the 'necessary condition' test – factual causation, and the 'scope of liability' – the normative component). As Edelman J explains, the common sense test of causation 'may be in decline', Justice James Edelman, 'Understanding Causation and Attribution of Responsibility' (Speech, Commercial Conference of the Supreme Court of Victoria/University of Melbourne, 7 September 2015) 1. The notion of 'common sense' is particularly incompatible with toxic tort cases where questions of causation almost always require the opinion of expert medical witnesses, rather than the application of the layperson's common sense. As neatly summarised by Gummow, Hayne and Crennan JJ in *Amaca v Booth,* 'many issues of causation…lie outside the realm of common knowledge and experience [because] They fall to be determined by reference to expert evidence, for example, medical evidence', *Amaca v Booth* (2010) 246 CLR 36 [67].

[26] *Third Restatement* (n 20) § 28, Comment *c(3)* and *(4) ('Third Restatement')*.

[27] See, eg, *Merck Sharp & Dohme (Australia) Pty Ltd v Peterson* [2011] FCAFC 128; (2011) 284 ALR 1
[195]: 'the primary judge held that across a population the consumption of Vioxx did involve an increase in risk, but that the extent of the risk in a particular case would depend on the conditions presumptively existing in the patient's vasculature'
[56]: 'Taken as a whole, his Honour concluded that the data referred to in the evidence warranted the generalisation that, over a population, the consumption of Vioxx increased the risk of MI "by a factor of about 2". His Honour also observed that the data took no account of issues of mechanism and related to people generally. As his Honour said (reasons at [476]): [476] The data may have a rather different utility when the circumstances of a particular person, suffering a particular condition, are required to be considered.'
[112]: 'In Amaca at [62] , the High Court emphasised that the significance of an epidemiological study depends upon whether the plaintiff is a typical member of the population which is the subject of the study.'
[113]: 'In this case, as has been seen, there was a clear basis for concluding that Mr Peterson does indeed stand apart from the ordinary case. His personal circumstances were such that they afford a ready explanation for the occurrence of his injury independent of the possible effects of Vioxx. The strength of the epidemiological evidence as a strand in the cable of circumstantial proof is seriously diminished by this consideration.'
See also *Amaca Pty Ltd v Ellis* [2010] HCA 5
[57]: 'Observing that by far the largest number of a population of lung cancer sufferers had been either smokers, or smokers and exposed to asbestos, does not, without more, provide a foundation for an inference about the probability that asbestos exposure was a cause of Mr Cotton's cancer'
[62]: 'To draw an inference about causation from what was established by the epidemiological studies, it would be necessary to decide whether the particular case under consideration should be treated as conforming to the pattern described by the epidemiological studies. Absent evidence which suggests that the individual may stand apart from the ordinary, there may be sufficient reason to assume conformity, but whether or not that is so, it is important to recognise that the first step that must be taken, if an inference is to be drawn from epidemiological studies, is to relate the results of studies of populations to the particular case at hand. That step is not inevitable.' [footnotes omitted]

[28] Steve Gold, 'The Reshapement of the False Negative Asymmetry in Toxic Tort Causation' (2011) 37(3) *William Mitchell Law Review* 1507, 1512.

be obtained[29]) or not necessary (because one type of evidence proves both, as with 'signature diseases').[30] For example, courts will generally accept that causation has been established in cases of well-known 'signature diseases' if the exposure and the manifestation of the disease are both established.[31] In other words, the courts draw an inference of specific causation based on general causation plus the fact of exposure. 'Signature diseases' are extremely rare diseases among the general population, with virtually all known cases arising from exposure to a particular substance. For example, the rare clear cell adenocarcinoma is a signature of *in utero* exposure to a drug called Diethylstilbestrol ('DES').[32] In contrast, lung cancer is a 'non-signature disease' and might be attributed to exposure to a multiplicity of substances (such as tobacco smoke, pollutants from a nearby factory or pollutants from traffic on a local highway), or it might result from no identifiable exposure at all.[33]

Regardless of jurisdiction and applicable law, there are several characteristics that typically complicate proof of general and specific causation in toxic torts. These characteristics all fall under the umbrella heading of causal indeterminacy (also described in the literature as 'causal uncertainty', 'indeterminate causation' and 'uncertain causation') which encompasses the following issues: (a) Long Latency; (b) Multiple & Varied Exposures (c) Poorly Understood Aetiology & Multiple Alternative Causes; and (d) Undermining Tort Objectives.

1.3.1. **Long Latency**

Due to the ubiquity of toxic substances, it is particularly difficult for plaintiffs to attribute the relevant injury to an isolated and clearly identifiable time and place.[34] This difficulty is often exacerbated by the existence of a considerable latency period, that may even be trans-generational, prior to the effect of exposure becoming apparent. The alleged injuries are

[29] Michael Green, 'The Future of Proportional Liability: The Lessons of Toxic Substances Causation' in Stuart Madden (ed), *Exploring Tort Law* (Cambridge University Press, 2005) 371.
[30] Gold, 'The More We Know' (n 3) 401.
[31] Ibid.
[32] For more on DES, see Part 1.3.1 of this chapter; see also Leslie Bender, 'An Overview of Feminist Torts Scholarship' (1993) 78(4) *Cornell Law Review* 575, 587. Mesothelioma has also long been argued to be a signature disease, only caused by asbestos exposure, but defendants are increasingly introducing gene mutations (such as *BAP1*) as possible causes of mesothelioma, see e.g, *Ortwein v. CertainTeed Corp., et al., Alameda County Superior Court* No. RG13701633 (12 December, 2014) (Lee J)*; Joseph Thrash, et al v The Boeing Co.* 2018 WL 2573097*; Dustin W. Holsten, et al. v. Amalgamated Sugar Co. LLC, et al.,* No. 18-L-1664, Ill. Cir., Madison Co*; Cynthia B. Cowger v. Qualitex Co.,* No. 2018-L-012099, Ill. Cir., Cook Co.
[33] Peter Menell, 'The Limitations of Legal Institutions for Addressing Environmental Risks' (1991) 5 *Journal of Economic Perspectives* 93, 102.
[34] Jane Stapleton, 'Compensating Victims of Disease' (1985) 5(2) *Oxford Journal of Legal Studies* 248, 249.

typically slow developing and often are not noticeable by the plaintiff until they manifest themselves in the form of a cancer, neurotoxic effect, birth defect, and other disease or development anomaly.[35] The issue is further intensified where plaintiffs experience a gradual contraction of the illness during prolonged exposure to a toxic substance.[36] These qualities of toxic torts distinguish them from many other common law claims, such as accidents or assaults, where the alleged harm is sudden, traumatically induced and immediately apparent.[37]

The DES cases are a prime example of the obstacles posed by long latency periods in toxic torts. Between 1941 and 1971, a synthetic female hormone called Diethylstilbestrol ('DES'), was frequently prescribed to prevent miscarriages.[38] DES was later found to cause clear cell adenocarcinoma in daughters exposed to the drug *in utero*. This rare form of cancer 'manifests itself after a minimum latent period of 10 or 12 years'.[39] The latency itself produced causal indeterminacy in these cases, because the lapse of time between maternal exposure and the daughter's cancer made it difficult to identify the manufacturer of the drug the mother consumed.[40] Plaintiffs could not identify and join all the hundreds of pharmaceutical companies that manufactured the unpatented drug.[41]

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[35] Michael Green, *Bendectin and Birth Defects: The Challenges of Mass Toxic Substances Litigation* (University of Pennsylvania Press, 1996) 16.
[36] Stapleton, 'Compensating Victims of Disease' (n 34) 249.
[37] Stuart Madden, *Toxic Torts Deskbook* (Taylor & Francis, 1992) 5.
[38] *Sindell v Abbott Laboratories* (1980) 26 Cal 3d 593, 593.
[39] Ibid 594.
[40] The *Third Restatement* explains that DES 'while posing a foreseeable risk of causing harm to the fetus of a woman taking the drug, also poses a risk of a genetic defect that could replicate itself generation after generation, the possibility of which was raised in the third-generation DES cases', *Third Restatement* (n 20) § 29, Comment *(m); Enright v Eli Lilly & Co* 570 N.E.2d 198 (NY, 1991); *Grover v Eli Lilly & Co* 591 N.E.2d 696 (Ohio, 1992). The *Third Restatement* argues that in such cases, it is appropriate for the courts to 'use a variety of techniques to cabin liability [in order to] exclude victims some distance in time or geography', *Third Restatement* (n 20) § 29, Comment *(m).* In contrast, some tortious conduct may result in a seemingly 'huge' scope of liability but this fact is not, of itself, a ground for imposing limits on the scope. Of particular relevance to toxic torts, the Third Restatement provides the example of asbestos products manufacturers who 'exposed hundreds of thousands to asbestos fibres, but no court has suggested the manufacturer's scope of liability should be confined because of the number of injured claimants or the magnitude of aggregate damages', ibid. An analogous situation is also provided of a negligent operator of a nuclear plant who should not have its liability limited based on the number of persons who were exposed to an escape of radiation or the magnitude of the damages, ibid.
[41] The question for the court then became: 'may a plaintiff, injured as the result of a drug administered to her mother during pregnancy, who knows the type of drug involved but cannot identify the manufacturer of the precise product, hold liable for her injuries a maker of a drug produced from an identical formula?', ibid 593. The court ultimately adopted a new 'market share liability' rule to better accommodate these cases. The plaintiff could recover against a group of manufacturers who comprised a 'substantial share' of the relevant market. This doctrine of market share liability imposes several liability, rather than joint and several, and limits a co-defendant's responsibility to their market share. In other words, a manufacturer that had 40% of the relevant market would be severally liable for 40% of the plaintiff's harm. See, eg, *Sindell v Abbott Laboratories* (1980) 607 P 2d 924, 937. Although a 'number of courts' have adopted market-share liability in DES cases, a 'roughly equal number of courts have declined to craft a new theory for DES plaintiffs, expressing concern that to do so would rend too great a chasm in the tort-law requirement of factual causation', see *Third Restatement* (n 20) §

Asbestos-related diseases also pose unique challenges for plaintiffs due to long latency periods between exposure to asbestos fibres and manifestation of a disease. Australia has one of the world's highest rates of the asbestos-related disease called mesothelioma and actuarial studies predict that mesothelioma cases will continue occurring until 2060.[42] The typical latency periods of asbestos diseases range from 20 to 40 years, depending on the particular disease and the circumstances of exposure.[43] The time between exposure and diagnosis will rarely be any less than 15 years and may even be up to 60 years.[44] As a result, asbestos-related disease is sometimes not apparent or diagnosed until examination is conducted after the person's death. By this time, there is an increased likelihood that the wrongdoer cannot be traced or, even if they can be traced, they may no longer be financially viable.

1.3.2. **Multiple & Varied Exposures**

This issue of latency is magnified in situations where plaintiffs have experienced exposure in multiple places, perhaps even in different jurisdictions.[45] This creates far greater difficulties than in cases of traumatic injury, such as accidents or assaults, where a single isolated causal agent could be verified via eyewitness accounts and other demonstrable evidence.[46] For example, asbestos diseases in Australia have primarily been caused by asbestos mining 'but it can equally be caused by working with a variety of asbestos materials and products, such as asbestos-cement sheeting, insulation containing asbestos, brake and clutch materials, and the

28, Comment *(o)*. In addition, this form of liability 'has very rarely been applied outside of DES cases' and, as the *Third Restatement* observes, 'the lack of activity in this area may reflect the declining significance of the issue', ibid § 28, Comment *(p)*. For a criticism of market share liability, see David Bernstein, 'Getting to Causation in Toxic Tort Cases' (2008) 74(1) *Brooklyn Law Review* 51, 52, 74; John Gray and Richard Faulk, 'Negligence in the Air? Should Alternative Liability Theories Apply in Lead Paint Litigation?' (2008) 25 *Pace Environmental Law Review* 147, 153; Sandy Steel, *Proof of Causation in Tort Law* (Cambridge University Press, 2015) 168. For an article in favour of market share liability, see, eg, Mark Geistfeld, 'The Doctrinal Unity of Alternative Liability and Market-Share Liability' (2006) 155 *University of Pennsylvania Law Review* 447; Noah Smith-Drelich, 'Performative Causation' (2020) 93(3) *Southern California Law Review* 379, 408-10.

[42] Australian Institute of Health and Welfare, *Mesothelioma in Australia* (Report, November 2018); New South Wales Law Reform Commission, *Compensation to Relatives* (Consultation Paper No 14, May 2011) 11.

[43] Safe Work Australia, *Mesothelioma in Australia: Incidence 1982 to 2006, Mortality 1997 to 2007* (Report, May 2010) 6.

[44] New South Wales Workers Compensation (Dust Diseases) Board, *Past and Future Incidence of Mesothelioma in Men in New South Wales* (Report, 2007); New South Wales Law Reform Commission (n 42) 9.

[45] Stapleton, 'Compensating Victims of Disease' (n 34) 252.

[46] Tan Golan, 'Epidemiology, Tort, and the Relations between Science and Law in the Twentieth-Century American Courtroom' in Mario Biagioli and Jessica Riskin (eds), *Nature Engaged: Science in Practice from the Renaissance to the Present* (Palgrave MacMillan, 2012) 168.

handling and transport of asbestos as a raw material'.[47] The multiplicity of potential sources of asbestos is particularly problematic for mesothelioma plaintiffs who experience a sequence of asbestos exposures.[48] These plaintiffs often cannot prove that the relevant defendant was a factual cause of their condition due to the existence of other exposures.[49]

An important effect of latency in both asbestos and DES cases is to create a problem of indeterminate defendants. Genetic markers of exposure and effect provide little benefit in these 'indeterminate defendant' scenarios because the plaintiff will still struggle to identify *which* defendants' toxic-substance-containing product caused their harm. As this thesis will demonstrate, these genetic markers do not change the nature of the causal inquiry. At best, they can only show exposure to a particular substance (eg asbestos) caused the plaintiff's illness. Where a plaintiff has experienced multiple exposures to the same substance, such markers cannot show *which* exposure caused their illness. In other words, genetic markers of exposure/effect cannot fill the evidential gap resulting from the limits of medical knowledge in these cases, leaving open the potential for injustice.[50]

This challenge is not confined to asbestos-related disease but encompasses many situations where there are multiple exposures and the effects caused by the substance differs 'depending on whether exposure was short-term (e.g., acute, single dose or a few days) or long-term (chronic, repeated over years)'.[51] As Professor David Eaton explains:

> Most chemicals that have been identified to have "cancer causing" potential (carcinogens) do so only following long-term, repeated exposure for many years. Single exposures or even repeated exposures for relatively short periods of time (e.g., weeks or months) generally have little effect on the risk of cancer, unless the exposure was remarkably high and associated with other toxic effects. Relatively infrequent exposure may also have negligible health consequences even if continued over time because of recovery between doses.[52]

So, individuals can usually tolerate or recover from brief short-term exposures and 'it is also possible that repeated, low dose exposures – even for many years – will have no consequence

[47] Neil Gunningham, 'Asbestos-Related Diseases and Workers' Compensation' (2011) 34 *Sydney Law Review* 269, 270.
[48] Jane Stapleton, 'The Two Explosive Proof-of-Causation Doctrines Central to Asbestos Claims' (2009) 74 *Brooklyn Law Review* 1011, 1023-1025.
[49] Ibid.
[50] This issue has been resolved in exceptional cases by abandoning the 'all or nothing' approach and allowing recovery of proportional damages where a plaintiff can prove exposure to a certain level of risk. For a detailed analysis of the cases, see, eg, Gold, 'When Certainty Dissolves into Probability' (n 3) 298-306. Probabilistic causation can be helpful in such exceptional cases where a significant evidential gap leads to a serious threat of injustice.
[51] David Eaton, 'Scientific Judgment and Toxic Torts: A Primer in Toxicology for Judges and Lawyers' (2003) 12(1) *Journal of Law and Policy* 5, 12.
[52] Ibid 13.

at all, since the body is often able to completely detoxify low doses before they do any damage'.[53] This creates significant obstacles for toxic tort plaintiffs who will struggle to identify defendants who were a cause of their illness.

1.3.3. Poorly Understood Aetiology & Multiple Alternative Causes

Poorly understood aetiology is another hallmark of the causal indeterminacy issue facing toxic tort plaintiffs. Idiopathic conditions place heavy burdens on plaintiffs to successfully prove causation. This burden is intensified by the ever-expanding number of environmental factors that are carcinogenic hazards. As at 27 November 2021, the International Agency for Research on Cancer classified 121 agents (substances, mixtures and exposure circumstances) as carcinogenic to humans; 90 agents as 'probably' carcinogenic to humans; and, 323 agents as 'possibly' carcinogenic to humans.[54] The combination of poorly understood aetiology and multiple alternative causes in toxic torts inevitably complicates proof of causation. Toxic torts merge scientific and legal causation 'in an uncertain network of feedbacks, variable inputs and outputs surrounded by different degrees of knowledge'.[55] This has the unfortunate result of discouraging otherwise meritorious claims because the causal chain is not within ordinary experience.[56]

This issue is reflected in the infamous *Dalkon Shield* litigation, which highlights the difficulties associated with possible alternative causes in cases of insidious medical injury.[57] The litigation involved a seriously flawed intrauterine device (IUD) which was linked to very severe complications to a disproportionately large number of its users including sepsis, infertility, miscarriage and death.[58] The aetiology of *individual* cases of disease was often murky because of the presence of multiple risk factors, such as a history of venereal disease, pelvic inflammatory disease or other independently caused infections.[59] Due to the prevalence of

[53] Ibid 12-13.
[54] International Agency for Research on Cancer, 'IARC Monographs on the Identification of Carcinogenic Hazards to Humans, Volumes 1-127' (World Health Organisation, 17 November 2021) <https://monographs.iarc.fr/agents-classified-by-the-iarc/>.
[55] Paolo Ricci and Natalie Gray, 'Toxic Torts and Causation: Towards an Equitable Solution in Australian Law – Part I: Legal Reasoning with Uncertainty' (1998) 21(3) *University of New South Wales Law Journal* 787, 787.
[56] Ibid.
[57] See, eg, *In re Dalkon Shield Cases*, 599 F Supp 1351, 1356-57 (D Md, 1984); *In re Dalkon Shield Punitive Damages Litigation*, 613 F Supp 1112 (ED Va, 1985).
[58] John Van Dyke, 'The Dalkon Shield: A "Primer" in IUD Liability' (1978) 6(1) *Western State University Law Review* 1, 2.
[59] Ibid 43. Peggy Pendergast and Harold Hirsh, 'The Dalkon Shield in Perspective' (1986) 5 *Medicine and Law* 35, 40.

alternative causes, much of the evidence was circumstantial and based on reasonable probability involving expert opinion testimony, which was often insufficient to establish causation.[60] This resulted in a number of plaintiffs failing to receive any compensation for their injuries.[61]

Similar to *Dalkon Shield*, the aetiological uncertainty of individual cases also prevented recovery in *June v Union Carbide Corp.* despite the demonstrable general connection between the radioactive contamination and the diseases in question.[62] This case involved twenty-seven former residents of Uravan, Colorado, a Uranium and Vanadium mining and milling town owned and operated by the defendants. The former residents alleged that they contracted thyroid disease and non-thyroid cancer as a result of radioactive contamination from operations in the company town. The plaintiffs successfully demonstrated that the products of Uranium and Vanadium radioactive decay, such as Iodine-131, are capable of causing cancer in the general population. The epidemiological evidence showed strongly that the defendants had exposed the populace of Uravan to radiation that increased their risk of cancer.

However, the defendants could only be held liable if: (1) the plaintiffs' medical conditions would not have occurred without exposure, or (2) such exposure was a necessary component of a causal set that would have caused their individual conditions. These two formulations both require 'but for' causation in lieu of 'substantial factor' causation or any other alternative basis for a finding of causation. The plaintiffs did not really attempt to satisfy the 'but for' standard but instead argued that their evidence sufficed to establish causation on a 'substantial factor' basis.[63] As the plaintiffs could not support a claim of more-likely-than-not 'but for' causation in any individual case, they could not recover any compensation for their injuries even though general causation was established.

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[60] Ibid.
[61] Ibid.
[62] *June v Union Carbide Corp*, 577 F 3d 1234 (10th Cir, 2009).
[63] In other words, in *June*, the Tenth Circuit endorsed the multiple-sufficient-causal-sets approach but ultimately held that the plaintiffs' failure to raise this approach at district court meant that they waived any argument that radiation was a necessary component of a causal set that probably caused their injuries, ibid 1242-43, 1247. If the plaintiffs were able to demonstrate their injuries were not produced solely by natural causes, even defendants who contributed only trivial amounts of radiological exposure would have been liable, ibid 1242, 1245. Such a result would have been contrary to the broader goals of the *Third Restatement*, as the multiple-sufficient-causal-sets provision is not intended to impose tort liability on negligent trivial contributors, see *Third Restatement* (n 20) § 27, Comment *(g)*. The trivial contributions provision provides a much-needed structural restraint on the operation of the causal set theory, see ibid § 36, Comments *(a)-(b); Illustrations 1-2*, see also Richard Wright, 'The NESS Account of Natural Causation: A Response to Criticisms' (2011) in Richard Goldberg (ed), *Perspectives on Causation* (Hart Publishing, 2011) 305.

These issues of causal indeterminacy are also reflected in the Australian case of *Amaca Pty Ltd v Ellis*.[64] This case involved a worker who was exposed to asbestos in the course of his employment with a sequence of two employers and subsequently died of lung cancer. The executor of his estate sued both employers and the manufacturer of some of the asbestos products. Causation was a central issue because the plaintiff only experienced relatively light asbestos exposure and had been a heavy smoker all his adult life. The Supreme Court of Western Australia and the Court of Appeal upheld liability, holding that the lung cancer was the cumulative product of both the tobacco smoking and asbestos exposure such that their effects could not be separated.

This decision was overturned by the High Court of Australia in a joint judgment by all members of the Court, ruling that causation had not been established against any defendant. The High Court noted that the plaintiff did not provide a sufficient basis for their argument that where an asbestos-exposed smoker develops lung cancer, the exposure must or would 'in the usual case' probably have been a cause of that cancer.[65] In addition, the plaintiff was unable to adduce evidence that the asbestos exposure doubled the risk of lung cancer relative to the remaining risk. [66] The expert testimony only showed, at most, 23 percent likelihood that asbestos was involved in his lung cancer, either acting alone or in synergy with smoking.[67]

Amaca Pty Ltd v Ellis[68] ultimately presents the same problem as *June v Union Carbide Corp*.[69] Negligently exposing smokers to asbestos is known to contribute to the risk of developing lung cancer, and thus to the population incidence of the disease, but no individual claimant can be compensated because the group-based epidemiologic evidence does not establish a greater than 50% attributable risk and no causation evidence particular to the individual (such as a genetic marker distinguishing the cause of cancer) is available. The Court in *Amaca* was at least honest about this seemingly 'paradoxical result'[70], as opposed to the court in *June.*

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[64] *Amaca Pty Ltd v Ellis* [2010] HCA 5.
[65] *Ellis v South Australia* [2006] WASC 270 [811]; *South Australia v Ellis* (2008) 37 WAR 1 [498] ('*Ellis*').
[66] *Amaca Pty Ltd v Ellis* [2010] HCA 5 [30], [59].
[67] Ibid; For an assessment of the epidemiologic evidence in *Ellis*, see, eg, David Hamer, 'Mind the Evidential Gap: Causation and Proof in Amaca Pty Ltd v Ellis' (2009) 31 *Sydney Law Review* 465.
[68] [2010] HCA 5.
[69] 577 F 3d 1234 (10th Cir, 2009).
[70] [2010] HCA 5 [69]-[70] (French CJ, Gummow, Hayne, Heydon, Crennan, Kiefel and Bell JJ):

> [69] It was submitted that the conclusion that causation was not established in this case entailed a paradox. If consideration of the results of the population studies described in evidence in this matter does not permit the inference that Mr Cotton's cancer was caused or contributed to by exposure to asbestos, no claim by an individual in Mr Cotton's position could succeed. And yet, the argument continued, the population studies showed that exposure to asbestos was a cause of cancer in some

The complicating role of epidemiologic evidence as proof of causation in cases of 'non-signature disease' was also highlighted in *Merck Sharp & Dohme (Australia) Pty Ltd v Peterson* ('*Merck*').[71] The primary issue in that case was whether the consumption of Vioxx caused or contributed to the plaintiff's myocardial infarction (heart attack). The trial judge found that causation was established on the basis of circumstantial evidence including statistical evidence derived from several epidemiological studies.[72] In particular, the trial judge relied upon epidemiological evidence which indicated that the consumption of Vioxx almost doubled the relative risk of heart attack in the general population.[73]

On appeal, the Full Court of the Federal Court of Australia held that the epidemiological studies failed to assist in resolving the question of specific causation.[74] The Court noted that an epidemiologic study adduced as 'proof of what may be expected to happen in the usual case is of no value unless it is proved that the particular applicant is indeed "the usual case"'.[75] The Court held that the plaintiff's 'personal circumstances were such that they afford a ready explanation for the occurrence of his injury independent of the possible effects of Vioxx'.[76] It is helpful to extract a significant portion of the court's observations on this point:

> The epidemiological evidence meant that it was possible that Vioxx consumption was a cause of Mr Peterson's MI. But there were other candidates as causes of his injury, and the claims of those candidates were strong. Shortly before Mr Peterson commenced taking Vioxx, he was, by reason of his age, gender, hypertension, hyperlipidemia, obesity, left ventricular hypertrophy and history of smoking, a member of a group within the community, 25% of whom were expected by the cardiologists to suffer a heart attack within 5 years. Mr Peterson may simply have been the unlucky one in four of this cohort to suffer a MI. We are unable to see how it can be said that it is more probable

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> cases. How then could it be right to reach a result that entailed the corollary that all individual claims would fail?
>
> [70] The answer to the question can be expressed in several different ways. All depend upon the basic and unpalatable fact that no scientific or medical examination can now say, with certainty, what caused Mr Cotton's cancer or lung cancer in any other particular case. As explained at the outset of these reasons, despite this uncertainty, the courts must, and do, "reduce to legal certainty [a question] to which no other conclusive answer can be given". The courts do that by asking whether it is more probable than not that X was a cause of Y. Saying only that exposure to asbestos may have been a cause of Mr Cotton's cancer is not a sufficient basis for attributing legal responsibility. Observing that a small percentage of cases of cancer were probably caused by exposure to asbestos does not identify whether an individual is one of that group. And given the small size of the percentage, the observation does not, without more, support the drawing of an inference in a particular case. The paradox, if there be one, arises from the limits of knowledge about what causes cancer. [footnotes omitted]

[71] [2011] FCAFC 128; (2011) 284 ALR 1.

[72] *Peterson v Merck Sharpe & Dohme (Australia) Pty Ltd* (2010) 266 ALR 1, 285-8 ('*Peterson*'); For a detailed analysis of *Peterson,* see Thomas Faunce, Ruth Townsend and Alexandra McEwan, 'The Vioxx pharmaceutical scandal: Peterson v Merke Sharpe & Dohme (Aust) Pty Ltd (2010) 184 FCR 1' (2010) 18(1) *Journal of Law and Medicine* 38.

[73] Ibid.

[74] *Merck* (n 71) [113].

[75] Ibid [106].

[76] Ibid [113].

> than not that Vioxx, whether alone or in combination with Mr Peterson's personal risk factors, was a necessary condition of the occurrence of his heart attack.[77]

It is notable that the Court relied on data showing that people with the plaintiff's underlying conditions had a 25% chance of having a cardiac event within five years, but seemingly without any analysis of how this risk compares to the risk in the general population. The Court's dismissal of the possibility that Vioxx acted in concert with the plaintiff's pre-existing risk factors is also noteworthy. The Court simply concluded that 'the strength of this strand' of epidemiological evidence 'did not rise above the possibility that it was "in the mix" of factors which may have caused Mr Peterson's heart attack'.[78] This ultimately meant that the Court could not conclude the plaintiff would not have suffered a heart attack 'but for' the consumption of Vioxx because such a conclusion 'is a matter of conjecture rather than reasonable inference on the balance of probabilities'.[79] This case ultimately demonstrates the difficulties associated with the historical reliance on epidemiological studies as proof of specific causation in toxic torts, as courts are willing to treat epidemiologic evidence as indispensable[80], but at the same time impose seemingly inflexible requirements on what epidemiologic evidence they will deem persuasive.[81]

1.3.4. **Undermining Tort Objectives**

This causal indeterminacy in toxic torts undermines the broader objectives of tort law. These objectives include:

> (1) assignment of responsibility, in money damages, to those responsible for creating a risk that produces harm;
> (2) compensation of persons for loss caused by another's substandard conduct;

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[77] Ibid [120].
[78] Ibid [123].
[79] Ibid [124]. Although the Court did 'not consider that it was more probable than not that the consumption of Vioxx was a necessary condition of Mr Peterson's heart attack', the Court noted that 'it does not follow from this conclusion that none of the other applicants represented in these proceedings can succeed in establishing the ingredient of causation in their claims'. In particular, the Court noted that 'there may be applicants in relation to whom there is no likely cause of their MI [myocardial infarction] other than the effects of their consumption of Vioxx', see ibid [126].
[80] See *Amaca Pty Ltd v Ellis* [2010] HCA 5.
[81] This tendency is also reflected in US courts. A notable example is the Supreme Court of Texas trilogy in *Merrell Dow Pharmaceuticals, Inc v Havner* 953 S.W.2d 706, *Merck & Co v Garza* 347 SW 3d 256, 265-66 (Tex, 2011) and *Bostic v Georgia-Pacific Corp* 439 SW 3d 332 (Tex, 2014), see, eg, Steve Gold, 'Drywall Mud and Muddy Doctrine: How Not to Decide a Multiple-Exposure Mesothelioma Case' (2015) 49 *Indiana Law Review* 117. For a detailed list of relevant US cases and commentary rejecting an epidemiologic threshold for causation, see *Third Restatement* (n 20) § 28, Reporter's Note to Comment *(c)(3).* For a detailed discussion of the merging of 'fact probability' and 'belief probability', see, eg, Steve Gold, 'Causation in Toxic Torts: Burdens of Proof, Standards of Persuasion, and Statistical Evidence' (1986) 96(2) *Yale Law Journal* 376; David Barnes, 'Too Many Probabilities: Statistical Evidence of Tort Causation' (2001) 64(4) *Law and Contemporary Problems* 191; Ian Freckelton, 'Epidemiology Evidence and Causation' (2004) 63 *Plaintiff: Journal of the Australian Plaintiff Lawyers Association* 18; Richard Wright, 'Proving Causation: Probability versus Belief' in Richard Goldberg (ed), *Perspectives on Causation* (Hart Publishing, 2011).

> (3) deterrence of further unreasonably hazardous conduct by the responsible party and others engaged in similar pursuits; and
> (4) encouragement of innovation, such as changes in design, formulation, packaging, labelling, transportation, disposal or the like, that will reduce or eliminate unreasonable hazards.[82]

Not only is tort law an instrument for compensation, providing incentives for safety and loss allocation, it also serves a 'corrective justice' function. This function aims to provide an aggrieved victim with a fair forum for pursuing his grievance.[83] As Dr Gemma Turton explains, corrective justice is 'interpersonal' and 'bipolar' such that 'the two parties are treated as equal' and 'the injustice can only be corrected by requiring the wrongdoer to repair the victim's loss'.[84] This is also reflective of the adversarial nature of the common law.

Tort law causation theory is crucial to achieving corrective justice because it establishes the crucial nexus between the parties by identifying the relevant victim and wrongdoer.[85] However, the toxic tort causation doctrine has been heavily criticised for undermining tort's broader objectives by allowing systematic under-compensation of plaintiffs and systematic under-deterrence of defendants.[86] This has led some to consider whether a probabilistic model of causation is better aligned to the objectives of the tort system and the improvement of the causal indeterminacy issue.[87]

Alternatively, others have suggested genetic evidence could be a potential solution to this problem.[88] As Professor Gary Marchant observes, 'By shifting the specific causation inquiry from statistical rules of thumb or subjective medical assessments to genetic changes within the plaintiff's own cells, genetic biomarkers such as gene expression signatures have the *potential* to make specific causation significantly more objective and reliable' (emphasis added).[89] As this thesis will demonstrate, sufficiently specific and sensitive markers do have *potential* to assist in the causal inquiry. However, scientific knowledge in the field of genetics is still

[82] Madden (n 37) 22.
[83] Green, *Bendectin and Birth Defects* (n 4) 7.
[84] Gemma Turton, *Evidential Uncertainty in Causation in Negligence* (Hart Publishing, 2016) 9.
[85] Andrew Klein, 'Causation and Uncertainty: Making Connections in a Time of Change' (2008) 49 *Jurimetrics* 5, 10-11.
[86] See, eg, Lin (n 2) 1452-1460; see Noah Smith-Drelich, 'Performative Causation' (2020) 93(3) *Southern California Law Review* 379, 393-395. For a discussion of how specific causation undermines the utilitarian goals of the tort system, see ibid 395-396.
[87] See, eg, Gold, 'When Certainty Dissolves into Probability' (n 3).
[88] See, eg, Brice and Christian (n 2); Marchant, 'Genetic Data in Toxic Tort Litigation' (n 2); Marchant, 'Genetic susceptibility and biomarkers in toxic injury litigation' (n 2); Grodsky (n 2); Lin (n 2); Hite (n 2).
[89] Marchant, 'Genetic Data in Toxic Tort Litigation' (n 2) 25.

evolving, so genetic markers as a method of proving factual causation is presently far from a 'solution' to the problem of causal indeterminacy in toxic torts.

1.4. Aim and Research Questions

This thesis aims to investigate the interpretations and applications of genetic evidence in supporting or refuting causation in toxic tort claims.

It ultimately strives to answer the question, '*Does genetic information alleviate or exacerbate the causal uncertainty in toxic torts?'* In order to answer this query, the following questions are considered:

- What are the similarities and differences between Australian and US approaches to establishing factual causation in toxic tort claims?
- What are the historical methods of proving or disproving causation in toxic torts? What are the limitations of these approaches?
- How has genetic data been used in toxic tort litigation? What impact has genetic evidence had on the outcome of toxic tort proceedings? Is genetic evidence superior to the more traditional methods of proof?
- How can genetic information assist litigants in proving or disproving causation in toxic torts? What are the means of obtaining genetic evidence in toxic torts, and for what purposes should its admission be sought and permitted?
- What are the policy implications of adducing genetic evidence, or compelling genetic testing, in toxic tort litigation? Do legal practitioners, litigants and courts require further guidance on the use of genetic data in toxic tort proceedings in order to ensure consistency and fairness?

1.5. Central Thesis Proposition

An analysis of Australian and United States ('US') case law focusing on genetic markers suggests incorporation of such markers in scientific research and clinical practice, let alone

trial and evidence, is still in its nascent stages.[90] There is still much variability in scientific interpretations of these markers, and there is limited usefulness where the markers are not sufficiently valid, sensitive or specific.[91] Inconsistencies in the case law suggest there is substantial judicial disagreement, stemming from broader scientific disagreement, regarding the utility and validity of genetic markers.

Tensions in the case law do not necessarily signal a need for doctrinal reform, rather they highlight that courts require greater guidance in assessing genetic information. A different approach to causation[92] would do little to remedy the *scientific* indeterminacy at the heart of toxic tort cases. Even if courts were to abandon the counterfactual inquiry and adopt a different approach to factual causation, the courts would still have to grapple with understanding the scientific evidence in order to reach a conclusion as to causal contribution. As Professor Steve Gold succinctly explains, the inevitably increasing reliance on genetic evidence means 'the train is coming, and courts cannot get off the tracks'.[93] This suggests there is a strong need for practice-oriented instruments[94] designed to assist courts, legal professionals and litigants in considering the strengths and weaknesses of genetic markers as a means of proving or disproving causation. In accordance with these findings, the final chapter of this thesis recommends the adoption of a reference guide.

1.6. Significance

The thesis provides an original contribution to knowledge, by critically examining Australian and United States ('US') case law and literature focusing on genetic evidence in toxic torts. A comprehensive analysis of the case law and literature is vital to inform best practice for the future by identifying the past, present and predicted impact and challenges of genetic evidence.

[90] See, eg, Edward Ramos et al, 'Genomic Test Results and the Courtroom: The Roles of Experts and Expert Testimony' (2016) 44 *The Journal of Law, Medicine & Ethics* 205, 228.
[91] For more information on the concepts of sensitivity and specificity, see Gold, 'When Certainty Dissolves into Probability' (n 3) 267-277. Even if a marker is sufficiently reliable, specific, and sensitive, plaintiffs could still struggle to show *which* exposure caused their harm where they have experienced multiple exposures to the same substance via different products.
[92] Such as a probabilistic approach, see, eg, Gold, 'When Certainty Dissolves into Probability (n 3).
[93] Gold, 'The More We Know' (n 3) 397.
[94] Perhaps through a judicial reference manual, such as an addition to the Federal Judicial Center, *Reference Manual on Scientific Evidence* (National Academy of Sciences, 3rd ed, 2011). Planning is currently underway for the next edition of this Manual. In addition, courts could benefit from independent scientific guidance through, for example, court-appointed experts, assessors (aka 'independent guides of the court'), referees or a 'science panel'. For more information, see Chapter 8.3.

The comparative case law analysis has ultimately demonstrated that issues of causal uncertainty affect both Australian and US toxic tort cases. However, US toxic tort litigants have exhibited a greater proclivity towards introducing genetic evidence to explore the issue of causation, with varying degrees of success. This reveals that genetic markers can provide valuable evidence of causation, or alternative causation, in addition to traditional forms of evidence such as epidemiological and/or toxicological studies. However, this thesis ultimately maintains that there is no single scientific method that can conclusively prove toxic tort causation. Despite the optimism of some scholars and practitioners, genetic evidence is presently by no means a solution to the problem of causal indeterminacy. Yet, if used properly, this evidence could shed light on causation, especially when viewed alongside all the other available evidence. Litigants, lawyers and courts should be aware of the limitations of this evidence and avoid overselling it as a solution to the causal indeterminacy problem.

Without further guidance on the utility of such markers, this evidence will only further confuse and mislead the judge or jury. This could exacerbate the problem of causal indeterminacy, leading to inconsistent case outcomes and posing further obstacles to meritorious claims. This thesis therefore concludes that there is a strong need for practice-oriented instruments designed to assist courts, legal professionals and litigants in considering the strengths and weaknesses of genetic markers as a means of proving or disproving causation. As articulated throughout the thesis, a Reference Guide would help to ensure that the probative value of genetic evidence is properly weighed against any potential harms. The original reference guide proposed in this thesis would promote a better understanding of how to assess the validity and utility of different types of genetic evidence in order to ensure that courts/litigants avoid misusing the evidence. The proposed guide would mimic the structure and contents of Chapters 4-7 of this thesis, containing a comprehensive survey of the case law and literature, and a detailed explanation and analysis of both the legal and scientific issues pertaining to genetic evidence.

The novel findings outlined in this thesis are not unique to toxic torts. In fact, they are relevant to a wide variety of legal areas where health-related genetic evidence is likely to be used

including employment law[95], criminal law[96], family law[97] and insurance claims[98] (such as worker's compensation or life insurance). This thesis focuses on toxic torts but also analyses personal injury cases more broadly (including medical negligence claims and workers' compensation claims). The original practice-oriented instrument proposed in the thesis therefore extends beyond toxic torts and can be applied in many areas of the law where health-related genetic evidence is used as a method to support or refute causation.

This study also provides a solid foundation for further research into potential solutions to the toxic tort causation problem. This is an area of the law requiring far greater academic attention in order to address the fundamental difficulties facing plaintiffs who are unable to recover compensation for their injury and defendants who are required to compensate plaintiffs for injuries that were not caused by their negligence.

1.7. Methodology & Thesis Chapter Structure

The research methodology employed in the thesis primarily involves a doctrinal approach, with a comparative element. This approach includes review of the literature, case law, and legislation, a comparative study of two countries, historical analysis, theoretical and ethical inquiry, and legal critique. A thesis focusing on decisions of trial/appellate courts and tribunals clearly lends itself to a doctrinal approach. The comparative approach also allows for the

[95] See, eg, Nunzia Cannovo, Mariano Paternoster and Claudio Buccelli, 'Predictive genetic tests for employment purposes: Why not?' (2010) 29 *Medicine and Law* 419; Anne Mainsbridge, 'Employers and Genetic Information: A New Frontier For Discrimination' (2002) 2 *Macquarie Law Journal* 61.

[96] See, eg, Rhanae Rego, 'A Critical Analysis of Post-Conviction Review in New South Wales' (2021) 2(3) *The Wrongful Conviction Law Review* 305; Scott Elder and Anderson Kemp, 'Genomics in the Courtroom: The Current Landscape of DNA Technology in Criminal and Civil Litigation' (2021) 88(1) *Defense Counsel Journal* 1; Maya Sabatello and Paul S Appelbaum, 'Behavioral Genetics in Criminal and Civil Courts' (2017) 25(6) *Harvard Review of Psychiatry* 289; Felix Ralph, 'Convictions through Kith and Kin: Legal, Policy and Ethical Issues in DNA Familial Matching and Genetic Metadata' (2018) 29(3) *Current Issues in Criminal Justice* 243; Stephen J Morse, 'Genetics and Criminal Responsibility' (2011) 15(9) *Trends in Cognitive Sciences* 378; Deborah Denno, 'Courts' Increasing Consideration of Behavioral Genetics Evidence in Criminal Cases: Results of a Longitudinal Study' (2011) 2011 *Michigan State Law Review* 967.

[97] See, eg, Maya Sabatello and M.D. Appelbaum, 'Psychiatric Genetics in Child Custody Proceedings: Ethical, Legal, and Social Issues' (2016) 4(3) *Current Genetic Medicine Reports* 98; Edward S Dove et al, 'Familial genetic risks: how can we better navigate patient confidentiality and appropriate risk disclosure to relatives?' (2019) 45(8) *Journal of Medical Ethics* 504.

[98] See, eg, Jean Macchiaroli Eggen, 'Toxic Reproductive and Genetic Hazards in the Workplace: Challenging the Myths of the Tort and Workers' Compensation Systems' (1992) 60(5) *Fordham Law Review* 843; Joan Flaherty, 'Toxicogenomics and Workers' Compensation: A Reworking of the Bargain' (2009) 12(2) *Journal of Health Care Law & Policy* 267; Kathryn J Sedo, 'Workers' Compensation, Social Security Disability, SSI and Genetic Testing' (2007) *Journal of Law, Medicine & Ethics* 74; Michael Baram, 'Genetic Testing for Susceptibility to Disease from Exposure to Toxic Chemicals: Implications for Public and Worker Health Policies' (2001) 41(2) *Jurimetrics* 165; Sara Golru, 'Regulating the Use of Genetic Information in the Life Insurance Industry' (2020) 7 *UNSW Law Journal Forum* 1.

extraction, and subsequent critique, of key legal principles. The historical approach contextualises the case law under discussion, and reveals that divergences in the case law are more likely to be a product of differences in judicial opinion, rather than differences in factors unique to each jurisdiction. The research primarily involved conducting Boolean searches on the following legal databases to locate relevant case law and literature: Lexis Advance AU, Lexis Advance US, Westlaw AU, Westlaw US, AGIS Plus Text, Austlii, Hein Online, JADE, NSW Case Law, SSRN and Google Scholar.[99]

This chapter has introduced the research problem, and presented background information. It has also outlined the research questions, the methodology and the central thesis proposition.

Chapter 2 and 3 examine the 'traditional' or 'historical' methods of proof of causation in toxic torts, and highlights the limitations of these methods.

Chapter 4 explores the history and science of genetics, and introduces the different types of genetic evidence used in toxic torts.

Chapter 5 analyses the advantages and disadvantages of adducing evidence of genetic markers of exposure and/or effect in toxic tort cases.

Chapter 6 investigates the utility of relying on evidence of genetic susceptibility markers in toxic torts, and personal injury cases more broadly.

Chapter 7 discusses the practice of court-ordered genetic testing in personal injury cases.

Chapter 8 concludes the thesis and provides recommendations for practice-oriented instruments and future research.

In short, the thesis first considers the value and limitations of traditional forms of evidence (epidemiology, toxicology and differential aetiology), which gives us insight into the issues courts need to be alert to with any scientific evidence and identifies issues that might be addressed by genetic evidence. The thesis then analyses genetic evidence and identifies the different ways it might be used, including as evidencing exposure to/the effect of a toxic substance, and as indicating a susceptibility to disease either independently of any exposure or

[99] An added benefit with the US position is that Lexis Advance (US) contains a record of jury verdicts and settlements. Although the information provided in this database is limited, it provides an indication of how frequently toxic tort settlements involve expert testimony relating to genetics and any impact this might have had on the settlement, see, eg, Diane Hoffman and Karen Rothenberg, 'Judging Genes: Implications of the Second Generation of Genetic Tests in the Courtroom' (2007) 66 *Maryland Law Review* 858, 868-869.

in making the plaintiff more susceptible to disease following exposure. The thesis concludes with an outline of the proposed reference guide to inform best practice for the future.

2. Chapter Two: Merging the Probabilities: Epidemiological Evidence and Toxic Torts

The previous chapter outlined the toxic tort causation problem. This chapter highlights the traditional importance of epidemiological evidence in elucidating the causal relationship between chemical exposure and development of disease. In doing so, it emphasises the complicated judicial treatment of this evidence where widespread misunderstandings have resulted in the merging of three distinct probabilities in toxic torts: fact probability, belief probability and sampling error probability. This chapter clarifies the applicable legal and scientific standards of proof in toxic torts, and cautions against merging the probabilities.

Part 2.1 will analyse the benefits and limitations of epidemiological evidence in toxic tort proceedings. Part 2.2 will emphasise the limited potential of Bayes' Theorem in solving the toxic tort causation problem. The chapter concludes that statistical evidence should not replace the fundamental legal inquiry in toxic tort litigation. It therefore joins the growing chorus of voices criticising judicial reliance on the doubles the risk rule in toxic tort litigation.

The following chapter will build on this analysis by examining the complementary role of toxicological studies as a method of proof of causation. These two chapters establish a 'framework' in which the thesis can locate its proposition that genetic evidence is not inherently dissimilar to more 'traditional' forms of evidence in toxic torts and there is no single scientific method that can conclusively prove factual causation in toxic torts. The thesis will ultimately reveal that genetic, toxicological, and epidemiological evidence complement each other in forming the overall picture of causation in a given case. It is crucial to first identify the aspects of epidemiological and toxicological evidence that present limitations, before moving on to make a more informed evaluation of the role of genetic evidence in potentially addressing these long-standing limitations.

2.1 Epidemiological Evidence in Toxic Torts

The epidemiological aim of disease prevention does not neatly align with the aims of tort law. Epidemiologists strive to control health problems and only seek to determine 'whether an agent

can cause a disease, not whether an agent *did* cause a specific instance of a disease'.[1] In other words, epidemiologists typically seek to determine whether certain substances are capable of causing disease in the *general* population, rather than whether a certain substance caused a *specific* individual's disease. Conversely, tort lawyers seek to determine *specific* causation in order to assign responsibility for harm caused to individuals.[2] Despite these conflicting aims, epidemiologic studies have proven to be particularly influential in toxic tort cases.

The PFAS[3] and PFOA[4] litigation in Australia and America provide a relatively recent example of the vital role of epidemiological studies in toxic tort claims. The Australian PFAS litigation involved

> claims made by group members, being either land owners or business owners, in relation to damages the group members are alleged to have suffered by reason of the use of a certain type of firefighting foam, containing per- and poly-fluoroalkyl substances (PFAS), at Royal Australian Air Force (RAAF) bases close to the localities in which the group members either reside and/or operate businesses.[5]

In approving the 2020 class action settlements for $212.5 million, Lee J noted that

> This was a case which, from the perspective of the applicants, was not without some degree of complexity and uncertainty. It is perhaps engaging in a degree of understatement to describe the proceedings as both factually and legally complex…Factually, there were a significant number of reports by experts and referees on issues [including] toxicology/*epidemiology'*.[6] [emphasis added.]

The role of epidemiology was more overt in the American PFOA class action lawsuits. In a $320 million class action settlement in 2004, a 'science panel' of three epidemiologists were employed to survey 70,000 residents who resided in districts where the water had been contaminated by PFOA released from a Du Pont manufacturing facility.[7] The 'survey was completed in 1 year at a cost of $70 million' and the epidemiologists then 'conducted 12 studies over 5 years', which cost 'around $35 million'.[8] However, they did not make any determinations until 2012, eight years after the settlement, at which time they determined that

[1] See Miquel Porta, *Dictionary of Epidemiology* (Oxford University Press, 2008) 120; Bertram K. C. Chan, *Biostatics for Epidemiology and Public Health using R* (Springer, 2016) 28-9.
[2] Douglas Weed, 'Causation: An Epidemiologic Perspective (in Five Parts)' (2003) 12(1) *Journal of Law and Policy* 43, 44; Michael Green, 'All You Ever Wanted to Know About Adequate Proof of Causation in Tort Law' (2018) 9(3) *Journal of European Tort Law* 308, 317.
[3] PFAS describes a group of chemicals known as per- and poly-fluorinated alkyl substances.
[4] PFOA denotes perfluorooctanoic acid, also known as C8, a fluorocarbon used in the production of Teflon.
[5] *Smith v Commonwealth of Australia (No 2)* [2020] FCA 837 [5].
[6] Ibid [60].
[7] *Leach v EI DuPont de Nemours & Co*, 01-C-608 (W Va, 2005). Kyle Steenland, David Savitz and Tony Fletcher, 'Class Action Lawsuits: Can They Advance Epidemiologic Research?' (2014) 2 *Epidemiology* 167, 168.
[8] Steenland, Savitz and Fletcher (n 7) 168.

there was a 'probable link….for 55 diseases'.[9] In a later publication, these epidemiologists revealed that

> Neither the judge not the plaintiffs were happy with the slow pace of epidemiology. The judge called us to court in 2011 to vent his frustration with our pace. He went so far as to suggest that the settling parties fire us, but fortunately they did not agree. We argued to the court, lawyers, and the public that it was better to take more time and get it right.[10]

This highlights the significant issues with efficiency, time and financial costs, associated with epidemiological evidence.[11] This section will firstly analyse the American usages of epidemiologic evidence in toxic torts followed by a comparison with the Australian position.

2.1.1 The American Position

The *Third Restatement* highlights the tension between the aims of epidemiology and tort law in the following passage:

> Applying the results of group studies to assess the probability of causation in an individual has become accepted by courts, this is especially true where, as is often the case, there is a lack of understanding about the other components of the causal chain necessary for a given disease. This acceptance has been necessitated by the legal requirement for proof of causation on an individual-plaintiff basis. Epidemiologists, however, do not seek to understand causation at the individual level and do not use incidence rates in group studies to determine the cause of an individual's disease. Epidemiologists may appreciate the conditions and caveats important to whether a study can appropriately be used to infer a probability of individual causation, but the process of doing so is not one that epidemiologists pursue outside the legal arena.[12]

This passage elucidates the relationship of necessity between epidemiology and toxic torts. Due to the sheer lack of understanding about the causes of certain diseases, tort lawyers have little choice but to rely on epidemiological evidence. As a result, this type of evidence has attained a clear position of superiority over all other forms of evidence in toxic torts.

As Professor Michael Green observes, there 'plainly is a hierarchy to these different indirect forms of toxic effect evidence. Epidemiology is at the top, and structural similarity, in vitro testing, and case reports are at the bottom'.[13] This is because not only is epidemiological

[9] Ibid.
[10] Ibid.
[11] For a comprehensive analysis of epidemiological evidence in the courtroom, see Federal Judicial Center, *Reference Manual on Scientific Evidence* (National Academy of Sciences, 3rd ed, 2011) ('*Reference Manual, 3rd ed*').
[12] The American Law Institute, *Restatement of the Law (Third), Torts: Liability for Physical and Emotional Harm* (The American Law Institute, 2010) *('Third Restatement')* § 28, Reporter's Note to *Comment (c)(4)*.
[13] Michael Green, 'Expert Witnesses and Sufficiency of Evidence in Toxic Substances Litigation: The Legacy of *Agent Orange* and Bendectin Litigation' (1992) 86 *Northwestern University Law Review* 643, 658. For more information on in vitro testing and toxic torts, see Chapter 3.

evidence used to prove general causation, it is also frequently relied upon to prove specific causation through probabilistic means. In particular, a number of American courts have held that specific causation can be inferred where the plaintiff adduces evidence of epidemiologic studies with a relative risk[14] (RR) greater than 2 to show that the relevant substance 'doubles the risk' of disease.[15] For example, in the Californian case of *Cook v United States*, the court required the plaintiffs to demonstrate a RR of at least 2 in order to prove that the swine flu vaccine was the cause of their Guillain-Barré Syndrome.[16]

However, the plaintiff need not always prove the relevant substance 'doubles the risk' of disease. There have been some cases where a doubling of the risk is not required so long as other known causes can be identified and eliminated.[17] For instance, some courts have recognised other individual risk factors (such as family history, diet, alcohol intake and smoking) that may modify the probability of causation based on RR.[18] Moreover, the *Third Restatement* suggests that 'any judicial requirement that plaintiffs must show a threshold increase in risk or a doubling in incidence in a group study in order to satisfy the burden of proof of specific causation is usually inappropriate'.[19] This is because 'differential aetiology' can provide 'probative evidence of specific causation' by 'Assessing whether other causes can be ruled out (or in) as potential causes of a plaintiff's disease'.[20]

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[14] Relative risk (RR), also called risk ratio, compares the group of individuals who were exposed to the risk factor with those who were not exposed in order to indicate the risk of developing a disease, see Penny Webb and Christopher Bain, *Essential Epidemiology: An Introduction for Students and Health Professionals* (Cambridge University Press, 2nd ed, 2010) 129; Sanders et al (n 59) 880. RR equals the disease incidence in the exposed group divided by the disease incidence in the non-exposed group:

RR = Disease Incidence in Exposed Group ÷ Disease Incidence in Non-Exposed Group
If RR = 1, there is no association between the risk factor and the disease
If RR >1, there is an increased risk of developing the disease when exposed to the risk factor
If RR<1, there is a decreased risk of developing the disease when exposed to the risk factor

Therefore, RR greater than 1 suggests exposure to the risk factor may be causal and RR less than 1 suggests exposure may protect against the disease, see, eg, Stewart (n 58) 113. In terms of signature diseases, the RR would be infinite because the toxin (such as DES) would explain 'all (or virtually all) of the disease that is found' and 'the incidence of disease in the unexposed group would be zero', Gold et al, *Scientific Evidence of Factual Causation: An Educational Module* (n 58) 44.

[15] See, eg, *DeLuca v Merrell Dow Pharms.,* Inc., 911 F 2d 941, 958–59 (3rd Cir, 1990); *Manko v United States*, 636 F Supp. 1419, 1434 (WD Mo, 1986) *aff'd in part*, 830 F 2d 831 (8th Cir, 1987); *Merrell Dow Pharms., Inc. v Havner*, 953 SW 2d 706, 718 (Tex, 1997); For extensive lists of relevant cases adopting this reasoning see, Federal Judicial Center, *Reference Manual on Scientific Evidence* (National Academy of Sciences, 2nd ed, 2000) 344 ('*Reference Manual, 2nd ed*') 384 and *Third Restatement* (n 12) 450-2.

[16] 545 F Supp 306, 315-17 (ND Cal, 1982).

[17] See, eg, *In re Hanford Nuclear Reservation Litigation* 292 F 3d 1124, 1137 (9th Cir, 2002); *Grassis v Johns-Manville Corp* 591 A 2d 671, 675 (NJ Super, 1991); *In re 'Agent Orange' Products Liability Litigation*, 818 F 2d 145, 437-41 (2nd Cir, 1987), cert. denied, 484 US 1004 (1988).

[18] See (n 17).

[19] *Third Restatement* (n 12) § 28, Comment *(c)(4)*.

[20] Ibid. For more on the role of differential aetiology in proving specific causation, see Chapter 3.3.

The doubles the risk requirement has also been criticised on the basis that it does not account for toxic substances that simply *accelerate* the time at which the plaintiff's disease occurs.[21] In such cases, a RR<2 might show that the toxic exposure *accelerated* the disease in the majority of individuals, and these individuals should subsequently recover damages to compensate for the acceleration.[22] In order to make such a claim, there would need to be 'evidence available to determine whether the biology and development of the disease is of the accelerative variety – perhaps because victims already have a genetic predisposition that merely requires a source to actuate the disease – or of the generative variety'.[23] The role of genetic predisposition will be further discussed in Chapter Six.

Epidemiological evidence has ultimately proven to be a crucial aspect of American toxic tort causation. For example, expert testimony can be excluded as unreliable if an expert ignores epidemiological studies that conflict with the expert's opinion.[24] In *Norris v Baxter Healthcare,*

[21] Michael Green, 'The Intersection of Factual Causation and Damages' (2006) 55(2) *DePaul Law Review* 671, 678.
[22] Ibid.
[23] Ibid.
[24] See, eg, *Norris v Baxter Healthcare* 397 F 3d 878, 882 (10th Cir, 2005) ('*Norris*'); For a contrasting case where epidemiological studies were deemed to be unnecessary in certain circumstances, see *Glastetter v Novartis Pharms. Corp*. 252 F 3d 986, 999 (8th Cir, 2001). For an explanation of the requirements for admissibility of expert evidence, see, eg, *Federal Rules of Evidence* (US) ('FRE') r 702. Most American states have either adopted the FRE, with or without local variations, or revised their existing statutes or court rules to at least partially conform with the FRE, Kenneth Graham Jr, 'State Adaptation of the Federal Rules: The Pros and Cons' (1990) 43(2) *Oklahoma Law Review* 293, 293. The Uniform Rules of Evidence, which attempts to achieve uniformity of the law of evidence between all American states, are also designed to be identical to the FRE, see especially rr 701-706 relating to opinions and expert testimony. Rule 702 reflects a heightened 'screening' or 'gatekeeping' role for judges in determining whether to admit expert evidence, see generally the '*Daubert* trilogy', *Daubert v Merrell Dow Pharmaceuticals Inc* (1993) 509 US 579; 113 S Ct 2786; *General Electric Co v Joiner* (1997) 522 US 136; 118 S Ct 512; *Kumho Tire Co Ltd v Carmichael* (1999) 526 US 137; 119 S Ct 1167. Some states have not adopted the *Daubert* test and still follow the *Frye* test, also known as the general acceptance test, was established prior to the enactment of the FRE in 1975, see *Frye v United States* 293 F 1013, 1014 (DC Cir, 1923). The states of California, Florida, Illinois, New Jersey, New York, Pennsylvania and Washington follow the *Frye* standard; Nevada, North Dakota and Virginia have not expressly adopted either the *Daubert* or *Frye* standard. All other states adopt the *Daubert* standard. This is particularly important to toxic torts because it means that the *Daubert* gatekeeping principles apply to all expert testimonies in those American states, irrespective of their discipline, whether scientific, engineering, medical or any other specialised knowledge. For example, experts testifying in pesticide litigation are often hydrologists, agricultural engineers, equipment specialists and farmers, all of whom would be subject to the *Daubert* criteria, see, eg, Mark Carpenter and George Ware, *Defending Pesticides in Litigation* (Thomson West, 2005) 221-258. In Australia, s 79(1) of the Uniform Evidence Legislation (see *Evidence Act 1995* (NSW); *Evidence Act 2001* (Tas); *Evidence Act 2004* (NI); *Evidence Act 2008* (Vic); *Evidence Act 2011* (ACT); *Evidence (National Uniform Legislation) Act 2011* (NT)) does not reflect the *Daubert* emphasis on reliability, but a challenge could be made to evidence relying on a new or emerging field of expertise on the basis that the purported 'field of expertise' does not fall within the ambit of 'specialised knowledge', see *Honeysett v The Queen* (2014) 253 CLR 122 [23]. In addition, in New South Wales, Western Australia and Victoria, the courts have held that expert evidence can be excluded where the evidence is unreliable, novel or the inferences drawn by the expert have not been tested or accepted by others, see *Tuite v The Queen* (2015) 49 VR 196 [72]-[73] where the Victorian Court of Appeal adopted the *Daubert* approach; *Liyanage v Western Australia* (2017) 51 WAR 359; *Mallard v The Queen* (2003) 28 WAR 1 where the Western Australian Court of Appeal adopted the *Frye* approach; *Chen v R* [2018] NSWCCA 106 [82]. In these jurisdictions, the evidence is not automatically inadmissible under s 79(1) of the UEL but can be

the US Court of Appeals for the Tenth Circuit affirmed summary judgment in favour of the defendant manufacturer because the plaintiff's experts simply 'ignored or discounted' all contrary epidemiological studies that found no reliable association between silicone breast implants and systemic disease.[25] The Court held that epidemiological evidence is not always required in a toxic tort case but 'where there is a large body of contrary epidemiological evidence', an expert must at the very least address this contrary evidence 'with evidence that is based on medically reliable and scientifically valid methodology'.[26] Merely relying on case studies and differential aetiology was insufficient to prove causation where this evidence was 'flatly contrary to all of the available epidemiological evidence'.[27]

Some American courts have gone so far as to imply that a plaintiff must adduce epidemiological evidence in order to meet their burden of proof.[28] The Bendectin litigation was the genesis for the requirement of an epidemiologic threshold for proof of causation in toxic torts.[29] Plaintiffs in this litigation were faced with a large body of epidemiological evidence that tended to exonerate Bendectin but little scientifically reliable evidence to support causation.[30] This led the US Court of Appeals for the Fifth Circuit to rule that '[S]peculation

excluded on discretionary grounds under s 135 (which is similar to r 403 of the *Federal Rules of Evidence* (US)) on the basis that it is untested, unverified or unsupported. It is unclear to what extent other Australian jurisdictions will unequivocally adopt a similar position in determining whether new scientific or medical theories and techniques should be admitted. Ian Freckelton QC suggests that 'at the very least', judges will likely 'focus upon the degree of dissension about any new technique within the scientific community and whether it is regarded as reliable' because the discretion to exclude evidence under s 135 affords an effective means of excluding any material that might be unduly misleading or confusing, Ian Freckelton, *Expert Evidence: Law, Practice, Procedure and Advocacy* (Thomson Reuters, 6th ed, 2019) 63. This argument reflects an earlier suggestion of the Australian Law Reform Commission that courts could rely on the general power under s 135 to exclude expert evidence where it 'has not sufficiently emerged from the experimental to the demonstrable', Australian Law Reform Commission, *Evidence*, Interim Report No 26 (1985) vol 1 [743]. These interpretations are more closely aligned with the emphasis on reliability underlying the *Daubert* principles.

[25] *Norris* (n 24).

[26] Ibid.

[27] Ibid.

[28] See, eg, *Brock v Merrell Dow Pharmaceuticals* 874 F 2d 307, 315 (5th Cir, 1989) ('*Brock*'); The *Third Restatement* observed that 'After *Brock*, several district courts in the Fifth Circuit employed it as a precedent, requiring epidemiological evidence, and courts have used a variety of techniques to squelch Bendictin plaintiffs in the face of a substantial body of exonerative epidemiology', see *Third Restatement* (n 12) § 28, Reporter's Note to Comment (c)(3); see also *Raynor v. Merrell Pharms. Inc.* 104 F 3d 1371, 1374 (DC Cir, 1997) where the court held that non-epidemiologic studies, 'singly or in combination, are not capable of proving causation in human beings in the face of the overwhelming body of contradictory epidemiological evidence' (quoting *Richardson v. Richardson Merrell, Inc.* 857 F 2d 823, 830 (DC Cir, 1988)).

[29] Ibid. The Bendectin litigation involved several toxic tort proceedings concerning birth defects that were allegedly caused by mothers ingesting Bendectin, a prescription anti-nausea drug marketed by Merrell Dow Pharmaceuticals.

[30] For a detailed analysis of *Bendectin* and review of the literature, see Gary Edmond and David Mercer, 'The Secret Life of (Mass) Torts; the "Bendectin Litigation" and the Construction of Law-Science Knowledges'(1997) 20(3) *UNSW Law Journal* 666.

unconfirmed by epidemiologic proof cannot form the basis for causation in a court of law'.[31] This view is also evident in the *Agent Orange* litigation where Judge Weinstein held that epidemiologic studies of exposed human populations were the 'only useful studies having any bearing on causation'.[32] The court in *Hupp v United States* made a similar ruling that only epidemiological evidence could prove causation in a case where the plaintiff alleged that a swine flu vaccine caused his multiple sclerosis ('MS').[33]

However, epidemiological evidence is not always necessary. In fact, the *Third Restatement* notes that 'a quite substantial body of case law and commentary rejects an epidemiologic threshold for sufficient proof of general causation'.[34] This is because, among other reasons, epidemiologic studies are expensive, time-consuming and cannot feasibly be conducted in a number of cases, such as where there are an insufficient number of persons exposed to the relevant substance or the incidence of the disease is so rare that epidemiologic studies are inadequate to reveal the effect of the substance.[35]

Even in toxic tort cases where epidemiological evidence has been adduced to support or refute causation, these cases have been plagued by widespread misunderstandings relating to the applicable legal and scientific standards of proof. These misunderstandings arguably stem from the merging of three distinct probabilities in toxic torts: fact probability, belief probability and sampling error probability.

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[31] *Brock* (n 28) 315.The Court was especially flawed in their requirement for 'statistically significant' studies. Statistical significance only addresses random error, and does not provide any information on bias or confounding. For more on the issues with this requirement, see Part 2.1.2 on merging the probabilities.

[32] *In re "Agent Orange" Products Liability Litigation* 611 F Supp 1223, 1231-32 (EDNY, 1985) where the court refused to consider any evidence other than epidemiologic studies of veterans.

[33] 563 F Supp 25 (SD Ohio, 1982); The plaintiff was only able to adduce circumstantial evidence to support causation and the lack of epidemiological evidence was fatal to the plaintiff's case. The circumstantial evidence included 'temporal proximity between vaccination and disease onset; known links between other vaccines and MS; known links between swine flu vaccine and neurological ailments other than MS; close physiological similarity between MS and GBS, an acknowledged result of the vaccine', see Steve Gold, 'The More We Know, the Less Intelligent We Are – How Genomic Information Should, and Should Not, Change Toxic Tort Causation Doctrine' (2010) 34(2) *Harvard Environmental Law Review* 369, 393. However, note that another court accepted circumstantial evidence 'as one type of several which, taken together, withstood a motion for summary judgment', see *Anderson v Cryovac, Inc*, No. 82-1672-S (D Mass, 1985)'; Gold (n 33) 393.

[34] See, eg, *Rider v Sandoz Pharms. Corp* 295 F 3d 1194, 1198 (11th Cir, 2002) where the court held that 'It is well-settled that while epidemiological studies may be powerful evidence of causation, the lack thereof is not fatal to a plaintiff's case'; *Norris* (n 24) 882-883; *Kennedy v Collagen Corp* 161 F 3d 1226, 1230 (9th Cir, 1998); David Faigman et al, 'How Good is Good Enough? Expert Evidence Under Daubert and Kumho' (2000) 50 *Case Western Reserve Law Review* 645, 663-4. For a detailed list of relevant cases and commentary rejecting an epidemiologic threshold, see *Third Restatement* (n 12) § 28, Reporter's Note to Comment *(c)(3).*

[35] See, eg, *Donaldson v Cent Ill Pub Serv Co* 767 NE 2d 314 (Ill, 2002) where the rarity of the plaintiff's form of cancer, neuroblastoma, meant that the 'relationship between coal tar and neuroblastoma has simply not been the subject of extensive study and research'. For a more detailed list of cases where the courts explored the various situations in which epidemiologic studies cannot feasibly be conducted, see ibid.

2.1.2 Merging the Probabilities

In 1986, Professor Steve Gold coined the terms 'belief probability' and 'fact probability' to delineate the probabilities that exist in toxic torts, respectively, 'as both a measure of strength of belief and a factual statistical quantity'.[36] In 2001, Professor David Barnes added the third probability, which he called 'sampling error probability' to describe a 'characteristic of statistical science'.[37]

'Fact probability' describes the statistical probability of a fact's occurrence or, more specifically, the statistical likelihood that the defendant's tortious conduct caused the plaintiff's harm.[38] Gold provides the example of a car accident where 'a traffic light fails to turn red and a crash ensues' but the council argues that the defective light was not the cause of the accident because the car was speeding and 'could not have stopped in time even had the light worked'.[39] In this example, the plaintiff could adduce evidence of a mathematical likelihood that '53% of cars would have stopped'.[40] This would be the 'fact probability', where the 'fact' being proven is that '*in most cases* the light *would have been* the cause'.[41] In a toxic tort case involving epidemiological evidence, the RR would usually be the relevant fact probability.[42]

On the other hand, 'belief probability' reflects the greater than 50% statistical probability required to persuade the factfinder to decide in favour of the plaintiff.[43] Both Australian and American authorities have traditionally interpreted the standard of proof to mean that the plaintiff must prove the facts supporting each element of the claim are 'more probable than not', or 'more *likely* than not', which typically requires a more than 50% probability.[44] In the car accident example, the fact is that there is a greater than 50% probability that the traffic light caused the accident, the decision-maker still needs to be able to form a probable belief in this

[36] Steve Gold, 'Causation in Toxic Torts: Burdens of Proof, Standards of Persuasion, and Statistical Evidence' (1986) 96(2) *Yale Law Journal* 376, 382.
[37] David Barnes, 'Too Many Probabilities: Statistical Evidence of Tort Causation' (2001) 64(4) *Law and Contemporary Problems* 191, 192.
[38] Gold (n 33) 383; see also Ibid.
[39] Ibid 382.
[40] Ibid 383.
[41] Ibid 384.
[42] Barnes (n 37) 193.
[43] Gold (n 33) 383.
[44] For a list of Australian judgments explicitly adopting this interpretation, see David Hamer, 'The Civil Standard of Proof Uncertainty: Probability, Belief and Justice' (1994) 16(4) *Sydney Law Review* 506, 509; For a list of American judgments explicitly adopting this interpretation, see Robert Ebert Jr, 'Damages for an Increased Risk of Developing Cancer Caused by Asbestos Exposure Are Only Recoverable if it is More Likely Than Not That Cancer Will Develop' (1986) 51(3) *Missouri Law Review* 847, 848.

fact, e.g., that the evidence of it is reliable, that it covers the particular traffic light in question and particular circumstances etc. In negligence cases, the plaintiff needs to prove the fact that the negligence was a cause of the damage, and the court must form a sufficient belief probability in that fact. In other words, 'a belief probability…measures the judge's degree of belief in a proposition so necessarily involves her assessment of how credible the assertion is'.[45] Whether the standard of proof is satisfied ultimately rests on the degree of persuasion of the decision-maker (the 'belief probability').[46]

A similar example highlighting the difference between fact and belief probability is Brachtenbach J's cab scenario:

> Assume there are two cab companies in a town; one has three blue cabs and the other has one yellow cab. A pedestrian is hit by a cab, but doesn't know what color it was. In a suit for personal injury, plaintiff wants to admit the statistical fact that there is a 75 percent chance that she was hit by a blue cab. This fact has relevancy; it is admissible. But is it sufficient to prove the blue cab company more probably than not committed the act? No. If this were not the case, the blue cab company could be held liable for every unidentified cab accident that occurred.[47]

In this example, Brachtenbach J emphasises the importance of a plaintiff being able to prove the fact that the negligence was a cause of their damage, and a fact-finder forming a sufficient belief probability in that fact.

Due to the prevalence of statistical correlations in toxic torts, 'fact probability' and 'belief probability' are often collapsed into the one enquiry.[48] This is because not only is the civil standard of proof expressed probabilistically, requiring greater than 50% probability, but 'the statistical causation evidence is also expressed probabilistically – as a factual estimate of the defendant's contribution to the plaintiff's risk'.[49] Moreover, Brachtenbach J's cab scenario does not neatly align with toxic torts because

> diseases are not like [cabs]. When trying to prove specific causation using epidemiological evidence, there is no possibility of eyewitness testimony. When only epidemiological evidence is used, that is generally because clinical science cannot produce anything better.[50]

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[45] Gemma Turton, *Evidential Uncertainty in Causation in Negligence* (Hart Publishing, 2016) 86.
[46] The factfinder should 'be persuaded from the evidence that factual causation more likely than not exists', see, eg, *Third Restatement* (n 12) § 28, Comment *(a)*; Uniform Evidence Legislation (see *Evidence Act 1995* (NSW); *Evidence Act 2001* (Tas); *Evidence Act 2004* (NI); *Evidence Act 2008* (Vic); *Evidence Act 2011* (ACT); *Evidence (National Uniform Legislation) Act 2011* (NT)) ss 140, 142; *Civil Liability Act 2002* (NSW) s 5E.
[47] *Herskovits v Group Health Cooperative of Puget Sound* (1983) 664 P 2d 474 [187]. For a more in-depth discussion of this scenario and how it relates to the standard of proof, see Michael Pardo, 'The Paradoxes of Legal Proof: A Critical Guide' (2019) 99(1) *Boston University Law Review* 233, 253-262.
[48] Gold (n 33) 383.
[49] Ibid.
[50] Alex Broadbent, 'Epidemiological Evidence in Proof of Specific Causation' (2011) 17 *Legal Theory* 237, 269.

Consequently, several US courts have merged the two probabilities so that causation will be established so long as the statistical evidence demonstrates a greater than 50% probability.[51] In other words, these courts will find that causation has been established where the relative risk is greater than 2. This collapsing of the probabilities has the indirect effect of promoting epidemiological evidence to a position of superiority in toxic torts and dismissing evidence that does not have a statistical value.[52] As Professor Susan Haack observes, 'by tempting us to confuse statistical probabilities with degrees of proof, legal probabilism can seduce us into forgetting that the statistical evidence in a case should be treated as *one piece of evidence among many*'.[53]

Undue emphasis on the fact probability carries great potential for unjust results. Professor Laurence Cohen provides the following helpful hypothetical scenario to illustrate the injustice that could result from adopting a purely mathematical approach:

> Consider, for example, a case in which it is common ground that 499 people paid for admission to a rodeo, and that 1,000 are counted on the seats, of whom A is one. Suppose no tickets were issued and there can be no testimony as to whether A paid for admission or climbed over the fence. So by any plausible criterion of mathematical probability there is a •501 probability, on the admitted facts, that he did not pay. The mathematicist theory would apparently imply that in such circumstances the rodeo organizers are entitled to judgement against A for the admission-money, since the balance of probability (and also the difference between prior and posterior probabilities) would lie in their favour. But it seems manifestly unjust that A should lose his case when there is an agreed mathematical probability of as high as •499 that he in fact paid for admission. Indeed, if the organizers were really entitled to judgement against A, they would presumably be equally entitled to judgement against each person in the same situation as A. So they might conceivably be entitled to recover 1,000 admission-moneys, when it was admitted that 499 had actually been paid.[54]

This approach therefore has the potential to produce absurdly unjust results where a fact could be 49% *improbable* but, if the fact and belief probabilities are merged, the legal standard of proof would still be satisfied because the fact is more than 50% *probable*.[55] As a result, it is problematic to merge these two very distinct probabilities.

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[51] Ibid 379, 386; Barnes (n 37) 205. For relevant cases, see, eg, the Supreme Court of Texas trilogy in *Merrell Dow Pharmaceuticals, Inc v Havner* 953 SW 2d 706, *Merck & Co v Garza* 347 SW 3d 256, 265-66 (Tex, 2011) and *Bostic v Georgia-Pacific Corp* 439 S W 3d 332 (Tex, 2014); see also, eg, Steve Gold, 'Drywall Mud and Muddy Doctrine: How Not to Decide a Multiple-Exposure Mesothelioma Case' (2015) 49 *Indiana Law Review* 117.

[52] Gold (n 33) 392; For examples of cases where the courts suggest epidemiological studies are the only type of evidence sufficient to prove causation, see, eg, *Brock* (n 28); *Agent Orange* (n 32); *Hupp* (n 33).

[53] Susan Haack, *Evidence Matters: Science, Proof and Truth in the Law* (Cambridge University Press, 2014) 72.

[54] Laurence Cohen, *The Probable and the Provable* (Oxford University Press, 1977) 75.

[55] Moreover, belief probability is not really susceptible to quantification in numerical terms in the way that the word 'probability' might suggest. Professor Richard Wright suggests that where the 'more likely than not' standard is employed, it is usually used to 'refer to the formation of a minimal belief in the truth of what actually happened on the particular occasion', rather than 'a mere statistical 50+ per cent probability', Richard Wright, 'Proving Causation: Probability versus Belief' in Richard Golberg (ed), *Perspectives on Causation* (Hart Publishing, 2011) 201.

This issue of collapsing fact and belief probability into one enquiry is further complicated by the 'sampling error probability'. Barnes uses this term to describe the 'likelihood that an observed statistical relationship was due to the random selection of subjects to include in the study' so that 'If statistical evidence based on a sample is used to establish a fact probability, the statistical evidence concerning the fact probability always has an associated sampling error probability'.[56] In toxic torts involving epidemiological studies, the 'sampling error probability' reflects the *p-value*.[57] The *p-value* affects the belief probability only to the extent that a higher *p-value* (closer to 1.0) reflects an increased probability that the RR (or fact probability) is due to the random selection of subjects. The belief probability is also affected by numerous factors that are not reflected in the *p-value,* such as the quality of the study, bias, confounding and the difficulties of extrapolating the results to a particular plaintiff's harm.[58] Moreover, the *p-value* relates to general causation, but the common problem in satisfying belief probability in toxic torts is specific causation. As a result, Barnes argues that the *p-value* should form part of the

[56] Barnes (n 37) 194.

[57] The product of significance testing, the p-value, provides a means of assessing the probability that, if the research were to be repeated many times, researchers would continue to find a difference at least as large as that observed in the current sample, see, eg, Erica Beecher-Monas, 'Lost in Translation: Statistical Inference in Court' (2014) 46(4) *Arizona State Law Journal* 1057, 1064-1065; Sanders et al (n 59) 869. The p-value ranges from 0 to 1.00 and a value closer to 0 means that there is a smaller probability that the result could have occurred even if there was no 'true association' between the agent and disease, see *Reference Manual,3rd ed* (n 11) 576. For example, 'a p-value of 0.1 means that there is a 10% chance that values at least as large as the observed relative risk could have occurred by random error, with no association actually present in the population', ibid. An outcome of an epidemiological study is usually only statistically significant when the observed p-value is less than 0.05. In other words, 'A 0.05 value means that the probability is 5% of observing an association at least as large as that found in the study when in truth there is no association', ibid 577. In such cases, the results of the study are 'statistically significant' because the observed difference is unlikely to have occurred by chance alone, see *Reference Manual, 2nd ed* (n 15) 354.

[58] Barnes (n 37) 200-5. In addition to chance, the results of an epidemiological study might exist merely because of bias, Ray Merrill, *Fundamentals of Epidemiology and Biostatistics: Combining the Basics* (Jones & Bartlett, 2013) 211. Unlike the 'random error' of chance where the errors have no particular pattern, bias involves 'systematic error' where the errors arise more uniformly and 'produce results which are systematically different from the real values', Antony Stewart, *Basic Statistics and Epidemiology: A Practical Guide* (Radcliffe Publishing, 3rd ed, 2010) 99. Bias usually occurs as a result of faults in the way a study is planned and conducted. The two primary types of bias are selection and information bias, see ibid. Confounding 'occurs when the relationship between an exposure and a disease outcome is influenced by a third factor, which is related to the exposure and, independent of this relationship, is also related to the health outcome', Merrill (n 58) 214. For example, where a study is investigating 'whether high alcohol consumption is a risk factor for coronary heart disease, smoking is a confounding factor (also known as a confounder)' because 'smoking is known to be related to alcohol consumption, and it is also a risk factor for coronary heart disease', Stewart (n 58) 101. Where randomisation is not possible, 'matching' can be used to address the problem of confounding by ensuring 'that two study groups are similar with regard to an extrinsic factor or factors that might distort or confound a relationship between an exposure and outcome being studied', Merrill (n 58) 215. Alternatively, stratified analysis could be used to divide subjects into groups at the analysis stage according to, for example, age, gender, lifestyle factors, and analysing the results on this basis, Stewart (n 58) 102. So, confounding factors can be controlled if they are identified by researchers during the study design, Steve C Gold, Michael D Green and Joseph Sanders, *Scientific Evidence of Factual Causation: An Educational Module* (The National Academics of Science, Engineering and Medicine, October 2016) 80.

fact probability as opposed to the belief probability.[59] As Barnes emphasises, 'Most importantly, the sampling error probability cannot be used to measure whether the evidence embodied in the fact probability is more likely true than not true'.[60]

However, legal academics, scientific experts and courts have confused *p-values*, confidence intervals and RR with the civil standard of proof.[61] For example, some scientific experts testifying in toxic torts[62] and legal academics[63] have erroneously interpreted the relevant scientific standard of proof as requiring 95% certainty, which clearly confuses the confidence interval[64] of 95% with the civil standard of proof.

In addition, US courts have described studies with a low RR as 'statistically insignificant' and subsequently insufficient to prove causation.[65] As statistical significance does not refer to RR, these courts have inadvertently merged sampling error probability and fact probability in an attempt to justify their belief probability and ultimately their decision to exclude epidemiological evidence. As Barnes notes, 'Notwithstanding the fervent wishes of courts, advocates, and expert witnesses, none of these three probabilities is equivalent to the

[59] Barnes (n 37) 205. Joseph Sanders et al, 'Differential Etiology: Inferring Specific Causation in the Law from Group Data in Science' (2021) 63 *Arizona Law Review* 851, 897.
[60] Barnes (n 37) 202.
[61] The civil standard of proof is here defined as the preponderance of the evidence standard in America and the balance of probabilities standard in Australia.
[62] See, eg, *Marmo v IBP Inc* 360 F Supp 2d 1019, 1021 (D Neb, 2005) where a toxicology expert testified that the scientific standard of proof required 95% certainty; *Merck Sharp & Dohme (Australia) Pty Ltd v Peterson* [2011] FCAFC 128; (2011) 284 ALR 1, 145 where a cardiologist testified in relation to the 'burden of proof required to prove causation for the general population, with scientific certainty' and explained that 'scientific certainty [requires] a conclusion that could be reached with a 95% probability of being valid'.
[63] See, eg, Dr Gemma Turton points out that Professor Richard Goldberg misinterpreted the standard of proof in science by suggesting that 'rules of epidemiology require evidential proof on a balance of probabilities of at least 95 per cent to establish causation', see Turton (n 45) 98 citing Richard Goldberg, 'Using Scientific Evidence to Resolve Causation Problems in Product Liability: UK, US and French experiences' in Goldberg (n 80) 150. See also Carl Cranor, *Regulating Toxic Substances: A Philosophy of Science and the Law* (Oxford University Press, 1993) 72-76 where Professor Cranor argues that 'the 95% rule' in science is far more stringent than the 50% civil standard; For a detailed critique of Cranor, see Michael Green, 'Science is to Law as the Burden of Proof is to Significance Testing' (1997) 37(2) *Jurimetrics* 205.
[64] Calculation of a confidence interval allows epidemiologists to assess the potential for random error in their results. A confidence interval of 95% is usually required in epidemiological studies because it indicates little random sampling error and suggests that these results would be expected '95% of the time if samples for new studies were repeatedly drawn from the same population', see *Reference Manual, 2nd ed* (n 15) 580; Webb and Bain (n 14) 156-7. When the confidence interval is wide, or includes a RR of 1, then it is less persuasive evidence of a causal relationship. Confidence intervals only provide information about 'the range of possible values that would be found due to random error if the true association is the study result', Gold et al, *Scientific Evidence of Factual Causation: An Educational Module* (n 58) 70. They do not provide any indication about the quality of the study design or whether there are other sources of error, such as bias and confounding, *Daubert v Merrell Dow Pharmaceuticals, Inc* (1993) 509 US 579, 593.
[65] See, eg, *In Re Joint Eastern and Southern District Asbestos Litigation*, 827 F Supp 1014, 1041-2 (SDNY, 1993); *Allison v McGhan Medical Corp* 184 F 3d 1300, 1315 (11th Cir, 1999); Barnes (n 37) 205-6.

probability that the defendant's act caused the plaintiff's harm'.[66] This reasoning is largely reflected in the Australian case law.

2.1.3 The Australian Position

In *Seltsam Pty Ltd v McGuinness* ('*Seltsam*'), Spigelman CJ criticised overreliance on statistical probabilities. His Honour observed that 'The predominant position in Australian case law is that a balance of probabilities test requires a court to reach a level of actual persuasion. This process does not involve a mechanical application of probabilities'.[67] His Honour questioned the American application of the doubles the risk doctrine 'as a rigid mathematical formula'.[68] His Honour subsequently provided the following helpful clarification of the Australian position:

> In Australian law, the test of actual persuasion does not require epidemiological studies to reach the level of a relative risk of 2.0, even where that is the only evidence available to a court. Nevertheless, the closer the ratio approaches 2.0, the greater the significance that can be attached to the studies for the purposes of drawing an inference of causation in an individual case. The "strands in the cable" must be capable of bearing the weight of the ultimate inference.[69]

This statement aligns with the views espoused by Gold and Barnes to the extent that it suggests the fact probability (RR) should not determine the belief probability ('an inference of causation in an individual case'). In other words, the epidemiologic studies, and their RR, are merely one of the 'strands in a cable' which may, alone or combined with other evidence, establish causation on the balance of probabilities.[70]

Applying *Seltsam* to a medical negligence case, Ipp JA in *Sydney South West Area Health Service v Stamoulis* ('*Stamoulis*') emphasised that there are 'dangers in applying epidemiological or statistical evidence in a mechanical way'.[71] In outlining the dangers of applying evidence that can be mathematically quantified, His Honour made reference to an English Court of Appeal judgment where Ormrod LJ noted:

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[66] Barnes (n 37) 197.
[67] (2000) 49 NSWLR 262; [2000] NSWCA 29 [136]; This case considered whether the plaintiff's exposure to asbestos caused his renal cell carcinoma. For a detailed explanation and analysis of the case, see Ian Freckelton, 'Epidemiology Evidence and Causation' (2004) 63 *Plaintiff: Journal of the Australian Plaintiff Lawyers Association* 18, 19-23. For a general explanation of statistical evidence in Australian legal proceedings, see John Goldring, 'An introduction to statistical "evidence"' (2003) 23 *Australian Bar Review* 239.
[68] [2000] NSWCA 29 [135]; Spigelman CJ provides a succinct summary of the American case law in this area, see [121]-[135]. For a list of the common-sense propositions , which 'should be viewed as guidelines', applied by Spigelman CJ in determining specific causation, see [139].
[69] Ibid [137].
[70] Ibid [89], [98]; see also *EMI Australia Ltd v BES* [1970] 2 NSWR 238, 242 (appeal dismissed (1970) 44 ALJR 360); *Fernandez v Tubemakers of Australia Ltd* [1975] 2 NSWLR 190, 239, 240.
[71] [2009] NSWCA 153 [135].

> The concept of 'probability' in the legal sense is certainly different from the mathematical concept: indeed, it is rare to find a situation in which these two usages co-exist although, when they do, the mathematical probability has to be taken into the assessment of probability in the legal sense and given its appropriate weight.[72]

While this passage highlights the disparity between mathematical and legal probabilities, Ipp JA confirmed that an Australian court may infer causation on a balance of probabilities even though experts do not infer causation to this standard.[73] Most importantly, His Honour rejected the argument that 'the statistical fact that a particular proposition is true of the majority of persons cannot of itself amount to legal proof on the balance of probabilities that the proposition is true of any given individual' and concluded that 'the matter is essentially one of degree'.[74] Therefore, consistent with Spigelman CJ's position in *Seltsam*[75], Ipp JA suggested that specific causation could be satisfied solely on the basis of epidemiologic evidence indicating the likelihood of causation in the general population.[76] His Honour expanded on this statement by suggesting that although 'the question is always whether the evidence as a whole establishes causation on a balance of probabilities', a 'finding of causal connection may be made even when the expert evidence does not rise above the possible'.[77] This implies that expert evidence does not need to satisfy the 'doubles the risk' threshold.

The Hon Justice Ian Freckelton QC questions the Australian approach to epidemiological evidence. His Honour concedes that the 'doubles the risk' rule may be 'arbitrary' but also emphasises that 'The advantage of such a rule is its clarity'.[78] His Honour asserts that, by contrast to the 'clarity' of the American approach, the Australian position of permitting 'epidemiological evidence that falls some distance short of 2.0' presents a 'risk…that courts will seek refuge in the imprecise language of "possibility" and "commonsense" which can result in inexact and impenetrable reasoning'.[79] This makes it especially difficult to determine the adequacy of a court's evaluation of the often 'complex and conflicting epidemiology evidence' and can subsequently lead to inconsistent decision-making.[80] Similarly, Dr Marc Stauch criticises the balance of probabilities test, by implying that this test prompts the courts to make a decision based on a feeling rather than on statistical facts.[81]

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[72] See ibid [134] citing *Re JS (a minor)* [1980] 1 All ER 1061, 1066.
[73] Ibid [138]; see also *Seltsam* (n 67) [143]-[144].
[74] *Stamoulis* (n 71) [137].
[75] *Seltsam* (n 67) [89], [98].
[76] *Stamoulis* (n 71) [137].
[77] Ibid [138]; see also *Seltsam* (n 67) [89], [94]-[96], [98]-[100], [102], [143], [144] and [153].
[78] Freckelton (n 67) 24.
[79] Ibid.
[80] Ibid.
[81] Marc Stauch, 'Loss of Chance in Medical Negligence' (1997) 17 *Oxford Journal of Legal Studies* 205, 219.

On the other hand, Dr Gemma Turton points out that 'It is essential to remember that these two types of probability are not mutually exclusive' because 'a rational belief probability must be based on an assessment of the credibility of the scientific evidence which includes, but is far wider than, the relative risk or fact probability'.[82] In short, 'While statistical probabilities may have an outward appearance of objectivity, they only tell part of the story and they certainly do not provide a definitive answer about causation in an individual case'.[83] Haack similarly maintains that:

> this kind of reliance on a whole mesh of evidence is ubiquitous – the rule, not the exception. It is commonplace in everyday life: when, for example, after reading a startling story in a newspaper, I buy a different paper, or turn on the television news, to check whether other sources confirm it.[84]

Haack ultimately suggests that 'the statistical evidence in a case should be treated as *one piece of evidence among many*'.[85] These arguments support the proposition that the 'doubles the risk' doctrine is inappropriate, as it supplants the vital role of the fact-finder's belief probability. Ultimately, although consistency in decision-making is important, it is also crucial to consider the ramifications of consistently applying a doctrine that might be 'clear' but carries significant potential for injustice.

Professor Richard Wright demonstrates how the doubling the risk doctrine can lead to substantial unfairness.[86] This unfairness arises because the defendant(s) would be held liable 'even if there is no evidence that the substance actually caused the injury on any particular occasion, and even though exposure to the substance could only have caused a portion of the injuries'.[87] For example, if epidemiologic studies prove that exposure to the substance causes harm in 51% of the population, this means that 49% of the population would not suffer injury as a result of exposure. Nevertheless, the defendant(s) would be required to compensate all injured parties in this scenario, because the plaintiff has demonstrated that exposure 'doubles the risk'. On the other hand, if epidemiologic studies demonstrate that exposure only caused harm in 49% of the population, the defendant(s) would not be liable for any of the injuries that occur following exposure. As Wright notes, 'It is remarkable that such a miniscule difference in statistical probability should be thought to result in such a dramatic difference in the

[82] Turton (n 45) 86.
[83] Ibid.
[84] Haack (n 53) 218.
[85] Ibid 71-2.
[86] Richard Wright, 'Proving Causation: Probability versus Belief' in Richard Goldberg (ed), *Perspectives on Causation* (Hart Publishing, 2011) 215-6; see also *McGhee v National Coal Board* [1973] 1 WLR 1, 12 (Lord Salmon); Ibid [26] (Lord Philips).
[87] Wright (n 86) 215-6.

supposed proof of specific causation and resulting liability'.[88] This 'all-or-nothing' system of compensation has rightly been the subject of some controversy[89] and solutions have been proposed, including award discounting or a comprehensive insurance scheme or system of proportional recovery.[90]

The 'doubles the risk' doctrine and the role of epidemiological evidence in establishing specific causation were also the subject of significant contention in *Merck Sharp & Dohme (Australia) Pty Ltd v Peterson* ('*Merck*').[91] The primary issue in that case was whether the consumption of Vioxx caused or contributed to the plaintiff's myocardial infarction (heart attack). The trial judge found that causation was established on the basis of circumstantial evidence including statistical evidence derived from several epidemiological studies, especially the VIGOR and APPROVe studies.[92] In particular, the trial judge relied upon epidemiological evidence which indicated that the consumption of Vioxx almost doubled the RR of heart attack in the general population.[93]

On appeal, the Full Court of the Federal Court of Australia expressed great scepticism towards the doubles the risk doctrine because 'it is apt to mandate an award of compensation to applicants who have not, in truth, been injured by the respondent'.[94] In a joint judgment, Keane CJ, Bennett and Gordon JJ pointed out a fundamental flaw in the doctrine because it requires defendants to compensate even individuals who were not in fact injured by the defendant's conduct.[95] This is because these individuals could also rely on the RR of greater than 2 'to

[88] Ibid. For a more recent article criticising the doubles the risk approach, see Per Laleng and Charles Feeny, 'Law and Epidemiological Evidence: Double, Toil and Trouble' (2022) 49(1) *UWA Law Review* 159, 167.
[89] See, eg, Gold (n 33) 398; Kinsley, 'Fate and Lawsuits: Litigation Doesn't Work. How about Socialism?' New Republic (June 14, 1980) 3 cited in Gold (n 33) 398.
[90] A discussion of these solutions is beyond the scope of this chapter. For a more in-depth discussion of potential solutions, Steve Gold, 'When Certainty Dissolves into Probability – A Legal Vision of Toxic Causation for the Post-Genomic Era' (2013) 70(1) *Washington & Lee Law Review* 237; Jennifer Champagne, 'Genetic Testing and Testimony in Toxic Tort Litigation' (2011) 13(1) *North Carolina Journal of Law & Technology* 1; Noah Smith-Drelich, 'Performative Causation' (2020) 93(3) *Southern California Law Review* 379; Alexandra Lahav, 'Chancy Causation in Tort Law' (2022) *Journal of Tort Law*; David Rosenberg, 'The Causal Connection in Mass Exposure Cases: A "PublicLaw" Vision of the Tort System' (1984) 97 *Harvard Law Review* 849, 925 where Rosenberg argues that the specific causation requirement should be replaced by class action-based proportional recovery; Sanders et al (n 59) where the authors propose an application of the Bradford-Hill Criteria, supplemented by considerations of internal and external validity, to assist courts in answering specific-causation questions and overcoming the 'G2i' problem (i.e. the problem of reasoning from group data to individual cases).
[91] [2011] FCAFC 128; (2011) 284 ALR 1.
[92] *Peterson v Merck Sharpe & Dohme (Australia) Pty Ltd* (2010) 266 ALR 1, 285-8 ('*Peterson*'); For a detailed analysis of *Peterson,* see Thomas Faunce, Ruth Townsend and Alexandra McEwan, 'The Vioxx pharmaceutical scandal: Peterson v Merke Sharpe & Dohme (Aust) Pty Ltd (2010) 184 FCR 1' (2010) 18(1) *Journal of Law and Medicine* 38.
[93] Ibid.
[94] *Merck* (n 91) [110].
[95] Ibid.

imply probability of greater than 50% that the respondent's actionable conduct was the cause of their loss'.[96] This is similar to Gold's assertion that the 'rigidity' of the doubles the risk test is 'particularly inappropriate' because 'the estimate of relative risk is a property of the studied population, not of an individual's case'.[97] The Court's observations ultimately reflect the concerns of Gold and Barnes to the extent that they reveal the unfairness that could arise from allowing the fact probability to be the sole determinant of the court's belief probability.

The Court ultimately held that the epidemiological studies failed to assist in resolving the question of specific causation.[98] The Court noted that an epidemiologic study adduced as 'proof of what may be expected to happen in the usual case is of no value unless it is proved that the particular applicant is indeed "the usual case"'.[99] The Court held that the plaintiff's 'personal circumstances were such that they afford a ready explanation for the occurrence of his injury independent of the possible effects of Vioxx' and subsequently 'The strength of the epidemiological evidence as a strand in the cable of circumstantial proof is seriously diminished by this consideration'.[100]

The Court emphasised that the power of the plaintiff's circumstantial case was substantially diminished by the plaintiff's failure to appreciate the degree of his attributable risk[101] from Vioxx in comparison with other factors.[102] Those other factors included age, lifestyle (history of smoking), obesity and hypertension.[103] As a result, 'the strength of this strand' of epidemiological evidence 'did not rise above the possibility that it was "in the mix" of factors which may have caused Mr Peterson's heart attack'.[104] This ultimately meant that the Court could not conclude the plaintiff would not have suffered a heart attack 'but for' the

[96] Ibid; The Court also observed that the trial judge found the RR to be 'about 2' which is problematic because 'while a relative risk of 2 might imply a 50% probability that the risk has come home in a typical case, a relative risk of less than 2 would imply a probability of less than 50%, that is to say less probable than not', see Ibid [111].
[97] Gold (n 33) 390; see also *Allen v United States* 588 F Supp 247, 416-18 (D Utah, 1984) where the Court warned against exclusive reliance on statistical estimates and explicitly rejected the doubles the risk rule. The plaintiffs alleged that they had contracted cancer as a result of exposure to radioactive fallout that drifted away from a nuclear test site and settled upon nearby communities.
[98] *Merck* (n 91) [113]. For more information on the Australian Vioxx class action, see Chapter 1.3.3.
[99] Ibid [106].
[100] Ibid [113].
[101] Attributable risk ('AR') is the 'excess risk of developing a disease in those who have been exposed to a risk factor compared with those who have not', Stewart (n 58) 114. See also Sanders et al (n 59) 880. In a formula: AR = Incidence of disease in exposed group – Incidence of disease in unexposed group. An AR of zero indicates that there is no excess risk from exposure.
[102] *Merck* (n 91) [111].
[103] Ibid [120]. For a more detailed quote from the judgment on this point, see Chapter 1.3.3.
[104] Ibid [123].

consumption of Vioxx because such a conclusion 'is a matter of conjecture rather than reasonable inference on the balance of probabilities'.[105]

Although the Court did 'not consider that it was more probable than not that the consumption of Vioxx was a necessary condition of Mr Peterson's heart attack', the Court noted that 'it does not follow from this conclusion that none of the other applicants represented in these proceedings can succeed in establishing the ingredient of causation in their claims'.[106] In particular, the Court noted that 'there may be applicants in relation to whom there is no likely cause of their MI other than the effects of their consumption of Vioxx'.[107] The Court is therefore suggesting that the strength of the epidemiological evidence in a particular case is ultimately determined by the plaintiff's personal circumstances.

In coming to this conclusion, the Court considered[108] the joint judgment of the High Court of Australia in *Amaca v Ellis.*[109] In that case, French CJ, Gummow, Hayne, Heydon, Crennan, Kiefel and Bell JJ held that the significance of epidemiologic studies was dependent upon whether the plaintiff conformed to the pattern described by the studies or was 'atypical'.[110] In particular, the High Court observed that:

> To draw an inference about causation from what was established by the epidemiological studies, it would be necessary to decide whether the particular case under consideration should be treated as conforming to the pattern described by the epidemiological studies. Absent evidence which suggests that the individual may stand apart from the ordinary, there may be sufficient reason to assume conformity, but whether or not that is so, it is important to recognise that the first step that must be taken, if an inference is to be drawn from epidemiological studies, is to relate the results of studies of populations to the particular case at hand. That step is not inevitable.[111]

This passage encapsulates the fundamental difficulty at the core of all epidemiological evidence in toxic torts, namely the need to extrapolate the results of an epidemiologic study to a particular individual's harm.

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[105] Ibid [124].
[106] Ibid [126].
[107] Ibid.
[108] Ibid [112].
[109] *Amaca Pty Ltd v Ellis; State of South Australia v Ellis; Millennium Inorganic Chemicals Ltd v Ellis* [2010] HCA 5; (2010) 240 CLR 111; (2010) 263 ALR 576 ('*Ellis*'). For a detailed analysis of the decision, see Basil Bitas, 'A Common Law View of Causation, Science and Statistical Evidence in the Courtroom' (2011) 23(1) *Singapore Academy of Law Journal* 307.
[110] *Ellis* (n 109) [62]-[63].
[111] Ibid [62].

As the plaintiff in *Ellis* was a smoker[112], a key issue in that case revolved around the 'synergistic or multiplicative' effects of tobacco smoke and asbestos.[113] The plaintiffs interpreted epidemiologic studies 'as showing that the numbers of lung cancer sufferers who were smokers and had been exposed to asbestos were higher than would have been expected if the incidence of lung cancer in smokers was added to the incidence in those exposed to asbestos'.[114] This interpretation was intended to reveal the 'synergistic effect' of tobacco and asbestos, with both carcinogens operating interdependently and 'asbestos exposure "multiplying" the risk of lung cancer due to smoking by a quantity greater than one'.[115] However, the High Court refused to permit the inference that smoking and asbestos 'must work together' merely because a greater number of people who are exposed to both carcinogens contract lung cancer than would be expected from those exposed only to one of the two carcinogens.[116] The Court also stressed that 'While the witnesses differed about the figures, all witnesses agreed that the risk from smoking was many times greater than the risk from asbestos inhalation'.[117] The plaintiff's case ultimately failed because the epidemiologic studies could only show that 'exposure to asbestos *may* have been a cause' of the plaintiff's cancer, but the studies could not reach the necessary standard of proving asbestos to be 'a probable cause'.[118]

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[112] Prior to his death, the plaintiff 'had smoked on average somewhere between 15 and 20 cigarettes a day for a bit over 26 years before he was diagnosed with lung cancer', see Ibid [3].

[113] Ibid [21], [31]-[37], [49], [51], [57]. For a thorough critique of the Western Australian Supreme Court and Court of Appeal's 'unwarranted' rejection of the epidemiological evidence in *Ellis*, see David Hamer, 'Mind the "Evidential Gap": Causation and Proof in *Amaca Pty Ltd v Ellis*' (2009) 31 *Sydney Law Review* 465.

[114] *Ellis* (n 109) [21].

[115] Ibid. The *Third Restatement* (n 12) § 28(a), Comment *(c)(5)* also addresses the 'synergistic effect' of tobacco and asbestos exposure. This comment stipulates that 'If the synergistic effect is sufficiently large, the excess incidence of disease due to the synergistic effect will be greater than the excess incidence of disease due to each of the agents separately. In such circumstances, factfinders may infer that the combined exposure is a cause of the plaintiff's disease'. The comment also stipulates that 'Only those causes attributable to tortious conduct are legally relevant in determining liability and apportioning liability for the plaintiff's harm' such that 'a natural condition, a genetic trait of the plaintiff, or a nonnegligent actors conduct' have no effect on apportionment of liability, see also *Restatement Third, Apportionment of Liability* § 26, Comment *m*. Illustrations 4 and 5 of *Third Restatement* (n 12) § 28(a), Comment *(c)(5)* demonstrate that apportionment of liability can only occur where the defendant successfully persuades the factfinder that the plaintiff's smoking constituted negligence on his/her part. In addition, the Reporter's Note to Comment *(c)(5)* states that allocation of the probability attributable to the synergistic effect of both agents 'requires normative judgment and cannot be calculated simply by mathematical technique'.

[116] *Ellis* (n 109) [49], [51], [57]. The Court also refused to accept the plaintiff's submission that exposure to both smoking and asbestos was 'more dangerous' than exposure to one or the other, see ibid [58]-[61].

[117] Ibid [31]. Professor David Hamer also observed this point, 'Despite some variation between the experts, the epidemiological evidence attributes virtually the entire risk of lung cancer to tobacco and background exposure rather than the workplace asbestos exposure. This strongly suggests that the lung cancer would have ensued even had the asbestos exposure not occurred', see Hamer (n 113) 484.

[118] Ibid [14], [51], [58]. For a similar case, see *Evans v Queanbeyan City Council* [2011] NSWCA 230 [19], [56]-[57], [67], [83] where the Court held that, even where there was evidence of a synergistic effect between tobacco and asbestos, the trial judge was entitled to reject the hypothesis that these carcinogens 'probably worked together in a majority of cases'. For an asbestos case where the plaintiff argued, 'independently of

Although *Ellis* focuses on issues arising from the effect of asbestos and tobacco on lung cancer, the High Court's careful treatment of statistical evidence extends far beyond this limited fact scenario. The High Court effectively established 'a road map for common law courts in Australia and perhaps elsewhere regarding the appropriate manner of integrating scientific proof into the courtroom while protecting the integrity of the legal inquiry'.[119] In particular, *Ellis* confirmed that statistical evidence 'cannot supersede the essential nature of the legal inquiry'.[120] This proposition rightly echoes the warning of an American judge, who cautioned that 'Judges and lawyers must approach with great care, the idea that court decisions can be justified solely on the findings of science, lest the quest for justice be lost along the way'.[121] As the following chapters will reveal, scientific evidence is a crucial aspect of toxic tort litigation but scientific methods have their shortcomings and it is therefore imperative that the courts consider all available evidence as a whole, rather than viewing each piece of evidence in isolation. The 'doubles the risk' doctrine is particularly inappropriate for this very reason - it places epidemiological evidence in a position of superiority and encourages courts to view this evidence in a vacuum. As mentioned earlier, such an approach carries great potential for injustice by overcompensating or undercompensating plaintiffs for their harm depending on whether they can meet the arbitrary cut off of RR>2. Even one percent less than 50% can leave a plaintiff with nothing. Conversely, one percent greater than 50% can provide a plaintiff with full compensation for their harm. This absurdly unjust result must not be allowed by the courts.

2.1.4 The Problem of 'Junk Science'

It is paramount that courts do not give undue weight to epidemiological evidence because, like any science, epidemiology is subject to disagreement.[122] A key example of this discord is the

epidemiological analysis, that exposure to asbestos was a cause of the cancer', see *Amaca v Booth* (2011) 246 CLR 36; (2011) 283 ALR 461; [2011] HCA 53, especially [40] where the court distinguishes the facts in *Ellis*.

[119] Bitas (n 109) 322. Similar to the Australian position, the United Kingdom Supreme Court also cautioned against exclusive reliance on statistical evidence to prove causation, see *Sienkiewicz v Greif* (UK) Ltd [2011] UKSC 10, [2011] 2 AC 229.

[120] Bitas (n 109) 321.

[121] *Allen v United States of America* 588 F Supp 247, 260 (D Utah, 1984) per District Judge Jenkins.

[122] There are also notable benefits of epidemiological studies, see, eg, Sanders et al (n 59) 881: 'Epidemiological studies have several advantages over other toxicological studies. They share with animal studies the advantage that they measure the effect of a substance on a whole organism, not simply the effect on a cell culture or an organ. And they sidestep the difficult cross-species comparisons confronting animal studies when those studies are used to predict effects on humans. In sum, they confront fewer external validity challenges to their results'. See also Noah Smith-Drelich, 'Performative Causation' (2020) 93(3) *Southern California Law Review* 379, 401-3 where Smith-Drelich; Claire McIvor, 'Debunking some Judicial Myths about Epidemiology and its Relevance to UK Tort Law' (2013) 21 *Medical Law Review* 553.

prolonged dispute over the role of oral contraceptives in causing (or preventing) breast cancer where multiple studies showed no increase in risk but other contradicting studies found significantly higher RRs.[123] Similarly, the RR of 'respiratory cancer resulting from occupational exposure to arsenic has been estimated at anywhere from 3 to 60'.[124] It is therefore imperative that experts seeking to rely on an epidemiologic study provide sufficient scientific explanation as to why any conflicting studies should be disregarded by the court.[125] As Professor Joseph Sanders et al explain, epidemiological studies are observational 'rather than true experiments', so 'there is always the possibility that the true relationship between a "cause" and an "effect" has been distorted by failure to account for some unmeasured confounder(s) linked to both'.[126]

It is also important that courts remain wary of studies that have not been subject to peer-review or publication. The *Bendectin* litigation demonstrated 'the dubious categories of evidence frequently relied on by expert witnesses in toxic tort cases', including 'preliminary, unpublished epidemiological studies that have not been scrutinized by peers in the scientific community'.[127] Unwarranted reliance on so-called 'junk science' could have far-reaching social impacts, including 'a grave risk of driving safe, useful products off the market, stifling innovation, sowing fear and confusion among consumers, and creating massive economic burdens for innocent companies'.[128] Examples include women who underwent painful and unnecessary removal of breast implants following media coverage of the association between implants and cancer.[129] Another example is the women who underwent abortions due to fears 'that their ingestion of Bendectin would lead to birth defects'.[130]

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[123] See, eg, Committee on the Relationship Between Oral Contraceptives and Breast Cancer, Institute of Medicine: Division of Health Promotion and Disease Prevent, *Oral Contraceptives & Breast Cancer* (National Academy Press, 1991).
[124] See Gold (n 33) 398.
[125] See, eg, *Lofgren v. Motorola Inc.*, No. CV 93-05521, 1998 WL 299925, 16-17 (Ariz Super Ct, June 1, 1998) cited in David Bernstein, 'Getting to Causation in Toxic Tort Cases' (2008) 74(1) *Brooklyn Law Review* 51, 66.
[126] Sanders et al (n 59) 881: 'This problem is one of internal validity—our confidence that the study design warrants a conclusion that an observed correlation reflects a causal relationship rather than one due to confounding or another source of methodological deficiency'. See also Noel Weiss, 'General Concepts in Epidemiology' in David Faigman et al, *Modern Scientific Evidence: The Law and Science of Expert Testimony* (West, 2019–2020 ed) §23.35.
[127] Bernstein (n 125) 61, 65. For more on the significance of peer reviewed publications in toxic torts, see Haack (n 53) 156-180.
[128] Bernstein (n 125) 74. For a critique of such concerns, see Steve Gold, 'The Reshapement of the False Negative Asymmetry in Toxic Tort Causation' (2011) 37(3) *William Mitchell Law Review* 1507.
[129] Bernstein (n 125) 73; see also *Norris* (n 24) 880.
[130] Ibid; Thomas Strong, 'Alternative Therapies of Morning Sickness' (2001) 33 *Clinical Obstetrics & Gynecology* 653, 656; Margaret A Berger & Aaron D Twerski, 'Uncertainty and Informed Choice: Unmasking *Daubert*' (2005) 104 *Michigan Law Review* 257, 259, 280-81, 289.

Professor David Bernstein outlines the significant societal impacts of the Bendectin and breast implant scandals:

> Even though there was overwhelming evidence by the late 1980s that Bendectin was safe, and even though its manufacturer eventually won every lawsuit filed against it (at a cost of over $100 million in direct litigation expenses), Bendectin remains off the market in the United Staes. As a result, "American patients tended to lose, on average, more weight during their NVP, were hospitalized more often than their Canadian counterparts [who can get prescriptions for the generic equivalent of Bendectin] despite similar distribution of the severity of symptoms, and lost more time from paid work"…"Phantom risk" litigation over products such as Bendectin and breast implants also inhibits innovation. Unjustified litigation claiming that products such as Bendectin, spermicides, and birth control pills caused birth defects spurred a decline in contraceptive research. Likewise, unjustified lawsuits against vaccines led to a decline in vaccine research.
>
> The economic costs to the companies involved in toxic tort litigation can also be enormous. Dow Corning, a leading breast implant manufacturer and Fortune 500 company, was forced into bankruptcy. Dozens of asbestos defendants have been forced into bankruptcy, and their remaining assets have been dissipated, plaintiffs have gone after thousands of solvent defendants with ever-more tenuous or marginal ties to asbestos, resulting in insurance chaos, financial uncertainty, and the loss of jobs.[131] [Footnotes omitted.]

Clearly, it is vital for courts to scrutinise scientific evidence in order to avoid the dire social, scientific and economic ramifications of admitting 'junk science'. The importance of such scrutiny is further underlined in chapters 5 to 7, and chapter 8 proposes a Reference Guide to assist legal professionals/litigants/courts in discerning the value of different types of genetic evidence.

2.2 Bayes' Theorem

Bayes' theorem has been proposed as a potential means of overcoming the inadequacies of epidemiological studies, by providing evidence of specific causation.[132] In particular, 'A "statistical chance" could be refined and personalised into a "personal chance" using Bayes' Theorem, which can modify evaluations of probability based on initial assumptions in the light of more data'.[133] This theorem seeks to enable the translation of a statistical probability into 'a

[131] Bernstein (n 125) 73-4. These issues are also reflected in the more recent mass torts, including the Bayer Monsanto Roundup Litigation, and the Johnson & Johnson Talcum Powder Litigation, see, eg, Tom Hals, 'Bayer to rethink Roundup in U.S. residential market after judge nixes $2 bln settlement' *Reuters* (online), 28 May 2021 <https://www.reuters.com/business/healthcare-pharmaceuticals/us-judge-rejects-bayers-2-bln-deal-resolve-future-roundup-lawsuits-2021-05-26/>; Mike Spector and Dan Levine, 'Special Report: Inside J&J's secret plan to cap litigation payouts to cancer victims' *Reuters* (online), 5 February 2022 <https://www.reuters.com/business/healthcare-pharmaceuticals/inside-jjs-secret-plan-cap-litigation-payouts-cancer-victims-2022-02-04/>.

[132] Richard Goldberg, *Causation and Risk in the Law of Torts: Scientific Evidence and Medicinal Product Liability* (Hart Publishing, 1999) 42; Richard Goldberg, 'Using scientific evidence to resolve causation problems in product liability' in Richard Goldberg, *Perspectives on Causation* (Hart Publishing, 2011) 163.

[133] Goldberg, 'Using scientific evidence to resolve causation problems in product liability' (n 132) 162.

probability statement that describes the probative force of that statistic'.[134] In short, Bayes' theorem can be used to predict the probability of an event's occurrence, based on prior knowledge of other probabilities. It does so by 'rigorously evaluating and combining related evidence…utilizing subjective probabilities [to measure] an individual's personal judgment about how likely a particular event is to occur or has occurred'.[135] Bayesian statistics therefore focuses on the probability of a hypothesis, where the hypothesis is treated as random (potentially true or not true but falling within a probability of 0 to 1) and is based on data which is treated as fixed (i.e. the presumption is that this data is the only relevant data that exists).

Bayes' theorem effectively compares 'the perceived probability before and after observing evidence'.[136] The calculation is as follows:

$$P(A/B) = \frac{P(A) \times P(B/A)}{P(B)}$$

A, B = Events

P(A), P(B) = Independent probabilities of A and B

P(A/B) = The Conditional Probability (the probability that A will occur if B is known certainly to have occurred, i.e. Posterior probability of A, after accounting for evidence B)

P(B/A) = probability of B given A is true

Ideally, this theorem could be used to translate general epidemiological studies into a probability of causation that is unique to the plaintiff.[137] For instance, the theorem could be used to translate generalised RR, obtained in epidemiological studies, into an individual probability that is personal to the plaintiff.[138] This individual probability would be calculated by relying on specific data that is unique to the plaintiff, including known risk factors such as the plaintiff's age, gender, genetic predispositions, lifestyle, socio-economic status, residential environment etc.[139] In effect, the personalised RR would be calculated by multiplying the original RR by all these additional, specific and statistically independent, factors.[140]

[134] See, Michael Finkelstein and William Fairley, 'A Bayesian Approach to Identification Evidence'(1969) 83(3) *Harvard Law Review* 489, 498. See also Haack (n 53) 73.
[135] Kevin Clermont, 'Death of Paradox: The Killer Logic beneath the Standards of Proof' 88(3) *Notre Dame Law Review* 1061, 1074.
[136] Ibid 1075. See also Jonathan Beach, 'Causation: The Interface Between the Scientific and Legal Methods' (2022) 49(1) *University of Western Australia Law Review* 113, 134.
[137] Goldberg, 'Using scientific evidence to resolve causation problems in product liability' (n 132) 163.
[138] Ibid.
[139] Ibid.
[140] Ibid.

However, as Haack notes, 'no theorem of the probability calculus could possibly perform such a miracle of "translation"'.[141] Moreover, Professor Kevin Clermont observes that Bayes' theorem has been subject to centuries of controversy such that 'even mathematicians cannot agree on how a fact-finder should perform the task of processing evidence, and so cannot unanimously guide the law on an ideal path to take'.[142] Turton explains that the theorem's 'practical significance is limited by it being premised on the assumption that the risk factors are independent rather than synergistic'.[143] This means that the theorem is largely redundant in toxic torts where 'many cases do involve synergistic interaction'.[144] Moreover, as Clermont highlights, 'Bayes' theorem leaves no place for indeterminacy, thus painting the world as black and white even though most of the world appears in shades of gray'.[145] In particular, the theorem does not provide for situations where there is 'conflicting or scarce information'.[146]

Bayesian statistics are also limited by their inherent subjectivity, as the fact-finder determines which factors are worthy of inclusion in the calculation and which factors should be excluded. Some of these factors (such as socio-economic status or lifestyle factors) are also not strictly quantitative and require interpretation by the fact-finder. In addition, Turton highlights that 'the end-product of this technique is still a statistic…so it espouses and lends itself to a quantitative interpretation of the balance of probabilities standard'.[147] In other words, 'Using Bayes' theorem encourages us to express every piece of information as a statistic to feed into the equation, but ultimately leaves us with a statistic'.[148] This means that Bayes' theorem effectively perpetuates the issues of merging fact and belief probability in toxic torts. Ultimately, Bayes' theorem is simply 'not realistic [because] It does not conform to the way intuitive humans arrive at prior probabilities or the way they combine them with new evidence to produce posterior probabilities'.[149] While the theorem can provide helpful information in some scientific contexts, it is of little relevance to the legal context of determining causation.[150]

[141] Haack (n 53) 73. See also, Turton (n 45) 119.
[142] Clermont (n 135) 1074.
[143] Turton (n 45) 119. See also Goldberg, *Causation and Risk in the Law of Torts* (n 132) 42.
[144] Ibid.
[145] Clermont (n 135) 1075.
[146] Ibid. See also Beach (n 136) 134; Lea Brilmayer and Lewis Kornhauser, 'Review: Quantitative Methods and Legal Decisions' (1978) 46 *The University of Chicago Law Review* 116, 135–48.
[147] Turton (n 45) 120.
[148] Ibid.
[149] Clermont (n 135) 1075.
[150] Beach (n 136)134-5.

2.3 Conclusion

This chapter has analysed the judicial treatment of epidemiological evidence in toxic torts. Part 2.1 highlighted the advantages and limitations of epidemiological evidence, particularly its inability to prove specific causation in toxic torts. Part 2.2 emphasised the significant inadequacies of Bayes' Theorem in toxic torts. There is clearly a plethora of misconceptions surrounding legal and scientific standards of proof. These misunderstandings, coupled with a lack of particularistic evidence and subsequent reliance on generalised epidemiological studies, has resulted in the merging of factual statistical probabilities and belief probabilities in toxic torts. Collectively, these issues serve to underline the urgent need to ensure statistical evidence does not replace the fundamental legal inquiry in toxic torts.

This chapter explained that epidemiological evidence seems to be the dominant method of proof of causation in toxic torts but it has limitations and is accompanied by an erroneous merging of fact and belief probabilities. The following chapter will build on this argument, by investigating the complicated judicial treatment of toxicological studies in toxic torts. The remainder of the thesis will highlight that, similar to epidemiological and toxicological evidence, genetic evidence should not be treated as determinative of causation but should simply be treated as 'one piece of evidence among'.[151] As chapters 4 to 7 will reveal, genetic evidence is increasingly being used in an attempt to personalise the more 'traditional' medical and scientific data so it has an important role to play. However, genetic evidence needs similarly close analysis of its role in proof of causation in order to avoid misuse of this evidence.

[151] Haack (n 53) 72.

3. Chapter Three: The Extrapolation Dilemma: Toxicological Evidence and Toxic Torts

The previous chapter highlighted the benefits and drawbacks of epidemiological studies as a method of proof of causation. This chapter examines the complicated judicial treatment of toxicological evidence to support or refute causation in Australian and US toxic tort litigation. Courts have typically been reticent to accept such evidence due to the difficulty of generalising results obtained from the artificial setting of animals and tissues in laboratories. Issues with extrapolation have therefore limited the utility of toxicological evidence as a method of proving the causal relationship between chemical exposure and development of disease in humans.

Part 3.1 will define the scientific discipline of toxicology. Part 3.2 will subsequently analyse the benefits and limitations of its role in toxic tort proceedings. Part 3.3 will discuss the importance of differential aetiology in examining toxic tort causation evidence. This chapter maintains that toxicological evidence can provide probative proof of causation but it also has limitations that could be addressed/complemented by other evidence, such as epidemiological evidence, genetic evidence, and testimony as to differential aetiology.[1] The following chapters will reveal that, like toxicological and epidemiological studies, genetic evidence also has notable limitations, but can nevertheless provide probative evidence of causation or alternative causation, especially when viewed in light of the other evidence.

3.1. Science of Toxicology

Toxicology refers to 'the study of the adverse systemic effects of chemicals'.[2] Toxicologists operate on the assumption that virtually all substances have the capacity to be toxic.[3] The toxicity of a substance is determined by the 'dose' received.[4] This concept is reflected in the oldest maxim in toxicology: 'the dose makes the poison'.[5] In particular, the toxicity of a

[1] For more information on the role of genetic evidence in toxic tort litigation, see Chapters 4-7 of this thesis. For more information on the role of epidemiology in toxic tort litigation, see Chapter 2 of this thesis.
[2] Patricia Frank and M Alice Ottoboni, *The Dose Makes the Poison: A Plain-Language Guide to Toxicology* (John Wiley & Sons, 3rd ed, 2011) 31, 191.
[3] David Eaton, 'Scientific Judgment and Toxic Torts – A Primer in Toxicology for Judges and Lawyers' (2003) 12(1) *Journal of Law and Policy* 5
[4] William Anderson, Lynn Levitan and Kieran Tuckley, 'The "Any Exposure" Theory Round II: Court Review of Minimal Exposure Expert Testimony in Asbestos and Toxic Tort Litigation Since 2008' (2012) 22(1) *Kansas Journal of Law & Public Policy* 1, 7.
[5] Bernard Goldstein, 'Toxic Torts: The Devil is in the Dose' (2008) 16 (2) *Journal of Law and Policy* 551, 551.

substance depends on whether the amount of that substance entering the body is sufficiently high to exceed the 'threshold dose'.[6]

A key tenet of toxicology is the concept of the 'dose-response' relationship. This describes the 'relationship between the magnitude or severity of the effect(s) and the dose' such that 'once a sufficient dose has been achieved to induce a toxic response, further increases in the dose may produce large increases in the response'.[7] The example of alcohol can be used to illustrate this scientific principle. Ingestion of a small amount of alcohol will merely result in a 'stimulatory' effect on the nervous system but further consumption will lead to greater effects, such as loss of coordination, and 'Continued consumption of alcohol beyond this level of intoxication may result in loss of consciousness and even death'.[8] Although there is inherent human variability in the body's response to the same dose of a chemical, 'the reaction of the population as a whole nevertheless follows a "dose-response relationship" such that the number of people in a population that respond to a chemical exposure increases with dose'.[9] Both acute and chronic exposures follow a dose-relationship[10], but the two kinds of exposure may produce very different results.[11] Some adverse effects are less likely to result from acute exposures.[12]

Experts on toxicology could be drawn from a number of 'sub-disciplines' within the field of toxicology.[13] For example, toxicologists might work in the pharmaceutical industry to conduct studies on products in order for these products to be registered and sold.[14] Alternatively, toxicologists might work in the chemical industry on issues surrounding occupational exposures or they might work in forensics to diagnose cases of suspected poisoning.[15] Toxicologists employ a wide variety of experimental techniques, depending on their area of specialisation, but toxicological evidence in toxic torts typically includes both *in vivo* ('in the animal') and *in vitro* ('in the test tube') research.[16] *In vivo* studies expose laboratory animals

[6] Ibid; 'Threshold dose' is also known as 'No observable effect level' or 'NOEL', see Federal Judicial Center and National Research Council, *Reference Manual on Scientific Evidence* (National Academy of Sciences, 3rd ed, 2011) ('*Reference Manual, 3rd ed*) 669-70.
[7] Eaton (n 3) 15. Steve C Gold, Michael D Green and Joseph Sanders, *Scientific Evidence of Factual Causation: An Educational Module* (The National Academics of Science, Module, October 2016) 110.
[8] Eaton (n 3).
[9] Ibid.
[10] This is not to say that a disease/condition is 'divisible' in the sense of being dose-related in severity.
[11] Gold et al, *Scientific Evidence of Factual Causation: An Educational Module* (n 7) 109.
[12] Ibid.
[13] Eaton (n 3) 9.
[14] Frank and Ottoboni (n 2) 44.
[15] Ibid.
[16] *Reference Manual, 3rd ed* (n 6) 640. The reliability of an *in vitro* test depends on 3 key criteria, see ibid 646.

to chemicals and *in vitro* studies use cells or tissues.[17] Both studies monitor the outcomes of exposure, such as cellular abnormalities, tumour formation or tissue damage, and compare these outcomes with those for unexposed control groups.[18]

The controllability of this laboratory-based testing is a primary advantage, as it allows for the collection of accurate data, such as exposure data.[19] In other words, researchers conducting animal and cell studies are able to 'isolate the effects of exposure to a single chemical or to known mixtures' and as a consequence 'toxicological findings offer unique information concerning dose–response relationships, mechanisms of action, specificity of response, and other information relevant to the assessment of causation'.[20] Another significant benefit of these controlled toxicological studies is that they can be completed over generations, with varying doses of exposure and 'following various periods of exposure'.[21] Toxicological studies arguably achieve the 'gold standard' of scientific evidence to the extent that the studies are randomised, controlled, and double-masked.[22] These studies are also simpler and cheaper than epidemiological studies.[23]

Despite its advantages, the utility of toxicological studies is significantly impeded by the difficulty of extrapolating the results of animal/cell studies to human populations. In brief, 'Humans are not rats, and it is far from clear how readily one may generalize from one mammalian species to another'.[24] For example, thalidomide is an anti-nausea drug that was later found to be a teratogen in humans.[25] The drug did not produce any malformations in the rats that were the subject of initial *in vivo* testing, but the drug did produce malformations in humans.[26] Even where a substance is found to cause toxicity in animals, the dose at which the substance causes this effect 'is modified by many internal factors, and the exact dose-response curve may be different from that for humans'.[27] Similarly, *in vitro* studies 'cannot account fully

[17] Frank and Ottoboni (n 2) 44.
[18] *Reference Manual, 3rd ed* (n 6) 639. See also Joseph Sanders et al, 'Differential Etiology: Inferring Specific Causation in the Law from Group Data in Science' (2021) 63(4) *Arizona Law Review* 851, 875 where the authors explain the process involved in *in vitro* studies.
[19] Jean Macchiaroli Eggen, *Toxic Torts in a Nutshell* (Thomson Reuters, 4th ed, 2010) 303-4; Sanders et al (n 18) 876; Jonathan Beach, 'Causation: The Interface Between the Scientific and Legal Methods' (2022) 49(1) *University of Western Australia Law Review* 113, 144.
[20] *Reference Manual, 3rd ed* (n 6) 658.
[21] Eaton (n 3) 17.
[22] Beach (n 19) 144; *Reference Manual, 3rd ed* (n 6) 658.
[23] Sanders et al (n 18) 875.
[24] *International Union, United Automobile, Aerospace and Agricultural Implement Workers of America, UAW v. Pendergrass*, 878 F.2d 389, 394 (D.C. Cir. 1989). See also Sanders et al (n 18) 874.
[25] Sanders et al (n 18) 876.
[26] Ibid 876-877.
[27] *Reference Manual, 3rd ed* (n 6) 646; Beach (n 19) 145; See also Sanders et al (n 18) 873.

for the environment in which events occur within the organism' such that 'effectiveness *in vitro* [can often fail] to translate into effectiveness in living animals'.[28] This creates doubts as to whether animal and cell experiments can accurately predict human responses to chemical exposures.[29]

However, even though extrapolation from non-mammalian species to humans is 'much more difficult', it 'can be done if there is sufficient information on similarities in absorption, distribution, metabolism and excretion'.[30] This information is becoming more readily available as a result of advances in computational toxicology.[31] As it is often unethical for researchers to intentionally expose humans to agents that are suspected to be harmful, 'toxicological evidence often provides the best scientific information about the risk of disease from a chemical exposure'.[32] The most persuasive combination of studies involves *in vivo* and *in vitro* data combined with additional toxicological information or positive human epidemiological data.[33]

3.2. Toxicological Evidence in Toxic Torts

It is important to briefly note that the following section of the chapter will primarily focus on the American case law and literature because, to the best of the author's knowledge, there is

[28] Sanders et al (n 18) 875.
[29] See, eg, Goldstein (n 5); Eggen (n 19) 304. See also Sanders et al (n 18) 873.
[30] *Reference Manual, 3rd ed* (n 6) 646-7. These are the four basic processes involved in toxicokenetics. See also Sanders et al (n 18) 875-6.
[31] *Reference Manual, 3rd ed* (n 6) 647, see in particular , 647 n 37.
[32] Ibid 639; see also United States Congress, Office of Technology Assessment, *Reproductive Health Hazards in the Workplace* (1985) 8.
[33] See *Reference Manual, 3rd ed* (n 6) s I.F.

minimal Australian literature on toxicological evidence in torts.[34] Australian case law discussing the admissibility and sufficiency of toxicological evidence in torts is also sparse.[35]

Toxicological evidence was 'extremely rare' in appellate civil litigation prior to the 1940s but, in contrast to Australia, 'toxicology has become an integral component of [American] civil litigation'.[36] Toxicologists have offered general evidence that supports or refutes causation in a variety of American toxic tort claims.[37] Although the following section will primarily refer to American case law and literature, the issues relate to the science of toxicology and subsequently are relevant to any jurisdiction that relies on toxicological evidence to prove causation, including Australia.

In forming their opinion on causation, toxicologists analyse three key issues:

1. Whether the disease can be related to chemical exposure by a biologically plausible theory;

[34] The literature on toxicology and expert evidence was almost exclusively focused on four areas:
(1) forensic toxicology in criminal contexts;
(2) toxicology in environmental, drug and food regulations;
(3) toxicology in product liability claims; and,
(4) toxicology in drug patenting.
For articles relevant to toxicological studies in torts, see, eg, John Childs, 'Toxicogenomics: A New Chapter in Proving Causation and Exposure in Toxic Tort Litigation' (2002) 13(1) *Australian Product Liability Reporter* 1; Judy Ford, 'A Potent Mix: Cautionary Tales of Chemical Mixtures' (2005) 69 *Precedent* 27; J Oosthuizen and M Cross, 'Establishing Cause, What Does that Mean from an Epidemiological and Legal Perspective?' (2018) 35(4) *Environmental and Planning Law Journal* 426; Gary Edmond and David Mercer, 'The Secret Life of (Mass) Torts: The "Bendectin Litigation" and the Construction of Law-Science Knowledges'(1997) 20(3) *UNSW Law Journal* 666; Paolo Ricci and Natalie Gray, 'Toxic Torts and Causation: Towards an Equitable Solution in Australian Law – Part I: Legal Reasoning with Uncertainty' (1998) 21(3) *University of New South Wales Law Journal* 787; Edward Christie, 'Toxic Tort Disputes: Proof of Causation and the Courts' (1992) 9(5) *Environmental and Planning Law Journal* 302; Randall Kune and Gabriel Kune, 'Proof of Cancer Causation and Expert Evidence: Bringing Science to the Law and the Law to Science' (2003) 11(1) *Journal of Law and Medicine* 112. The latter two articles contain a more substantive discussion of toxicological studies in torts. These two articles will be interwoven throughout the following discussion of toxicological evidence.

[35] Many of the cases were irrelevant because they related to torts such as defamation, passing off, malicious prosecution, negligent misrepresentation, road accidents, slip and fall etc. At least 16 cases were identified as involving toxicological evidence adduced in toxic torts, see, eg, *Amaba Pty Ltd v Booth; Amaca Pty Ltd v Booth* [2010] NSWCA 344 ('*Amaba*'); *BHP Billiton Ltd v Hamilton & Anor* (2013) 117 SASR 329; *Lo Presti v Ford Motor Co of Australia Ltd* [No 2] [2008] WASC 12 ('*Lo Presti*'); *Lowes v Amaca Pty Ltd* [2011] WASC 287 ('*Lowes*'); *Gill v Ethicon Sarl (No 5)* [2019] FCA 1905; *Peterson v Merck Sharpe & Dohme (Australia) Pty Ltd Ltd* (2010) 184 FCR 1 ('*Peterson*'); *Hamilton v BHP Billiton Ltd* [2012] SADC 25 ('*Hamilton*'); *Larsen v Grace Worldwide (Aust) Pty Limited (No 2)* [2015] NSWSC 1224; *Ellis v The State of South Australia* [2006] WASC 270 ('*Ellis*'); *Parker v BHP Billiton Ltd* [2011] SADC 104; *Koljibabic v BHP Billiton Nickel West Pty Ltd* [2008] WADC 165 ('*Koljibabic*'); *Forbes v Selleys Pty Ltd* [2002] NSWSC 547; *Forbes v Selleys Pty Ltd* [2004] NSWCA 149; *Van Soest v BHP Billiton Ltd* [2013] SADC 81; *John William Suthern v Unilever Australia Ltd* [2007] ACTSC 81; *Julia Farr Services Inc v Hayes* [2003] NSWCA 37 ('*Julia Farr*'). However, only 8 cases were identified by the author as raising substantive issues relating to causation in toxic torts: *Amaba* (n 35); *Hamilton* (n 35); *Lo Presti* (n 35); *Lowes* (n 35); *Peterson* (n 35); *Ellis* (n 35); *Koljibabic* (n 35); *Julia Farr* (n 35). These cases will be embedded into the following broader discussion of toxicological evidence.

[36] Gold et al (n 7) 185-6. For two early civil cases involving toxicological evidence, see *Tindall v American Furniture Co* 306 4 SE 2d 894 (NC, 1939) and *Boal v Electric Storage Battery* 98 F 2d 815 (3rd Cir, 1938).

[37] See, eg, *General Electric Co v Joiner* 522 US 136 (1997); *Daubert v Merrell Dow Pharmaceuticals Inc*, 509 US 579 (1993); *Bonner v ISP Techs Inc*, 259 F 3d 924, 928-31 (8th Cir, 2001).

2. Whether the plaintiff was exposed to the chemical in a manner that can lead to absorption into the body; and,
3. Whether the dose to which the plaintiff was exposed is sufficient to cause the disease.[38]

However, the aims of toxicology and tort law are far from compatible. Toxic tort cases seek to determine the cause of a particular individual's harm. Conversely, toxicological studies typically seek to determine the adverse impacts of a substance on general human populations or the environment.[39] As a result, toxicological studies alone are rarely sufficient to provide direct evidence of specific[40] causation.[41]

Toxicological evidence is further complicated by three key factors. First, the effect, or toxicity, of a chemical varies as it travels through the body.[42] This means that issues of 'absorption, distribution, metabolism and excretion are central to understanding the toxicology of an agent'.[43] Second, these 'central' issues are all genetically determined such that human sensitivity to a toxic substance can greatly differ among individuals.[44] Third, extrapolation is usually required not only across species but also across doses.[45] In short, it is difficult to extrapolate from animal data to humans and from high doses to low doses. For example, 'proffered toxicological expert opinion on potentially cancer-causing chemicals almost always is based on a review of research studies that extrapolate from animal experiments involving doses significantly higher than that to which humans are exposed'.[46] These extrapolation issues are crucial because expert testimony can be excluded where the expert fails to relate the toxicological study to the plaintiff's case. Toxicologists testifying about toxic tort causation can attempt to overcome issues with extrapolation by relying on 'additional background information' including the plaintiff's medical history.[47] Therefore, despite the complexity of extrapolation, toxicologists can provide probative evidence of causation. Ultimately, toxicological evidence should be considered alongside all other evidence in a case, including

[38] *Reference Manual, 3rd ed* (n 6) 661.
[39] Ibid 635, 637.
[40] For an explanation of specific and general causation, see, eg, Chapter 1.3.
[41] *Reference Manual, 3rd ed* (n 6) 637, n 8 notes that 'There are exceptions, for example, when measurements of levels in the blood or other body constituents of the potentially offending agent are at a high enough level to be consistent with reasonably specific health impacts, such as in carbon monoxide poisoning'.
[42] Ibid 668.
[43] Ibid 636.
[44] Ibid. For more on the role of genetic evidence in toxic torts, see Chapters 4-7.
[45] *Reference Manual, 3rd ed* (n 6) 636, 646.
[46] Ibid 645. See also Robert C James, 'Role of Toxicology in Toxic Tort Litigation: Establishing Causation' (1994) 61(1) *Defense Counsel Journal* 28, 30.
[47] *Reference Manual, 3rd ed* (n 6) 645; For a general outline of statistical analyses that assist with extrapolation from animal data to human exposure, see Shayne C Gad, *Statistics and Experimental Design for Toxicologists and Pharmacologists* (CRC Press, 4th ed, 2005).

personal and familial medical history, lifestyle factors, any available epidemiological/genetic evidence, and testimony as to differential aetiology.

3.2.1. Advantages of Toxicological Evidence

Toxicological studies are useful in a number of toxic tort cases. Such studies can contribute to 'the weight of evidence supporting causal inferences by explaining how a chemical causes a specific disease through describing metabolic, cellular, and other physiological effects of exposure'.[48] They can also reveal 'the increased risk of contracting a disease at any given dose and help rule out other risk factors for the disease'.[49]

Professor Bernard Goldstein strongly criticises courts that 'inappropriately exclude' toxicological evidence.[50] He highlights the 'reductionist and overly simplistic approach' of some courts that exclude 'animal toxicology and mechanistic information of pertinent value in evaluating a toxic tort'.[51] He elaborates that 'the American judicial system appears to be responding to the increasing breadth and complexity of environmental health science by searching for simple uni-dimensional solutions for toxic tort issues which increasingly exclude modern scientific reasoning'.[52] He concludes that 'Unfortunately, as judges attempt to simplify complex issues related to causality, there are too many instances in which relatively simple and straightforward scientific understanding concerning dose is being discarded or obfuscated'.[53] The crux of Goldstein's criticism is that 'this attempt at simplification does not excuse the almost total disregard of the scientific discipline of toxicology' because 'The failure to consider toxicology does a disservice to defendants as well as plaintiffs'.[54]

Although some American courts have adopted a largely dismissive[55] approach to toxicology, other courts have accepted toxicological evidence. As Supreme Court Justice Stephen Breyer observed, 'A judge is not a scientist and a courtroom is not a scientific laboratory,' but judges 'must aim for decisions that, roughly speaking, approximately reflect the scientific state of the

[48] *Reference Manual, 3rd ed* (n 6) 637.
[49] Ibid.
[50] Goldstein (n 5) 553.
[51] Ibid.
[52] Ibid 568.
[53] Ibid 587.
[54] Ibid 571, 580. See also Carl Cranor, *Toxic Torts: Science, Law, and the Possibility of Justice* (Cambridge University Press, 2006) 248-255.
[55] See, eg, *Joiner* (n 37); *Re "Agent Orange" Product Liability Litigation*, 611 F Supp 1223, 1241 (EDNY, 1985); *Parker v Mobil Oil Corp* 793 NYS 2d 434 (NY App Div, 2005), *aff'd* NE 2d 1114 9 (NY, 2006), *reargument denied*, 861 NE 2d 104 (NY, 2007). See also Goldstein (n 5) 559, 577.

art'.[56] This 'scientific state of the art' was arguably reflected in *Ruff v Ensign-Bickford Industries, Inc.* because, even where there was a contradictory epidemiological study, the District Court of Utah admitted multiple *in vivo* studies showing that exposure to the same substance to which the plaintiffs were exposed caused the same harm from which the plaintiffs suffered.[57] Similarly in *Re Heparin Products Liability Litigation,* the District Court for the Northern District of Ohio observed that:

> Defendants point to two epidemiological studies, neither of which were designed to determine whether there was an association between contaminated heparin and any of the conditions identified in defendants' motion for summary judgment. Absence of proof is not proof of absence, and while these [epidemiological] studies do not provide support for plaintiffs' theories, neither do they contradict them. I will not, therefore, exclude plaintiffs' [non-epidemiological] evidence on these grounds.[58]

Moreover, in the Australian Full Federal Court decision in *Tobacco Institute of Australia Ltd v Australian Federation of Consumer Organisations Inc,* Hill J described the difference between epidemiological and toxicological evidence of cancer causation:

> The former is concerned with the study of the incidence of disease in human populations. Its approach is observational in character. The latter is an experimental discipline concerned with investigating in what form, by what mode of exposure and at what level of dose a substance may induce tumours in animals. Each discipline approaches the investigation of causes of disease from a different perspective. It is not possible to accept one approach as in some way preferable to the other.[59]

Therefore, although some courts have asserted the superiority of epidemiological evidence and subsequently undermined the utility of toxicological evidence[60], others have recognised that this type of evidence also has its obvious advantages.[61] A primary advantage of toxicological evidence is that 'It is much easier, and more economical, to expose an animal to a chemical or to perform in vitro studies than it is to perform epidemiological studies'.[62] Moreover, *in vivo* and *in vitro* studies can be 'rigidly controlled in a way that is not possible in epidemiological studies'.[63]

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[56] The Associated Press, 'Justice Breyer Calls for Experts To Aid Courts in Complex Cases', *The New York Times* (online, 17 February 1998) < https://www.nytimes.com/1998/02/17/us/justice-breyer-calls-for-experts-to-aid-courts-in-complex-cases.html>.
[57] 168 F Supp 2d 1271, 1281 (D Utah, 2001); see also *Sterling v Velsicol Chemical Corporation* 647 F Supp 303, 480-483 (WD Tenn, 1986), where the court noted that 'The use of animals is a valid scientific basis to identify potential human carcinogens and to attempt to quantify such a risk'.
[58] 803 F Supp 2d 712, 729 (ND Ohio, 2011).
[59] (1992) 38 FCR 1, 59–60, quoted in Kune and Kune, (n 34) 117.
[60] For more information, see below Parts 3.2.2-3.2.7.
[61] For more on the advantages and disadvantages of toxicology, see above Part 3.2.
[62] *Reference Manual, 3rd ed* (n 6) 659; see also Goldstein (n 5) 581; Christie (n 34) 204.
[63] Goldstein (n 5) 582; see also Christie (n 34) 204. Eg, 'matching is more readily achieved [in animal studies] because the animals are genetically similar and have identical environmental histories': see *Reference Manual, 3rd ed* (n 6) 658.

Toxicological evidence is particularly useful when there is little or no epidemiological evidence, or the epidemiological evidence has a relative risk of less than 2.0.[64] However, the two scientific disciplines of toxicology and epidemiology ultimately 'complement each other' because:

> In essence, epidemiological findings of an adverse effect in humans represent a failure of toxicology as a preventive science or of regulatory authorities or other responsible parties in controlling exposure to a hazardous chemical or physical agent. A corollary of the tenet that, depending upon dose, all chemical and physical agents are harmful, is that society depends upon toxicological science to discover these harmful effects and on regulators and responsible parties to prevent human exposure to a harmful level or to ensure that the agent is not produced. Epidemiology is a valuable backup approach that functions to detect failures of primary prevention.[65]

This complementary relationship between epidemiology and toxicology has led to the development of the 'Epi-Tox' approach where these disciplines are described as 'complementary methods of detecting whether a chemical causes harm to humans' and can be aligned 'with framing the legal causal inquiry'.[66] As noted by Haack, 'the statistical evidence in a case should be treated as *one piece of evidence among many*'.[67] Haack elaborates that:

> if courts decide *with respect to each expert* whether his testimony should be admitted, in whole or in part, they may fail to recognize that the testimony of several experts might, in some instances, fit together in an explanatory story to give more credibility to a fact in issue than the testimony of any one would do.[68]

In other words, the overall body of evidence may be greater than the sum of its parts. While an individual study might have limitations, when viewed alongside other evidence it can still give valuable evidence of causation so, as Haack argues, we should not be too demanding in respect of each piece of evidence.

In relation to toxicology, litigants/lawyers/courts should be aware of both the benefits and drawbacks of this method of proof of causation in toxic torts. Despite its clear advantages, toxicological evidence is subject to some notable limitations. Expert toxicological testimony has typically been declared inadmissible in American case law when the testimony falls in one or more of the following areas: (a) lack of similarity between species; (b) lack of similarity between substances; (c) lack of similarity between injuries; (d) lack of similarity between

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[64] Goldstein (n 5) 582; see also Sanders et al (n 18) 899.
[65] *Reference Manual, 3rd ed* (n 6) 660.
[66] For more information, see, eg, See Hans-Olov Adami et al, 'Toxicology and Epidemiology: Improving the Science with a Framework for Combining Toxicological and Epidemiological Evidence to Establish Causal Inference' (2011) 122(2) *Toxicological Sciences* 223; For an article advocating the alignment of "Epi-Tox' principles 'with framing the legal causal inquiry', see Oosthuizen and Cross (n 34) 429.
[67] Susan Haack, *Evidence Matters: Science, Proof and Truth in the Law* (Cambridge University Press, 2014) 71-2.
[68] Ibid 43.

doses; (e) reliance on regulatory standards; and, (f) reliance on the no-threshold theory.[69] The following section will analyse each of these limitations and misconceptions. The final section of this chapter will consider how these issues can be addressed by other evidence, including differential aetiology testimony. This chapter ultimately demonstrates that, despite its limitations, toxicological evidence can provide valuable evidence of causation, when viewed alongside the other evidence in a case.

3.2.2. Lack of Similarity Between Species

Generalising from animals to humans is complicated by the notable differences between species. For example, lab animals are often anatomically different to human beings.[70] There are also 'mechanistic differences that can exist in a species response to exposure'.[71] To illustrate, male rats will develop kidney tumours when exposed to 'perchloroethylene, a chlorinated solvent frequently found at hazardous waste sites'.[72] However, 'This response is so specific that it cannot be extrapolated to female rats or mice of either sex' and 'is only possible in the male rat' which begs the question, 'How could one possibly attempt to extrapolate such a response to human beings, a species far more phylogenetically removed from rats than are mice?'[73]

These differences have led some courts to entirely dismiss the relevance of animal studies in toxic torts. In *Brock,* the Court suggested that animal studies have 'very limited usefulness…when confronted with questions of toxicity'.[74] A more extreme position was adopted by Judge Weinstein in the *Agent Orange* litigation where he held that 'The animal studies are not helpful in the instant case because they involve different biological species. They are of so little probative force and are so potentially misleading as to be inadmissible'.[75] Similarly, in *National Bank of Commerce v Dow Chemical Company*, the court held that due to 'the difference in animal species, the methods and routes of administration of the suspect

[69] Differences in susceptibility (due to, eg, genetic, environmental, and toxicokinetic effects) are also relevant.
[70] James (n 46) 30. Eg, 'rodent species also possess an additional structure with no known human correlate - the forestomach', ibid 31.
[71] Ibid 32-33.
[72] Ibid.
[73] Ibid.
[74] *Brock v Merrell Dow Pharmaceuticals* 874 F 2d 307, 313 (5th Cir, 1989).
[75] *Agent Orange* (n 55). Judge Weinstein also observed that 'There is no evidence that plaintiffs were exposed to the far higher concentrations involved in both animal and industrial exposure studies'.

chemical agent, maternal metabolisms and other factors, animal studies, taken alone, are unreliable predictors of causation in humans'.[76]

This position was also reflected in the Commonwealth of Australia Royal Commission into the Use and Effects of Chemical Agents on Australian Personnel in Vietnam.[77] Professor Edward Christie notes that the Commission not only 'ignored relevant research linking cancer in animal studies to chemicals such as 2,4,5-T' but the Final Report also stated that 'animal data…offers a doubtful basis from which to determine retrospectively whether a particular past exposure was sufficient to provide toxic effects in man'.[78] Jessup J in *Peterson v Merck Sharpe* came to a similar conclusion when he held that 'There appears to be no data from studies involving humans…To the extent they might be useful, the animal stidies [sic] are at best equivocal, and…contradictory in situations in which Vioxx itself was used'.[79] Toxicological studies are therefore more likely to be dismissed or excluded where the expert is unable to cite supporting epidemiological studies and evidence that their opinions have been 'generally accepted by the scientific community'.[80]

Despite the complexity of extrapolation, 'there is sufficient information to permit reliable extrapolation in many situations'.[81] Professor Bernard Goldstein explains that there is a 'particularly strong' likeness 'in cellular and organ function… among mammals such that extrapolation of effects from one species to another is accepted by the scientific community as a means of evaluating the toxicity of external agents'.[82] In addition, 'In terms of general causation, the specificity of toxic effects on organs is relatively similar across mammals'. [83]

More recent American decisions have taken the more moderate approach of suggesting that the difficulty of extrapolation in itself is not sufficient to make an animal study inadmissible. In *Metabolife International Inc v Wornick*, the Court of Appeals held that animal studies are not inadmissible as a matter of law merely 'due to the uncertainties in extrapolating from effects

[76] 965 F Supp 1490, 1527 (ED Ark, 1996), *aff'd,* 133 F 3d 1132 (8th Cir, 1998). In vitro animal studies have also been met with scepticism by the courts, see, eg, *Wade-Greaux v Whitehall Laboratories* 874 F Supp 1441, 1456-57 (VI, 1994), *aff'd* 46 F 3d 1120 (3rd Cir, 1994).
[77] J. McCulloch, 'Whistling in the Dark: The Royal Commission into Agent Orange', in Kenneth Maddock and Barry Wright (eds), *War: Australia and Vietnam* (Harper & Row, 1987) 262-280 cited in Christie (n 34) 308.
[78] Commonwealth, Royal Commission into the Use and Effects of Chemical Agents on Australian Personnel in Vietnam, *Final Report* (1985) vol 2, 23 quoted in Christie (n 34) 308.
[79] *Peterson* (n 35) 266 ALR 1, 215 [544].
[80] *Johnson v Arkema Inc*, 685 F 3d 452 (5th Cir, 2012); *Allen v Pennsylvania Engineering Corporation*, 102 F 3d 194, 197 (5th Cir, 1996) ('*Allen*').
[81] Goldstein (n 5) 557; see also Christie (n 34) 307.
[82] Goldstein (n 5) 556.
[83] Ibid.

on mice and rats to humans', and consequently 'the district court erred in rejecting the animal studies proffered by Metabolife merely because of the species gap'.[84] Similarly, the court in *Allen* held that animal studies can be useful so long as they are 'carefully qualified in order to have explanatory potential for human beings'.[85] Toxicologists should therefore review similarities and differences between humans and the animal species being tested in the relevant study, in order to determine the suitability of extrapolating from animal data to the plaintiff's case.[86] In some instances, this extrapolation is particularly burdensome, such as where the plaintiff alleges 'subjective symptoms' that are difficult to assess in animals, such as 'nausea, headache and weakness'.[87] The American Federal Judicial Center's Reference Manual on Scientific Evidence ('Reference Manual') provides a helpful list of questions that can help in extrapolating from animals to humans.[88]

3.2.3. Lack of Similarity Between Substances

In order for toxicological studies to assist in supporting or refuting causation, there must be some similarity between the substance used in the *in vivo* or *in vitro* study and the substance to which the plaintiff was exposed. In *Johnson v Arkema Inc,* the United States Court of Appeals for the Fifth Circuit confirmed that 'in forming a reliable opinion regarding the effects of exposure to a particular chemical, an expert may extrapolate data from studies of similar chemicals' but they must also 'attempt to explain any direct correlation' between the particular chemical that is the subject of litigation and the similar chemicals that are the subject of the study.[89] Therefore, there cannot be 'too great an analytical gap between the data and the opinion proffered'.[90]

Such an analytical gap has occurred in a number of American cases. For example, in *Re Accutane Products Liability*, the plaintiff's expert relied on two rat studies involving 'high doses of vitamin A, not Accutane' but made 'no effort to analogize the effect of high doses of

[84] 264 F 3d 832, 842 (9th Cir, 2001).
[85] *Allen* (n 80) 197.
[86] Ibid; Failure to compare similarities and differences across animals and humans could lead to the exclusion of evidence, see *Re Silicone Gel Breast Implants Products Liability Litigation,* 318 F Supp 2d 879, 891 (CD Cal, 2004); *Fabrizi v Rexall Sundown Inc.* 2004 WL 1202984, 8 (WD Pa, 4 June 2004); *Hall v Baxter Healthcare Corporation* 947 F Supp 1387, 1410 (D Or, 1996).
[87] *Reference Manual, 3rd ed* (n 6) 662; see also Eaton (n 3) 21.
[88] *Reference Manual, 3rd ed* (n 6) 661-664. For a similar list, see also, Eaton (n 3) 38-41.
[89] *Johnson* (n 80).
[90] *Joiner* (n 37).

vitamin A to the effect of Accutane on rats, much less on the human body'.[91] Similarly, in *DeLuca v Merrell Dow Pharmaceuticals Inc*, the court held that toxicological studies revealing drugs with similar chemical structures are associated with birth defects is insufficient to prove that Bendectin is associated with birth defects.[92] Therefore, courts have exhibited a tendency to exclude evidence where the expert relies on data concerning one chemical to determine the carcinogenicity of a different chemical.[93]

3.2.4. Lack of Similarity Between Injuries

There must also be some similarity between the plaintiff's harm and the harm documented in the toxicological study. In *Ruff v Ensign-Bickford Industries Inc*, the District Court of Utah excluded expert testimony that was based on an animal study showing 'that female mice contracted liver cancer when injected with RDX', because the plaintiffs failed to show 'how this correlates with their lymphomas or why it is scientifically valid to extrapolate from the study that liver cancer in female mice are predictive of human lymphomas'.[94] However, the court did admit the same expert's testimony regarding Hydrazine because the animal studies indicated Hydrazine causes Non-Hodgkin's lymphoma in mice, which is the same type of cancer that affected the plaintiffs.[95]

Toxicologists should also consider whether the toxic substance affects the relevant target organ. This is difficult to assess *in vitro* because, for example, 'In a test tube, the radiation from radioactive iodine can affect the genetic material obtained from any cell in the body, but in the intact laboratory animal or human, only the thyroid is at risk'.[96] Therefore, *in vitro* studies are presently limited by 'the frequent inability to relate doses that cause cellular toxicity to doses that cause whole-animal toxicity' but this fact alone should not affect the admissibility of such evidence.[97] Inferences can still be made from *in vitro* and *in vivo* studies so long as the inferences are based on plausible, 'even if inconclusive, scientific data'.[98]

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[91] 511 F Supp 2d 1288, 1294 (MD Fla, 2007), *aff'd, Rand v. Hoffman La Roche Inc.*, 291 Fed App'x 249 (11th Cir, 2008).
[92] 791 F Supp 1042, 1054 (DNJ, 1992), *affd*, 6 F 3d 778 (3rd Cir, 1993).
[93] *Lofgren v Motorola, Inc*, 1998 WL 299925, 15 (Ariz Super Ct, No CV 93-05521, 1 June 1998).
[94] 168 F Supp 2d 1271, 1280 (D Utah, 2001).
[95] Ibid 1281.
[96] *Reference Manual, 3rd ed* (n 6) 663.
[97] Ibid 664.
[98] *Re Ephedra Products Liability Litigation* 393 F Supp 2d 181, 194 (SDNY, 2005); *Kumho Tire Co v Carmichael* 526 US 137, 152 (1999), where the Court required that the expert opinions be formed with 'the same level of intellectual rigor that characterizes the practice of an expert in the relevant field'.

3.2.5. Lack of Similarity Between Doses

There must be some correlation between the dosage and durations of exposure in the *in vivo* and *in vitro* studies and the plaintiff's case.[99] In *General Electric Co v Joiner,* the Supreme Court affirmed the District Court's rejection of an expert's reliance on animal studies where the studies involved vastly different dosage and harm than the plaintiff had experienced.[100] The relevant study involved infant mice who had massive doses of PCBs [Polychlorinated biphenyls] injected directly into their peritonea or stomachs in a highly concentrated form but the plaintiff was exposed to a much smaller dose and PCB concentration than the exposure in the animal studies.[101] The infant mice developed a different type of cancer ('alveologenic adenomas') than that suffered by the plaintiff ('small-cell carcinomas') and 'No study demonstrated that adult mice developed cancer after being exposed to PCBs'.[102] Therefore, the court concluded that 'The studies were so dissimilar to the facts presented in this litigation that it was not an abuse of discretion for the District Court to have rejected the experts' reliance on them'.[103]

Similarly in *Re Rezulin Products Liability Litigation*, the United States District Court for the Southern District of New York suggested that 'In assessing the reliability of an extrapolation from in vitro results to effects in live humans, two crucial considerations are the type of cell on which the in vitro experiment was performed and the dose to which the cells were exposed'.[104] In that case, the plaintiffs were unable to rely on *in vitro* studies to support their claim that Rezulin caused their liver injury because 'In the cited studies, the cells in which Rezulin was found to produce apoptosis were not normal human liver cells. They were either healthy liver cells of rats, cancerous human liver cells, and cancerous or otherwise abnormal cells from other human organs'.[105] Moreover, the cells in the relevant studies were exposed to higher concentrations than 'those to which cells in the liver of a living human are exposed'.[106]

[99] *Johnson* (n 80); Sanders et al (n 18) 877-878.
[100] *Joiner* (n 37) 144–45. For more information on dose rates in animal studies, see, eg, Christie (n 34) 305-6.
[101] Ibid.
[102] Ibid.
[103] Ibid.
[104] 369 F Supp 2d 398, 429 (SDNY, 2005).
[105] Ibid.
[106] Ibid 431-5.

These concerns around dose differences were also highlighted in the Parlodel[107] litigation. In *Soldo v Sandoz Pharmaceuticals Corp*oration, the District Court for the Western District of Pennsylvania emphasised 'that the doses administered to these animals were hundreds and thousands of times higher than would obtain in a woman using Parlodel'.[108] In another Parlodel case, *Dunn v Sandoz Pharmaceuticals Corporation,* the District Court for the Middle District of North Carolina reiterated that 'the high doses customarily used in animal studies make extrapolating the effect on much lower doses in humans very difficult to determine'.[109]

As a result, a number of American courts have rightly held that experts cannot rely on the 'extrapolation down' argument. This argument suggests that 'if high dose exposure is bad for you, then surely low dose exposure (indeed, no matter how low) must still be bad for you'.[110] However, an expert cannot simply extrapolate down from high doses to low doses because this violates the fundamental toxicological principle that 'the poison is in the dose'.[111]

On a practical note, determining dosage exposure of plaintiffs is inherently easier in toxic tort cases involving 'pharmaceutical products or devices', compared to environmental chemicals, because 'the dose of a pharmaceutical agent such as Vioxx or Bendectin is assumed to be that on the drug label, and someone either has or does not have a silicon breast implant or a medical device'.[112] In addition, pharmaceutical agents usually come with a wealth of 'pre-marketing information', including 'a reasonably substantial amount of animal toxicology and human epidemiological data already available before the drug is marketed' but the same 'is not true for a chemical not intended for use as a drug'.[113] This means that 'Exposure is frequently disputed in occupational-disease cases and hazardous-waste cases, while it is less often an issue in pharmaceutical cases'.[114] In the former occupational-disease and hazardous-waste cases,

[107] Parlodel is a drug used to suppress lactation in postpartum women.
[108] 244 F Supp 2d 434, 530 (WD Pa, 2003).
[109] 275 F Supp 2d 672, 683 (MDNC, 2003), quoting Federal Judicial Center, *Reference Manual on Scientific Evidence* (National Academy of Sciences, 2nd ed, 2000) 346.
[110] *Re Toxic Substances Cases*, 2006 WL 2404008, 6–7 (Pa Ct Com P, No AD 03-319, 17 August 2006), quoted in David Bernstein, 'Getting to Causation in Toxic Tort Cases' (2008) 74(1) *Brooklyn Law Review* 51, 68.
[111] Ibid; see also, Sanders et al (n 18) 878. For more information on this fundamental principle, see Part 3.1 of this thesis.
[112] Goldstein (n 5) 562.
[113] Ibid.
[114] American Law Institute, *Restatement of the Law Third, Torts, Liability for Physical and Emotional Harm* (2010) 405.

dosage is typically difficult to ascertain, and it is important to 'understand the bioavailability of the substance and attributes such as the age of the exposed individual'.[115]

3.2.6. Regulatory vs Private Law

These issues are further complicated by the fact that toxicological studies are also commonly relied on as a basis for regulating chemicals. As toxicology can predict the adverse effects of toxic substances on human populations and environments, it often provides the foundation for 'government regulations concerning a chemical or class of chemicals'.[116] As a result, toxicological evidence is typically adduced in litigation challenging these regulations.[117] However, personal injury litigants should be careful to avoid generalisations from regulatory standards because 'Regulatory standards are set for purposes far different than determining the preponderance of evidence in a toxic tort case'.[118] For example, 'an agency charged with health or safety might well ban a non-essential substance…simply because it is "better to be safe than sorry"'.[119] Therefore, a regulatory agency's 'threshold of proof is reasonably lower than that appropriate in tort law'.[120] In particular, 'there is a great deal of variability in the extent of evidence required to support different regulations' depending upon factors such as the law, societal impacts, specific end points of concern, 'costs, politics' and the inclusion of 'protective factors to reasonably ensure that susceptible individuals are not put at risk'.[121] Therefore, 'the mere fact that an individual has been exposed to a level above a standard does not necessarily mean that an adverse effect has occurred'.[122]

For example, risks assessments are used by regulatory authorities to measure the risks of hazardous chemicals and establish guidelines for acceptable levels of exposure.[123] Although these assessments are 'not an exact science', they provide a useful framework for policymaking purposes.[124] However, risk assessments are of limited relevance to determining toxic tort

[115] Sanders et al (n 18) 879.
[116] *Reference Manual, 3rd ed* (n 6) 635. In particular, '…more than 90 percent of the compounds considered to be carcinogens are classified solely on the basis of animal studies': see James (n 46) 30.
[117] *Reference Manual, 3rd ed* (n 6) 638.
[118] Ibid 665.
[119] *Re Ephedra* (n 98) 195.
[120] *Allen* (n 80) quoting *Wright v Willamette Industries, Inc*., 91 F 3d 1105, 1107 (8th Cir, 1996).
[121] *Reference Manual, 3rd ed* (n 6) 666.
[122] Ibid.
[123] Ibid 649. For an explanation of toxicology in risk assessments, see ibid 650-1.
[124] Ibid 649.

causation because 'there are substantial differences in approach'.[125] Robert James highlights the limited circumstances where regulatory standards might be appropriate in toxic torts:

> The regulatory goal – to err well on the side of safety – can be used reasonably to exclude chemical causation when the exposure is so low that estimated risks fall within regulatory guidelines for acceptably small and safe risk levels. It must be stressed that because of the conservative nature of the risk assessment process, however, the converse is not true. It cannot be concluded that an exposure exceeding some regulatory standard necessarily means cancer is likely to be caused. Indeed, regulators have not served the public well if the regulatory level embodies so little a margin for safety that any excursion above this value actually places human beings at a significant risk.[126]

Therefore, regulatory risk assessments are conservative in nature because they are designed to maximise 'the perceived risk and forc[e] it to stay within those bounds considered to be "acceptably safe" or "virtually safe"' but it also means that such standards could only be used 'as a means to rule out causation, rather than as a tool to establish causation'.[127] While conformity with such standards could certainly be used to suggest that there is no breach of duty, the issue of causation becomes more relevant where the substance that complies with regulatory standards is a competing potential cause. In such cases, the mere fact that exposure has occurred within safe regulatory limits is not necessarily sufficient to disprove causation because experts have suggested that individuals could still contract an illness when they are exposed to a substance 'at levels which are well within legislated safety limits'.[128] As succinctly stated by the court in *Parker v Mobil Oil Corporation*, 'standards promulgated by regulatory agencies as protective measures are inadequate to demonstrate legal causation'.[129]

3.2.7. No-Threshold Assumption

Both Australian and American toxic tort plaintiffs have relied on an assumption in toxicology that 'there is no safe threshold with respect to substances that are known carcinogens'.[130] This assumption 'has caused a considerable amount of controversy in lawsuits where a defendant has exposed an individual to minimal amounts of some carcinogen'.[131] The Reference Manual raises the issue of the 'no-threshold model of carcinogenesis', which suggests that

[125] Ibid; Eaton (n 3) 34.
[126] James (n 46) 37.
[127] Ibid 36.
[128] *Koljibabic* (n 35) (Dr Andrew Harper).
[129] 857 NE 2d 1114 (NY, 2006).
[130] Gold et al, *Scientific Evidence of Factual Causation: An Educational Module* (n 36) 150. See also *Hamilton* (n 35) [73] where plaintiff's expert suggested that 'most authorities assumed no level [of exposure to asbestos] was safe'; *Lowes* (n 35) [709] where the plaintiff's expert observed that 'Australian studies of dose response between lung fibre content and mesothelioma risk were consistent with a "no threshold" model'.
[131] Gold et al, *Scientific Evidence of Factual Causation: An Educational Module* (n 36) 123.

> certain genetic mutations, such as those leading to cancer and some inherited disorders, are believed to occur without any threshold. In theory, the cancer-causing mutation to the genetic material of the cell can be produced by any one molecule of certain chemicals. The no-threshold model led to the development of the one-hit theory of cancer risk, in which each molecule of a cancer-causing chemical has some finite possibility of producing the mutation that leads to cancer.[132]

However, this 'no-threshold theory' has been rejected by many American courts as 'merely a hypothesis'.[133] For example, the court in *Cano v Everest Mineral Corporation* observed that 'Several courts have considered and rejected the use of the linear no-threshold model in the litigation context'.[134] Similarly, the court in *Sutera v Perrier Group of America Inc.* held that there 'is no scientific evidence that the linear no-safe threshold analysis is an acceptable scientific technique used by experts in determining causation in an individual instance'.[135] Therefore, American courts have consistently rejected the no-threshold theory as proof of causation.[136] Conversely, Australian courts appear to have been more receptive to the no-threshold theory, especially in the context of asbestos.[137]

The 'no-threshold' theory has also underpinned the assertions of many asbestos plaintiffs who claim that 'any exposure' or 'every exposure' to asbestos caused their asbestosis or mesothelioma.[138] This is particularly problematic because, as Beech J in *Lo Presti v Ford Motor Co of Australia [No 2]* noted, 'it is not enough, in order to make a diagnosis of asbestosis, to identify that there has been some exposure to asbestos, without having any regard to the level or extent of exposure'.[139] American courts applying the 'substantial factor' test of causation have not only questioned whether the different exposure theories match scientific opinion, but they have also been particularly sceptical of how this maps on to the legal test of causation. For example, the District Court for the Eastern District of Louisiana observed that 'Although there may be no known safe level of asbestos exposure, this does not support [the]

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[132] *Reference Manual, 3rd ed* (n 6) 642, 670; see also Eaton (n 3) 18; Goldstein (n 5) 555. For more information on the role of genetic evidence in toxic torts, see Chapters 4-7 of this thesis.
[133] Ibid; *Parker v Mobil Oil Corporation*, 16 AD 3d 648, (NY App Div, 2005), aff'd on other grounds, 857 NE 2d 1114 (NY, 2006). See also *National Bank of Commerce v. Associated Milk Producers, Inc.*, 22 F Supp 2d 942 (ED Ark, 1998), aff'd, 191 F 3d 858 (8th Cir, 1999); *Burleson v Texas Department of Criminal Justice*, 393 F 3d 577 (5th Cir, 2004). The theory has also been rejected by Australian experts testifying in toxic torts, see, eg, *Amaba* (n 35) [50].
[134] 362 F Supp 2d 814, 849 (WD Tex, 2005).
[135] 986 F Supp 655 (D Mass, 1997).
[136] Bernstein (n 110) 67.
[137] See, eg, *Ellis* (n 35) [622] where the court held 'The unequivocal state of the medical and scientific opinion throughout was that there was no safe threshold [to asbestos] and that exposure levels less than those prescribed by the regulations could still lead to serious consequences, for example, mesothelioma'; *Julia Farr* (n 35) where Spigelman CJ agreed with Giles JA and held that decisions of the NSW Court of Appeal 'established the proposition that breach of duty can be made out on the basis that there is no known safe dose of asbestos'.
[138] See, eg, Joseph Sanders, 'The "Every Exposure" Cases and the Beginning of the Asbestos Endgame' (2014) 88 *Tulane Law Review* 1153; Bernstein (n 110) 72.
[139] *Lo Presti* (n 35).

leap to the conclusion that therefore every exposure [the plaintiff] had to asbestos must have been a substantial contributing cause of his mesothelioma'.[140] Plaintiffs cannot simply equate the no-threshold assumption with the legal test of causation in an attempt to 'both sidestep the necessity of quantifying the dose to which plaintiff was exposed by defendant and to neutralize epidemiologic evidence that fails to demonstrate a connection between work in certain occupations and asbestos-related disease'.[141] As a result, like the 'no-threshold' theory, the 'any exposure' theory has been rejected by several American courts.[142]

3.3. Differential Aetiology

Neither epidemiology nor toxicology alone is sufficient to prove specific causation. Differential diagnosis, more aptly described as differential aetiology, is often required to eliminate other known and competing causes of the plaintiff's disease.[143] The process of differential aetiology involves 'ruling in' then 'ruling out' many potential causes, including personal and family medical history, genetic predispositions and susceptibilities and exposure to other known causes by conducting patient examinations and various diagnostic and laboratory tests as well as tissue samples and biopsies.[144]

It should briefly be noted at the outset that the following section will exclusively focus on American literature and case law. To the best of the author's knowledge, Australian literature discussing differential aetiology is non-existent. In fact, the term differential aetiology does not appear to have been adopted in Australian case law or academic literature.[145]

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[140] *Comardelle v Pennsylvania General Insurance Co.,* 76 F Supp 3d 628, 632, 634 (ED La, 2015).
[141] Gold et al, *Scientific Evidence of Factual Causation: An Educational Module* (n 36) 151.
[142] See, eg, *Bartel v John Crane, Inc*, 316 F Supp 2d 603, 610-11 (ND Ohio, 2004), *aff'd sub nom. Lindstrom v. A-C Product Liability Trust*, 424 F 3d 488 (6th Cir, 2005); *Re WR Grace & Co.,* 355 BR 462, 474-78 (Bankr D Del, 2006); *Brooks v Stone Architecture*, PA, 934 So 2d 350, 352-54 (Miss Ct App, 2006); *Georgia-Pacific Corporation v Stephens*, 239 S.W.3d 304, 320-21 (Tex App, 2007); *Butler v Union Carbide Corporation* 712 SE 2d 537, 539-40 (Ga. Ct. App, 2011); *Betz v PneumoAbex LLC* 44 A 3d 27, 55-7 (Pa, 2012); Bernstein (n 110) 59; Sanders (n 138).
[143] *Reference Manual, 3rd ed* (n 6) 617; See, eg, *Re Ephedra* (n 98) 187; *Easum v Miller*, 92 P 3d 794, 802 (Wyo, 2004); *Westberry v Gislaved Gummi AB*, 178 F 3d 257, 262 (4th Cir, 1999); *McCullock v H.B. Fuller Co*., 61 F 3d 1038, 1044 (2nd Cir, 1995) where the court noted that differential diagnosis 'requires listing possible causes, then eliminating all causes but one'. For an extensive list of American courts endorsing the use of differential aetiology, see *Third Restatement* (n 114) § 28 Reporter's Note to Comment (c)(4) 454.
[144] David Faigman et al, *Modern Scientific Evidence: The Law and Science of Expert Testimony* (Thomson West, 2009) § 21:31-21:39 cited in Joseph Sanders, 'Applying Daubert Inconsistently? Proof of Individual Causation in Toxic Tort and Forensic Cases' (2010) 75(4) *Brooklyn Law Review* 1367, 1391.
[145] A search for "differential aetiology", conducted on 26.11.2020, returned zero results in the general search on Westlaw AU, LexisAdvance AU and AGIS Plus Text, except for Austlii which returned one case, *Amaca v Booth*. The only relevant aspect of this HCA transcript is the defendant's complaint that 'there is no differential aetiology' attributable to the products of Amaca and those of Amaba: see Transcript of Proceedings, *Amaca Pty Ltd (Under*

Moreover, Australian literature discussing differential diagnosis exclusively relates to the medical diagnostic technique, rather than the legal interpretation of the term which is used to determine causation.[146] However, there appears to be at least one Australian case adopting the term 'differential diagnosis' in the context of causation in toxic torts. [147]

It should be kept in mind that although the following section predominantly draws from the American literature and case law, the analysis of differential aetiology remains relevant to any jurisdiction that relies on the medical technique of differential diagnosis to establish causation, including Australia.

The American literature and case law have identified three key issues with differential aetiology: (a) the contrast between medical and legal approaches; (b) the difficulty of applying differential aetiology when the causes of a disease are largely unknown; and, (c) the insufficiency of differential aetiology to prove general causation.

3.3.1. Medical vs Legal Approaches: Differential Diagnosis vs Differential Aetiology

There is a substantial discrepancy between the medical profession's understanding of 'differential diagnosis' and the legal profession's interpretation of this term. The medical approach to differential diagnosis involves determining 'the patient's disease rather than its cause'.[148] Differential diagnosis in litigation involves an expert who attempts to determine the

NSW Administered Winding Up) v Booth [2011] HCATrans 276, [865]; Transcript of Proceedings, *Amaca Pty Ltd (Under NSW Administered Winding Up) v Booth* [2011] HCATrans 277, [1470].

[146] A search for "differential diagnosis", conducted on 26.11.2020, returned the following results on Westlaw AU – 'journals' search (26 articles), LexisAdvance AU – 'AU Secondary Materials' search (8 articles), Austlii – 'All Law Journals Databases' search (12 articles) and AGIS Plus Text general search (2 articles). The author was unable to identify any relevant articles, as they all related to the diagnostic technique and had no mention of the legal technique used to establish causation.

[147] *Amaca Pty Ltd v Tullipan* [2014] NSWCA 269 [32] ('It should also be noted that the analysis relevant to competing causes for a known disease may be quite different from that applicable to the differential diagnosis of an unknown disease, where there are only two competing candidates'). A search for "differential diagnosis" AND tort, conducted on 26.11.2020, returned the following results on Westlaw AU – 'cases' search (117 cases), LexisAdvance AU – 'cases' search (85 cases), Austlii – 'All Case Law Databases' search (92 cases). These cases almost exclusively related to the clinical diagnostic technique of differential diagnosis in medical negligence. However, the term was adopted in *Tullipan* (n 147) in the context of determining causation.

[148] *Third Restatement* (n 114) § 28, Reporter's Note to Comment *(c)(4)* 454; see also, Thomas Jayne, 'The Use and Abuse of the Differential Diagnosis to Prove Causation in Toxic Torts' (2010) 60(3) *FDCC Quarterly* 204, 212 where he states that 'the correct medical view is that differential diagnosis identifies diseases, not the agents causing disease'. See also *Creanga v Jardal* 886 A 2d 633, 639 (NJ, 2005) quoting *Clausen v M/V New Carissa* 339 F 3d 1049, 1057 n.4 (9th Cir, 2003); Sanders et al (n 18) 857. Eg, the court in *Zandi v Wyeth a/k/a Wyeth Inc*, 2007 WL 3224242 (Minn Dist Ct, No 27-CV-06-6744, 15 October 2007) noted that physicians do not attempt to determine the cause of breast cancer. As noted in the *Third Restatement,* physicians will only attempt

cause of the plaintiff's illness by 'ruling in' and 'ruling out' potential causes.[149] As a result, 'although courts persist in calling it a differential diagnosis', the technique is more aptly described as 'differential aetiology'.[150] Courts should emphasise that a doctor's 'skill and experience in diagnosing an illness does not always translate to skill and experience in attributing background causation'.[151] However, Professor Joseph Sanders et al highlight that 'There are important exceptions to this general position', such as doctors who search for a genetic cause of an individual's illness.[152]

The difficulty of applying the technique of differential diagnosis in litigation is exacerbated by the fact that clinical medicine is not always scientifically reliable. As Thomas Jayne observes, 'doctors continue to base their clinical decisions on habit, common practice, peer practice, and their prior experiences with patients all of which frequently rely on out-dated studies or sub-optimal treatments in light of the ever-increasing technology'.[153] However, the court of appeals noted in *Heller v Shaw Industries Inc* that this does not necessarily affect the reliability of such evidence because:

> experience with hundreds of patients, discussions with peers, attendance at conferences and seminars, detailed review of a patient's family, personal, and medical histories, and thorough physical examinations are the tools of the trade, and should suffice for the making of a differential diagnosis even in those cases in which peer-reviewed studies do not exist to confirm the diagnosis of the physician.[154]

This position is only acceptable to the extent that it does not contravene the admissibility requirements outlined in *Kumho* and *Joiner.*[155] In any case, the potentially unreliable foundations of clinical medicine and the different legal and medical approaches to differential diagnoses have led to the concern that 'The label "differential diagnosis" should not open the courthouse door to unscientific opinions on causation'.[156] This is particularly important considering the significant problem of unknown causes in toxic torts.

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to determine the cause of the patient's condition 'when the cause may have some continuing effect on the patient's health, as when a rash may be the result of a continuing occupational exposure', see *Third Restatement* (n 114) § 28, Reporter's Note to Comment *(c)(4)*.

[149] *Reference Manual, 3rd ed* (n 6) 617-618.

[150] Anthony G. Hopp, Jeremy S. Goldkind and David M. Cummings, 'Differential Diagnosis and Daubert: Preventing the Misuse of Differential Etiology to Prove Causation in Toxic Tort Cases' (2017) 84(1) *Defense Counsel Journal* 1, 3; Jayne (n 148) 212.

[151] Sanders et al (n 18) 860. See also *Polaino v Bayer Corporation*, 122 F Supp 2d 63, 70 (D Mass, 2000); *Re Breast Implant Litigation*, 11 F Supp 2d 1217, 1230 (D Colo, 1998); *Tamraz v Lincoln Electric Co*, 620 F 3d 665, 673 (6th Cir, 2010) ('*Tamraz*').

[152] Sanders et al (n 18) 859; For more information on genetic evidence and toxic torts, see Chapters 4-7 of this thesis.

[153] Jayne (n 148) 209.

[154] 167 F 3d 146, 155 (3rd Cir, 1999).

[155] See Jayne (n 148) 210.

[156] Ibid 219. It should also be noted that, despite the suggestions of some courts, the vast majority of American states do not require that expert testimony should be held to a 'reasonable degree of medical or scientific

3.3.2. Unknown Unknowns

Differential aetiology depends upon most causes of the disease being known, so this technique 'is of little benefit' for diseases with unknown causes.[157] For example, it has been estimated that the cause of approximately two-thirds of all birth defects[158] and between 70-80% of Acute Myeloid Leukaemia (AML) cases are unknown.[159] This has led some courts to conclude that differential aetiology is 'inherently unreliable'[160] and 'insufficient as the sole basis of an opinion'[161] where unknown causes account for the majority of the cases of the disease at issue.

It is important to note that experts are not required to eliminate all conceivable competing causes in order for their testimony to be admissible.[162] However, the 'more likely than not' standard may not be met if competing causes cannot be ruled out.[163] The arduousness of this task is limited by the fact that a competing cause is only relevant to differential aetiology if there is sufficient evidence that it is, in fact, a cause of the disease.[164]

certainty', see, eg, *Third Restatement* (n 114) § 28, Comment (e), § 28, Reporter's Note to Comment (e). There is also no such requirement under Australian law, although some experts do explain their opinions in these terms, see, eg, *Peterson* (n 35) 297–8 [768] where one of the applicant's experts (Professor Douglas Zipes) stated 'I think we are dealing with statistics and the likelihood of [the applicant] having an infarct is increased by him taking Vioxx, so I think *to a reasonable degree of medical probability* Vioxx played a substantial contributing role' (emphasis added). On the other hand, one of the respondent's experts (Professor David Celermajer) concluded that 'We do not believe *with a reasonable degree of scientific certainty*, that Vioxx played a role in causing [the applicant's] heart attack': at 298–9 [770] (emphasis added).

[157] *Reference Manual, 3rd ed* (n 6) 618; *Third Restatement* (n 114) § 28 Comment *(c)(4)* 409. See also *Perry v Novartis Pharms. Corp*., 564 F Supp 2d 452, 469 (ED Pa, 2008); *Soldo* (n 108).

[158] See, eg, *Third Restatement* (n 114) § 28 Reporter's Notes to Comment *c(4)*.

[159] See, eg, *Milward v Acuity Specialty Products Group Inc*, 969 F Supp 2d 101, 109 (D Mass, 2013), affd sub nom *Milward v Rust-Oleum Corporation*, 820 F 3d 469 (1st Cir, 2016); *Henricksen v ConocoPhillips Co*, 605 F Supp 2d 1142, 1149 (ED Wash, 2009).

[160] *Hall v Conoco Inc*., 886 F 3d 1308, 1315 (10th Cir, 2018) where the court held that 'Because idiopathy accounts for more than half of the cases of [the relevant disease], a differential diagnosis could be considered inherently unreliable here'.

[161] *Johnson & Johnson Talcum Powder Cases*, 249 Cal Rptr 3d 642, 676 (Cal App, 2019) where the court acknowledged that 'a differential diagnosis alone may be insufficient as the sole basis for an opinion on the etiology of a largely idiopathic disease' but 'that is not the situation before us'.

[162] See, eg, *Wendell v GlaxoSmithKline LLC*, 858 F 3d 1227, 1237 (9th Cir, 2017); *Best v Lowe's Home Centers, Inc.*, 563 F 3d 171 (6th Cir, 2009); *Stubbs v City of Rochester*, 134 NE 137, 140 (NY, 1919); *Easum* (n 143); *Reference Manual, 3rd ed* (n 6) 618.

[163] See, eg, *Moore v Ashland Chemical Inc*, 151 F 3d 269, 278 (5th Cir, 1998).

[164] See, eg, *Cooper v Smith & Nephew, Inc*., 259 F3d 194, 202 (4th Cir, 2001); *Ranes v Adams Laboratories In.*, 778 NW 2d 677, 690 (Iowa, 2010); *Reference Manual, 3rd ed* (n 6) 618.

Finally, 'like any scientific methodology', differential aetiology 'can be performed in an unreliable manner'.[165] The Court in *Best v Lowe's Home Centers, Inc*. provided the following 'differential-diagnosis test':

> A medical-causation opinion in the form of a doctor's differential diagnosis is reliable and admissible where the doctor (1) objectively ascertains, to the extent possible, the nature of the patient's injury…, (2) "rules in" one or more causes of the injury using a valid methodology, and (3) engages in "standard diagnostic techniques by which doctors normally rule out alternative causes" to reach a conclusion as to which cause is most likely.[166]

If the doctor does 'engage in very few standard diagnostic techniques by which doctors normally rule out alternative causes', the doctor must offer a 'good explanation as to why his or her conclusion remain[s] reliable'.[167] Moreover, the doctor must provide sufficient explanation as to why any alternative causes raised by the defence are not the sole cause of the plaintiff's harm.[168] However, the utility of the steps provided in *Best* is limited by the absence of any explanation of the third step, i.e. 'standard diagnostic techniques by which doctors normally rule out alternative causes'.[169]As Sanders et al explain, 'courts have made relatively little progress in developing a systematic analytical approach'.[170] Despite the court's intention to formulate a legal 'test', the steps outlined in *Best* cannot possibly be a 'test', because it is no more than a description of how doctors perform a differential diagnosis.[171] The description in *Best* is further limited by a lack of detail regarding who should be testifying as to differential aetiology.

3.3.3. General Causation

Although differential aetiology is often crucial in determining specific causation, it is usually insufficient to establish general causation.[172] Differential aetiology is typically inadmissible without further scientific proof of general causation because the expert must 'rule in' the

[165] See *Reference Manual, 3rd ed* (n 6) 618 where it states 'Numerous courts have concluded that, based on the manner in which a differential diagnosis was conducted, it was unreliable and the expert's testimony based on it is inadmissible'; see, eg, *Glastetter v Novartis Pharmaceuticals Corporation*, 252 F 3d 986, 989 (8th Cir, 2001).
[166] *Best* (n 162); For a critique of *Best*, see Hopp, Goldkind and Cummings (n 150) 14.
[167] Ibid; *Re Paoli RailRoad Yard PCB Litigation*, 35 F 3d 717, 758, 760 (3rd Cir, 1994).
[168] Ibid.
[169] Sanders et al (n 18) 892-3.
[170] Ibid 860.
[171] Ibid 862.
[172] *Third Restatement* (n 114) § 28 Comment *(c)(4)* 409-10 and Reporter's Note to Comment *(c)(4)* 457; see also *Zuchowicz v United States*, 140 F 3d 381 (2nd Cir, 1988); *Westberry v Gislaved Gummi AB*, 178 F 3d 257 (4th Cir, 1999). See also *Third Restatement* (n 114) § 28 Comment *(c)(4)* 409-10 where it provides some exceptions.

suspected cause as well as 'rule out' other potential causes.[173] In other words, a differential aetiology focuses on what did not cause the plaintiff's disease, rather than what did.[174] Professor Joseph Sanders and Julie Machal-Fulks adopted a similar position in their assertion that, 'one cannot make a Sherlock Holmes-like deduction that simply because all other known causes have been eliminated, the only known cause left, no matter how improbable, must be the actual cause'.[175] A Florida Supreme Court Justice provided the following rather extreme example, where a:

> patient suffering from depression sees a doctor because her arm hurts. She does not know why her arm hurts. The doctor diagnoses a broken arm. The patient cannot tell the doctor how she broke her arm. The doctor may, through performing tests and interviewing the patient, conclude that it could not have been a car accident (the patient was not involved in an accident) and it could not have been playing sports (the patient does not play sports), but the doctor cannot then conclude that it must have been the depression that caused the broken arm-unless, of course, the doctor can show that the theory that depression can cause a broken arm is generally accepted in the scientific community.[176]

As a result of this significant potential for injustice, experts are usually required to 'rule in' the suspected cause.[177] This has the result that 'Although differential etiologies are a sound methodology in principle, this approach is only valid if general causation exists and a substantial proportion of competing causes are known'.[178] The most persuasive case therefore requires a combination of evidence, including toxicological, epidemiological and genetic evidence, as well as testimony as to differential aetiology. The limitations of each method of proof can be addressed/complemented by the other methods. For example, toxicological and/or epidemiological evidence can be used to show general causation and differential aetiology testimony can be used to show specific causation.

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[173] See, e.g., *Seaman v Seacor Marine L.L.C*., 326 Fed Appx 721, 726-28 (5th Cir, 2009); *Moore* (n 163) 279-81; *Hall* (n 86) 1413. For cases where differential aetiology testimony was admitted even without sufficient scientific studies demonstrating an association between the relevant substance and disease, see, eg, *Bonner* (n 37) 928-29; *Heller* (n 154) 154, 158.

[174] Bernstein (n 110) 65-6; See also Sanders et al (n 18) 893.

[175] Joseph Sanders and Julie Machal-Fulks, 'The Admissibility of Differential Diagnosis Testimony to Prove Causation in Toxic Tort Cases: The Interplay of Adjective and Substantive Law' (2001) 64(4) *Law and Contemporary Problems* 107, 133-34.

[176] *Marsh v Valyou*, 977 So 2d 543, 565 (Fla, 2007) (Cantero, J., dissenting) quoted in Bernstein (n 110) 65.

[177] See, eg, *Chapman v Procter & Gamble Distributing LLC*, 766 F 3d 1296, 1311 (11th Cir, 2014); *Kilpatrick v Breg Inc*, 613 F 3d 1329, 1343 (11th Cir, 2010); *Tamraz* (n 151) 675; *Re Rezulin Products Liability Litigation*, 2004 WL 2884327, 3 (SD NY, MDL No 1348, 00 Civ 2843 (LAK), 10 December 2004); *Cavallo v Star Enterprise*, 892 F Supp 756, 771 (ED Va, 1995), affd on this issue, revd in part on other grounds, 100 F 3d 1150 (4th Cir, 1996); *Glastetter* (n 165); *Meister v Medical Engeenering Corporation*, 267 F 3d 1123, 1129 (DC Cir, 2001); *Caraker v Sandoz Pharmaceuticals*, 188 F Supp 2d 1026, 1030 (SD Ill, 2001) where the court ruled that when a differential diagnosis is employed 'in the practice of science (as opposed to its use by treating physicians in the practice of medicine out of necessity) it must reliably 'rule in' a potential cause'.

[178] *Reference Manual, 3rd ed* (n 6) 618. It should be kept in mind that a 'rose by another name may smell as sweet − but simply calling an analysis a differential diagnosis doesn't make it so': *Re Lipitor (Atorvastatin Calcium) Marketing, Sales Practices & Products Liability Litigation [No II]* MDL 2502, 892 F 3d 624, 643 (4th Cir, 2018).

3.4. Conclusion

This chapter has analysed the judicial treatment of toxicological evidence in Australian and American toxic tort litigation. Part 3.1 provided a brief introduction to this complex scientific discipline. Part 3.2 examined the advantages and inadequacies of toxicological evidence, particularly its inability to prove specific causation in toxic torts. Part 3.3 assessed how differential aetiology could be used to provide evidence of specific causation and examined the limitations of this technique.

Ultimately, toxicological evidence has been a controversial method of proving causation in toxic tort litigation. Nevertheless, this chapter has argued that such evidence can provide probative proof of the causal relationship between chemical exposure and development of disease. Although this evidence certainly has its weaknesses, it is nevertheless a valuable means of establishing or refuting causation, particularly when viewed in conjunction with all the other evidence, including epidemiological evidence and testimony as to differential aetiology. The following chapter will introduce the role of genetic information as a method of proof of causation in toxic torts. Chapters 4 to 7 will then highlight the limitations and advantages of genetic evidence, concluding that litigants/lawyers/courts should not consider genetic evidence in isolation but should analyse the evidence alongside all the other medical and scientific evidence in the case.

4. Chapter Four: A Brief Introduction to Genetic Evidence

The previous chapters highlighted the advantages and disadvantages of toxicological and epidemiological evidence to support or refute causation in toxic tort litigation. The remainder of the thesis will consider whether genetic evidence is a potential solution to the toxic tort causation problem. This chapter will provide a brief introduction to genetic evidence. Part 4.1 will outline the correlation between genetics and human diseases, including the role of genetic mutations, epigenetics, gene expression and genetic markers. Part 4.2 will introduce the different types of genetic testing and their purposes, with an emphasis on the increasing importance of pharmacogenomics, personalised medicine and toxicogenomics. Part 4.3 will explain the different types of genetic evidence employed in toxic torts.

The following chapters will consider the impact of these health technologies on toxic tort litigation. These chapters will show that genetic information derived from family medical history and/or genetic test results can have a variety of applications and interpretations in toxic tort claims. As a result, the thesis concludes that a Reference Guide is needed to promote a better understanding of how to assess the validity and utility of different types of genetic evidence in order to ensure that courts/litigants/lawyers avoid misusing the evidence.

4.1. Genetics & Disease

4.1.1. Brief History of Genetics

On 26 June 2000, President Bill Clinton announced the completion of the first survey of the entire human genome by declaring, 'Today we are learning the language in which God created life…With this profound new knowledge, humankind is on the verge of gaining immense, new power to heal'.[1] This exuberance was tempered by Prime Minister Tony Blair's notable concern that 'We have to focus on the possibilities, develop them and then face up to the hard ethical and moral questions that are inevitably posed by such an extraordinary scientific discovery'.[2] As Chapter Seven will demonstrate, these ethical and moral questions have been

[1] 'Text of the White House Statements on the Human Genome Project', *The New York Times* (online), 27 June 2000 <https://archive.nytimes.com/www.nytimes.com/library/national/science/062700sci-genome-text.html>.
[2] 'What they said: Genome in quotes', *BBC News* (online), 26 June 2000 <http://news.bbc.co.uk/2/hi/science/nature/807126.stm>.

the subject of significant debate since the completion of the Human Genome Project (1990-2003), the world's largest collaborative biological project.

Commencing in 1990, the international Human Genome Project signified a 13-year quest to uncover the 'blueprint of life' by sequencing the entire human genome and effectively creating a map of the genetic structure of the whole human species.[3] Although the human genome was only sequenced relatively recently[4], the science of genetics has a long history spanning over almost two centuries and is rooted in Charles Darwin's theory of natural selection and Gregor Mendel's principles of inheritance.[5] The modern science of genetics was born in 1953 when James Watson and Francis Crick discovered the double helix structure of DNA, igniting widespread interest in uncovering the components of the human genome and the genetic basis for disease, effectively laying the groundwork for the Human Genome Project.[6] In turn, the Project then paved the way for detection of genetic diseases through the use of diagnostic and predictive genetic testing.

The sheer rapidity of scientific and technological advancements in the field of genetics is truly remarkable, as it was a mere fifty years from the discovery of the DNA double helix in 1953 to the effective mapping of the entirety of the human genome in 2003 and only another decade before the discovery of technologies that allowed researchers to potentially edit the human genome.[7] These technologies gained further international recognition in the award of the 2020 Nobel Prize in Chemistry to Professors Emmanuelle Charpentier and Jennifer Doudna for developing the genome-editing tool, CRISPR-Cas9.[8] As Professor Edwin Kirk recently

[3] International Human Genome Sequencing Consortium, 'Finishing the Euchromatic Sequence of the Human Genome' (2004) 431 *Nature* 931, 931; Craig venter et al, 'The Sequence of the Human Genome' (2001) 291 *Science* 1304.

[4] The Environmental Genome Project commenced in 1998, the first draft of the human genome was sequenced in 2001 and the Human Genome Project was completed in 2003. See, eg, Kimberly Gray, 'NIEH's Environmental Genome Project' (2004) 15(4) *Epidemiology* 139, 139; Francis Collins et al, 'Human Molecular Genetics and Genomics – Important Advances and Exciting Possibilities' (2021) 384 *New England Journal of Medicine* 1, 2.

[5] Siddhartha Mukherjee, *The Gene: An Intimate History* (The Bodley Head, 2016) 46.

[6] Francis Crick and James Watson, 'Molecular Structure of Nucleic Acids; a Structure for Deoxyribose Nucleic Acid' (1953) 171 *Nature* 737.

[7] Ibid; International Human Genome Sequencing Consortium (n ?); Jennifer Doudna and Samuel Sternberg, *A Crack in Creation: Gene Editing and the Unthinkable Power to Control Evolution* (Houghton Mifflin Harcourt, 2017).

[8] Nobel Prize Outreach, *Press release: The Nobel Prize in Chemistry 2020* (7 October 2020) <https://www.nobelprize.org/prizes/chemistry/2020/press-release/>. CRISPR was first used to edit DNA *in vitro* in 2012, see Francis Collins et al, 'Human Molecul9ar Genetics and Genomics – Important Advances and Exciting Possibilities' (2021) 384 *New England Journal of Medicine* 1, 2. CRISPR stands for Clustered Regularly Interspaced Short Palindromic Repeats. It is a form of genome editing allowing scientists to modify the genes of an organism by acting as a pair of genetic scissors to target a genetic sequence of a specific gene or alter the expression of a specific gene. See, eg, Susan Brice and Whitney Christian, 'The Use of Genetic

observed, 'Remarkable things are happening in genetics, a quiet revolution that has already dramatically changed some parts of medicine, and is coming for the rest'.[9]

4.1.2. Meaning of Genetic Information

By way of brief scientific background, the human genome is contained in the nucleus of almost all of the trillions of cells of the human body.[10] The human genome is (typically) comprised of twenty-three chromosome pairs, 3.3 billion DNA base pairs and approximately 20,000-25,000 protein-coding genes.[11] DNA itself is comprised of four nucleic acid bases called Adenine (A), Thymine (T), Cytosine (C) and Guanine (G).[12] In essence, the genome is a set of instructions for the human body, written in the A, T, C, G alphabet of the nucleotides.[13] The order of the A, T, C, G alphabet is what determines the instructions or, in other words, the genetic code.[14] Protein-coding genes effectively act as a blueprint instructing cells on how to make proteins, but these protein-coding genes only account for approximately 1-2 per cent of the human genome.[15] The non-coding regions of DNA are often referred to as 'non-coding DNA' and their precise function is still unclear, but researchers are discovering that some non-coding DNA plays important cellular roles.[16]

The World Health Organisation differentiates between genomics (the study of genomes) and genetics (the study of genes), by observing that

> The main difference between genomics and genetics is that genetics scrutinizes the functioning and composition of the *single* gene whereas genomics addresses *all* genes and their interrelationships in order to identify their combined influence on the growth and development of the organism.[17] [Emphasis added.]

Evidence to Defend Against Toxic Tort Claims - Part III' (2017) 29(11) Intellectual Property & Technology Law Journal 3, 5.

[9] Edwin Kirk, 'The Genes That Make Us: Human Stories from a Revolution in Medicine' (Scribe Publications, 2020) 1-2.

[10] Richard Dawkins, *The Selfish Gene* (Oxford University Press, 2016) 27-8; Kirk (n 9). Every living thing has a genome, including humans, animals, plants and microbes (such as bacteria and fungi), see, eg, Kirk (n 9) 9-10. Viruses also have genomes, see, eg, Kirk (n 9) 10.

[11] Dawkins (n 10) 27-8. The chromosomes are coiled around proteins named histones and this DNA-protein combination is called chromatin, see, eg, Kirk (n 9) 10.

[12] Dawkins (n 10) 27-8.

[13] Ibid.

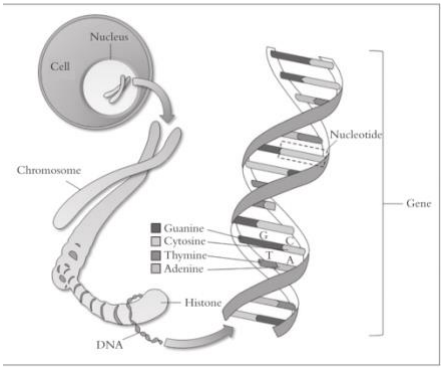
[14] Ibid.

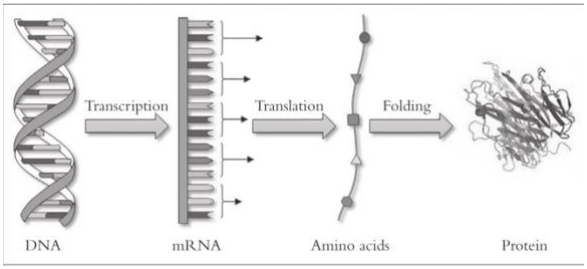
[15] Kirk (n 9) 26.

[16] Benjamin Pierce, *Genetics: A Conceptual Approach* (Macmillan Learning, 7th ed, 2020) 637-8. Although subject to continuing controversy, the Encyclopaedia of DNA Elements (ENCODE) project assigned 'biochemical functions for 80% of the genome, in particular outside of the well-studied protein-coding regions', see, eg, The ENCODE Project Consortium, 'An integrated encyclopaedia of DNA elements in the human genome' (2012) 489 *Nature* 57.

[17] World Health Organization, *WHO definitions of genetics and genomics* <https://www.who.int/genomics/geneticsVSgenomics/en/>.

Essentially, genetics describes the study of *single* genes whereas genomics describes the study of *all* genes in the genome.[18]





Images extracted from Susan Brice and Whitney Christian, 'The Use of Genetic Evidence to Defend Against Toxic Tort Claims - Part I' (2017) 29(9) *Intellectual Property & Technology Law Journal* 3, 5.

4.1.3. Genetic Mutations

Generally speaking, a genetic mutation refers to a change in the DNA sequence or structure.[19] Mutation can occur spontaneously (natural mutation) or on exposure to mutagens, i.e. agents that induce mutation (induced mutation).[20] A mutation could include base substitution (the alteration of a single nucleotide base in the DNA) or deletion, insertion or duplication of a segment of a gene.[21] Potential causes of mutation include, but are by no means limited to, 'spontaneous [occurrence], radiation, ultraviolet rays, x-rays, α-rays, β-rays, temperature, chemical exposure, caffeine [and] formaldehyde'.[22] Somatic mutations only involve somatic cells and are not heritable.[23] Germline mutations involve gametes (sex cells) and are heritable because germline mutations become incorporated into the DNA of every cell in the body of the offspring.[24] Therefore, variations in DNA sequence (also known as the genetic code or genome) primarily arise through inheritance or changes occurring during one's lifetime.

[18] In addition, cytogenetics describes the study of chromosomes, see, eg, Kirk (n 9) 14.
[19] Yogesh Ashok Sontakke, *Principles of Clinical Genetics* (Jaypee Brothers Medical Publishers, 2018) 38.
[20] Ibid 38.
[21] Benjamin Pierce, *Genetics: A Conceptual Approach* (Macmillan Learning, 7th ed, 2020) 528.
[22] Sontakke (n 19) 38.
[23] See, eg, ibid; Pierce (n 21) 527.
[24] See, eg, Sontakke (n 19) 38; Pierce (n 21) 528.

4.1.4. Genetic Susceptibilities & Predispositions

There are a number of common polymorphisms and rare mutations that underlie individual susceptibility to specific phenotypes[25] of disease. For example, approximately 5 to 10 percent of cancers 'have a hereditary or familial component'.[26] There are currently over 50 known forms of hereditary cancer.[27] A relatively well-known example is familial forms of breast cancer associated with mutations in the *BRCA1* and *BRCA2* genes that predispose carriers to early onset breast, and often ovarian, cancer.[28] *BRCA1* and *BRCA2* mutations are often highly penetrant, which means an individual carrying these genes has a relatively high probability (greater than 50 percent) of developing cancer.[29] However, inherited cancer-susceptibility alleles[30] are insufficient in themselves to trigger cancer, as mutations in other genes are usually required to fully express the cancer phenotype.[31]

It is possible to draw a distinction between 'two types of susceptibility genes: those that increase the risk of disease in everyone with that gene…and those that increase the risk of disease only in the presence of a triggering exposure'.[32] In either case, these genes only indicate the *increased likelihood* of developing a particular disease. Susceptibility genes do not indicate that a carrier is certain to develop the disease. Chapter 6 provides a detailed discussion of susceptibility genes.

[25] Phenotype describes an individual's physically observable traits, such as height, eye colour or blood type. Conversely, genotype describes the actual alleles present in an individual, i.e. the genetic contribution to the phenotype, see, eg, Oscar Wambuguh, *Examining the Causal Relationship Between Genes, Epigenetics, and Human Health* (IGI Global, 2019) 116.

[26] William Klug et al, *Concepts of Genetics* (Pearson Education, 11th ed, 2015) 385. Simple Mendelian patterns of inheritance describe the manner by which genes and traits are passed from parents to their offspring but specific diseases with these patterns of inheritance 'tend to be relatively uncommon or frequently rare, with early ages of onset, such as phenylketonuria, sickle cell anemia, Tay-Sachs disease, and cystic fibrosis', see, eg, Committee on Assessing Interactions among Social, Behavioral, and Genetic Factors in Health, *Genes, Behavior, and the Social Environment: Moving Beyond the Nature/Nurture Debate* (The National Academy of Sciences, 2006) 45.

[27] Klug et al (n 26).

[28] Committee on Assessing Interactions among Social, Behavioral, and Genetic Factors in Health (n 26) 45.

[29] Ibid.

[30] An allele is a variant in the DNA sequence at a single gene or locus. In other words, an allele describes 'alternative forms of the same gene responsible for a given trait', see, eg, Wambuguh (n 25) 116.

[31] In particular, 'Usually, at least one other somatic mutation in the other copy of the gene must occur to contribute to tumorigenesis' and typically 'other somatic mutations in proto-oncogenes or tumor-suppressor genes are necessary for the development of hereditary cancers', see, eg, Klug et al (n 26) 385-6. Proto-oncogenes and tumour-suppressor genes are two types of cancer-causing genes.

[32] Andrew Askland and Gary Marchant, 'Genetic Data and Toxic Torts: Intimations of Statistical Reductionism' in Richard Sharp, Gary Marchant and Jamie Grodsky (eds), *Genomics and Environmental Regulation* (The John Hopkins University Press, 2008) 87-8.

4.1.5. Gene Expression & Epigenetics

Gene expression describes the process whereby genes are activated or silenced (turned 'on' or 'off') in different cells, meaning that they do or do not produce functional gene products such as proteins.[33] Cellular gene expression ultimately depends on several factors, namely the

1. internal cell environment (inherited DNA);
2. immediate internal cell environment (neighbouring cells or tissues);
3. integrity of DNA (due to damage from physical and/or age-related factors); and
4. external (outside cell) environment comprised of signals from other parts of the body including chemicals, nutrients, and/or mechanical stress.[34]

This is because 'genes and their products do not act in isolation; rather, they frequently interact with other factors, including environmental factors'.[35]

Epigenetics refers to 'changes in gene expression that are not due to changes in the DNA sequence'.[36] Simply put, '"Epi" means above, and so epigenetics refers to modifications above the genetic code' where changes are made 'to the DNA molecule or associated proteins that affect gene expression without changing the genetic code itself'.[37] Epigenetic modifications are 'inheritable, modifiable or erasable in response to developmental cues [including cell or tissue type and age] or [exposure to] external and environmental stimuli'.[38]

The study of epigenetics is increasingly crucial to understanding development and treatment of disease. For example, 'defects in epigenetic regulation have been linked to developmental defects, metabolic disorders, and cancer in humans' as well as potentially also 'more common complex diseases including psychosis, diabetes and asthma'.[39] Moreover, 'Growing evidence suggests that environmental pollutants may cause diseases via epigenetic mechanism-regulated gene expression changes' and mounting research has also linked epigenetic alterations with exposure to organic toxicants (such as benzene, BPA and DES), heavy metals (such as arsenic, cadmium and chromium) and pesticides (such as endocrine disruptors, herbicides and

[33] Wambuguh (n 25) 187.
[34] Ibid.
[35] Peter Donaldson et al, *Genetics of Complex Disease* (Taylor & Francis, 2016) 29.
[36] Ibid 30. 'Epigenomics is the identification of all epigenetic modifications implicated in gene expression', see Wambuguh (n 25) 240.
[37] Gary Marchant, 'Genetic Data in Toxic Tort Litigation' (2016) 45(2) *The Brief* 22.
[38] Wambuguh (n 25) 240. 'The best-studied epigenetic changes are methylation of the cytosine base in DNA, which tends to suppress gene expression', see Marchant, 'Genetic Data in Toxic Tort Litigation' (n 37).
[39] Wambuguh (n 25) 240. See also an influential rat study published in 2004 which revealed the crucial role of environmental factors in shaping epigenetics, Ian Weaver et al, 'Epigenetic Programming by Maternal Behaviour' (2004) 7 *Nature Neuroscience*
847.

insecticides).[40] As Professor Marchant notes, 'The important significance for toxic tort litigation is that environmental exposures exert epigenetic changes that could affect the exposed individual's risk of future disease, and may even impact the disease risks of future generation progeny of the exposed individual'.[41]

4.1.6. Genetic Biomarkers

Biological markers (biomarkers) are molecular changes in blood or some other tissue of a person that can be objectively measured and evaluated as an indicator of normal or abnormal biological processes, pathogenic processes or pharmacologic responses to therapeutic interventions.[42] There are a number of biomarkers in genetics (known as genetic, genomic or DNA biomarkers), 'including chromosomal rearrangements, mutational spectra, or gene expression patterns'.[43] Essentially, genetic or epigenetic markers are DNA or RNA characteristics that may influence, explain or predict the incidence, risk, severity or outcome of disease or susceptibility to disease.[44] Genetic or epigenetic markers can also detect or measure exposure.

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[40] See, eg, Wambuguh (n 25) 254-8; Pierce (n 21) 664-7. In addition, 'Numerous studies report that modification of lifestyle factors, especially increasing physical activity levels, can influence the epigenetic patterns involved in human cancer, metabolic, cardiovascular and neurodegenerative diseases', see Wambuguh (n 25) 254. Moreover, 'Research has shown that life experiences, especially those early in life, can have long-lasting effects on behaviour, in some cases into future generations. Increasingly, research hers are finding that these long-term effects are mediated through epigenetic processes', see Pierce (n 21) 664.

[41] Marchant, 'Genetic Data in Toxic Tort Litigation' (n 37).

[42] See, eg, Wambuguh (n 25) 359. Basic examples of biomarkers include pulse, blood pressure, heart rate or glucose levels.

[43] Marchant, 'Genetic Data in Toxic Tort Litigation' (n 37).

[44] Giuseppe Novelli et al, 'Genetic tests and genomic biomarkers: regulation, qualification and validation' (2008) 5(2) *Clinical Cases in Mineral and Bone Metabolism* 149, 150 where genetic and epigenetic biomarkers are defined as DNA or RNA characteristics that indicate 'normal biological processes, pathogenic processes, and/or response to therapeutic or other intervention' where:

> DNA characteristics include, but are not limited to:
> • Single nucleotide polymorphisms (SNPs)
> • Variability of short sequence repeats
> • DNA modification, e.g. methylation
> • Insertions
> • Deletions
> • Copy number variation
> • Cytogenetic rearrangements, e.g. translocations, duplications, deletions or inversions.
> RNA characteristics include, but are not limited to:
> • RNA sequence
> • RNA expression levels
> • RNA processing, e.g. splicing and editing
> • MicroRNA levels.

See also Andreas Ziegler et al, 'Personalized medicine using DNA biomarkers: a review' (2012) 131 *Human Genetics* 1627, 1629 which defines a 'DNA biomarker' as 'A germline biomarker, such as SNPs, STRs, deletions, insertions, or other variation on the DNA sequence level' and an 'Epigenetic biomarker' as 'A

There are three key types of these biomarkers in clinical medicine:

1. Biomarkers of exposure (an individual's 'level or type of exposure to an environmental factor');
2. Biomarkers of effect (an individual's 'genetic [or epigenetic] responses to environmental exposures'); and
3. Biomarkers of susceptibility (an individual's genetic or epigenetic susceptibility to disease or their susceptibility to toxic effects of environmental exposures).[45]

For instance, 'blood lead concentration has been used as a marker for lead exposure', 'somatic mutations have been used as biomarkers of effect after exposure to carcinogens' and susceptibility genes, such as *BRCA1*, have been used as biomarkers of susceptibility.[46] Susceptibility markers may indicate inherent biological susceptibility to disease (eg, a *PAH* genotype causes phenylketonuria, or a *CFTR* genotype causes cystic fibrosis) or such markers could indicate susceptibility to toxic effects of exposure (eg a *NAT2* genotype increases the risk of breast cancer in smokers).[47]

The significance of these biomarkers lies in the fact that 'Robust, reproducible accessible' genetic markers can be useful for (1) diagnosis; (2) identification of causal factors; and (3) treatment.[48] Of these, the first and third seem much more highly developed at this point. As genetics is an emerging field, the validity of genetic markers for causal assessment is especially unclear where they are insufficiently sensitive or specific to be used on their own for diagnostic, screening, monitoring or therapeutic purposes.[49] At the same time, a biomarker may be useful for diagnosis and/or treatment but meaningless for causal assessment.[50]

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biomarker that measures epigenetic alterations, such as DNA methylation, histone methylation, histone acetylation, microRNAs, or other non-coding RNA'. See also Wambuguh (n 25) 545.

[45] Xiao-He Chen, Shuwen Huang and David Kerr, 'Biomarkers in clinical medicine' (2011) 163 *IARC Scientific Publications* 303, 303-4.

[46] Ibid.

[47] For more information, see, eg, Steve Gold, 'The More We Know, the Less Intelligent We Are – How Genomic Information Should, and Should Not, Change Toxic Tort Causation Doctrine' (2010) 34(2) *Harvard Environmental Law Review* 369, 385-390; Steve C Gold, Michael D Green and Joseph Sanders, *Scientific Evidence of Factual Causation: An Educational Module* (The National Academics of Science, Engineering and Medicine, October 2016) 168; Joseph Sanders et al, 'Differential Etiology: Inferring Specific Causation in the Law from Group Data in Science' (2021) 63 Arizona Law Review 851, 883.

[48] Novelli et al (n 44) 150.

[49] See, eg, Rotem Ben-Hamo et al, 'Predicting and affecting response to cancer therapy based on pathway-level biomarkers' (2020) 11(3296) *Nature Communications* 1, 2; Garrett Green et al, 'Specificity of Genetic Biomarker Studies in Cancer Research: A Systematic Review' (2016) 11(7) *PLoS ONE* 1; Committee on Applications of Toxicogenomic Technologies to Predictive Toxicology and Risk Assessment, *Applications of Toxicogenomic Technologies to Predictive Toxicology and Risk Assessment* (National Academy of Sciences, 2007) 54-6. For the stages of biomarker cancer development, see, eg, Margaret Pepe et al, 'Phases of Biomarker Development for Early Detection of Cancer' (2001) 93(14) *Journal of the National Cancer Institute* 1054.

[50] For example, in breast cancer, the presence or absence in the tumor of estrogen, progesterone and HER2 receptors is an important piece of diagnostic information that critically informs treatment decisions. The presence of estrogen and progesterone receptors have been used to support claims that hormone replacement therapy caused the cancer, see, eg, *In re Prempro Products Liability Legislation* 586 F 3d 547 (8th Cir, 2009). The absence of these receptors may tend to negate a claim of causation by hormone therapy, but provides no information about whether some other exposure (eg tobacco smoke or PFOA which is a perfluorooctanoic acid,

4.2. Genetic Testing

Chromosome analysis, also known as karyotyping, can be described as 'the original genetic test'.[51] It examines a person's chromosomes to determine if the right number is present and to determine if each chromosome appears normal. Although karyotyping is still used today, it only 'provides a bird's eye view' and a wide variety of more detailed genetic tests have since been developed.[52] These newer genetic tests include whole exome and whole genome sequencing, as well as arrays and microarrays. In fact, as Professor Kirk notes, genetic testing has become so advanced and increasingly routine that, over the next decade or two, genetic information will likely be a part of all patient files, 'as much a part of your record as your blood pressure, your weight, and the medications you take'.[53]

4.2.1. Microarrays, Single gene tests and Gene Panel Sequencing

In contrast to the bird's eye view of karyotypes, microarrays analyse specific regions of the genome.[54] Examples of microarrays include:

- SNP microarrays - used to detect single nucleotide polymorphisms (SNP), a variation at a single site in DNA, which is the most frequent type of variation in the genome;
- chromosomal microarrays (CMA) - used to detect copy number variants (including microdeletions and microduplications, i.e., missing (deleted) or extra (duplicated) segments of DNA)
- gene expression microarrays - used to detect gene expression patterns for specific genes; and
- array comparative genomic hybridisation (CGH) - used to detect copy number variants.[55]

However, the issue with some microarrays, including CMA and CGH, is that they cannot 'recognize translocations or inversions[56] that can contribute to genetic diseases'.[57]

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also known as C8, a fluorocarbon used in the production of Teflon) might have caused the cancer. For more information, see Gold, 'The More We Know' (n 47) 414-415.

[51] Kirk (n 9) 11.

[52] Ibid.

[53] Kirk (n 9) 1-2. In addition, direct-to-consumer genetic testing seeks to provide consumers with information about their risk of diseases and disorders, without involving a healthcare provider, see, eg, Pierce (n 21) 167.

[54] Philip Meneely et al, *Genetics: Genes, Genomes, and Evolution* (Oxford University Press, 2017) 393.

[55] For more information, see,eg, Klug et al (n 26) 583-585.

[56] Tiny duplications and deletions of DNA segments within a single gene.

[57] Klug et al (n 26) 587.

In general, the issue with microarrays, single gene testing (identifies variants in a single gene) and gene panel sequencing (identifies variants in more than one gene) is that they confine their focus to those specific regions of the genome that are known to be polymorphic, they do not look at the entire DNA sequence. This means these tests are cheaper and quicker than other genetic tests, but they also provide less information about a person's genome, which can have implications for litigants who rely on these tests in toxic torts. These implications will be discussed in greater detail in Chapters 6 and 7.

4.2.2. Whole Exome & Whole Genome Sequencing

Whole exome sequencing (WES) or whole genome sequencing (WGS) can be used when microarrays, single gene testing and/or gene panel testing have not provided a diagnosis, or the patient's suspected condition or genetic cause is unclear. WES and WGS are collectively known as 'next generation sequencing'. Instead of focusing in on only a select few genes, WES identifies variations in all the exons (protein-coding regions of any gene).[58] WES focuses on sequencing the exons of individuals, rather than their entire genome. The advantage of this approach is that 'Exons comprise less than 2% of the total genome sequence, so focusing on them greatly reduces the amount and the complexity of sequence information that is compiled and analyzed'.[59] This makes WES 'much cheaper and faster than sequencing entire genomes'.[60] Despite this 'reduced complexity', a drawback of this type of testing 'is that any mutations affecting regulatory regions are missed'.[61] However, this is not a major drawback in the case of 'many single-gene genetic diseases (i.e. monogenic diseases, such as Huntington's Disease or Cystic Fibrosis, where the disease results from a mutation in a single gene) with severe phenotypes' because 'Mutations in exons are likely to be the mutations with the most profound effects on the function of the gene's protein product'.[62] In fact, 'most severe genetic disease will be due to mutations in the exons that produce deleterious changes in the amino acid sequence'.[63] For example, whole exome sequencing has been used to identify genes associated

[58] Meneely et al (n 54) 390. See also Alejandro Iglesias, 'The usefulness of whole-exome sequencing in routine clinical practice' (2014) 16(12) *Genetics in Medicine* 922.
[59] Meneely et al (n 54) 390.
[60] Ibid 393. See also Katharina Schwarze, 'Are whole-exome and whole-genome sequencing approaches cost-effective? A systematic review of the literature' (2018) 20(10) *Genetics in Medicine* 1122.
[61] Meneely et al (n 54) 390.
[62] Ibid.
[63] Ibid 393.

with diseases such as Charcot-Marie-Tooth Disease[64], Inflammatory Bowel Disease[65] and Parkinson Disease[66] and has also been used in the discovery of cancer-driver genes.[67] In addition, it has been shown to have clinical and diagnostic utility in children with developmental disorders and intellectual disability.[68] So, whole exome sequencing is still an efficient method to identify many possible disease-causing mutations.

In order to capture the regulatory regions that would be missed in WES, whole genome sequencing ('WGS') can be used 'to identify all of the possible causative mutations' by 'examining the entire genome, both the exons and the regulatory regions'.[69] A key limitation to WGS 'is that the databases of common polymorphisms focus primarily on exons; thus, it is more difficult to filter out common polymorphisms in other parts of the genome, at least until many more entire individual human genomes are sequenced'.[70] Another limitation is that, generally speaking, 'Diseases that are caused by multiple genes are much harder to diagnose and treat based on sequencing data'.[71] For instance, WGS of individuals affected by 'autism spectrum disorder (ASD) has revealed the involvement of more than 100 different genes'.[72]

[64] See, eg, Kleita Michaelidou, 'Whole exome sequencing establishes diagnosis of Charcot-Marie-Tooth 4J, 1C, and X1 subtypes'(2020) 8(4) *Molecular Genetics & Genomic Medicine* 1; Gladys Montenegro et al, 'Exome sequencing allows for rapid gene identification in a Charcot-Marie-Tooth family' (2011) 69(3) *Annals of Neurology* 464.

[65] See, eg, Eileen Crowley et al, 'Prevalence and Clinical Features of Inflammatory Bowel Diseases Associated With Monogenic Variants, Identified byWhole-Exome Sequencing in 1000 Children at a Single Center' (2020) 158(8) *Gastroenterology* 2208; Katja Christodoulou, 'Next generation exome sequencing of paediatric inflammatory bowel disease patients identifies rare and novel variants in candidate genes' (2013) 62 *Gut* 977; Elizabeth Worthey, 'Making a definitive diagnosis: Successful clinical application of whole exome sequencing in a child with intractable inflammatory bowel disease' (2011) 13(3) *Genetics in Medicine* 255.

[66] See, eg, Alessandro Gialluisi et al, 'Whole Exome Sequencing Study of Parkinson Disease and Related Endophenotypes in the Italian Population' (2020) 10(1362) *Frontiers in Neurology* 1; Eman Al Yemni et al, 'Integrated Analysis of Whole Exome Sequencing and Copy Number Evaluation in Parkinson's Disease' (2019) 9(3344) *Scientific Reports* 1; Janice Farlow et al, 'Whole-Exome Sequencing in Familial Parkinson Disease' (2016) 73(1) *JAMA Neurology* 68; Jose Bras and Andrew Singleton, 'Exome Sequencing in Parkinson's Disease' (2011) 80(2) *Clinical Genetics* 104.

[67] See, eg, Manon Reda et al, 'Implementation and use of whole exome sequencing for metastatic solid cancer' (2020) 51(10264) *EBio Medicine* 1; Áron Bartha and Balázs Gyorffy, 'Comprehensive Outline of Whole Exome Sequencing Data Analysis Tools Available in Clinical Oncology' (2019) 11 *Cancers* 1725; Chee-Seng Ku, David Cooper and George Patrinos, 'The Rise and Rise of Exome Sequencing' (2016) 19 *Public Health Genomics* 315; Ignacio Varela, 'Exome sequencing identifies frequent mutation of the SWI/SNF complex gene PBRM1 in renal carcinoma' (2011) 469(7331) *Nature* 539.

[68] See, eg, Jelena Rumi Stojanovic et al, 'Diagnostic and Clinical Utility of Clinical Exome Sequencing in Children With Moderate and Severe Global Developmental Delay / Intellectual Disability' (2020) 35(2) *Journal of Child Neurology* 116; Siddharth Srivastava et al, 'Meta-analysis and multidisciplinary consensus statement: exome sequencing is a first-tier clinical diagnostic test for individuals with neurodevelopmental disorders' (2019) 21(11) *Genetics in Medicine* 2413.

[69] Meneely et al (n 54) 393.

[70] Ibid.

[71] Klug et al (n 26) 591.

[72] Ibid. The genetics of ASD is further complicated by 'the broad range of phenotypes associated with this disorder', see ibid.

This complexity is exacerbated by the fact that WGS of individuals affected by ASD has not only 'revealed inherited mutations, it has also identified sporadic *de novo* mutations'.[73] This makes it especially difficult to pinpoint the genes involved in causing ASD.[74]

4.3. Genome-Wide Association Studies

Genome-wide association studies ('GWAS') are increasingly powerful tools in helping geneticists 'identify genes that may influence disease risk'.[75] These studies have resulted in scientific publications linking thousands of genetic variations to hundreds of traits.[76] For instance, there have been 'GWAS for height differences, autism, obesity, diabetes, macular degeneration, myocardial infarction, arthritis, hypertension, several cancers' etc.[77] GWAS involve analysis of 'the genomes of thousands of unrelated individuals with a particular disease, typically by microarray analysis' and subsequent comparison 'with genomes of individuals without the disease as an attempt to identify genetic variations that may confer risk of developing the disease'.[78]

A primary limitation of GWAS is that they are 'association' studies. This means that 'Although they identify the regions of the chromosomes that are likely to contain the genes for particular traits, they do not identify the specific causative gene within that region' and the issue of 'Identifying the causative gene is not a trivial problem'.[79] As a result, 'Fewer than half of the GWASs listed at the genome.gov website have pinpointed the specific causative gene within that region'.[80] Another limitation is that 'not all populations can be easily studied' and this creates difficulties because 'a region of the genome that is polymorphic in one population could show an association with the disease, whereas the same region might not be polymorphic in another population and thus would not show an association with the disease'.[81]

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[73] Ibid.
[74] For a detailed discussion of the difficulties with using genetic tests in toxic torts, see Chapters 6 and 7.
[75] Klug et al (n 26) 592.
[76] Ibid.
[77] Ibid.
[78] Ibid. 'By determining which copy number variations, standard nucleotide polymorphisms, or epigenome changes co-occur in individuals with the disease, scientists can [rely on statistical analysis to] calculate the disease risk associated with each variation'.
[79] Meneely et al (n 54) 412. For an explanation of different approaches to identifying the causative gene, see ibid 412-3.
[80] Ibid 412. For a complete list of GWASs that meet certain criteria for population size and strength of association, see National Human Genome Research Institute, *GWAS Catalog: The NHGRI-EBI Catalog of human genome-wide association studies* < http://www.genome.gov/gwastudies>.
[81] Meneely et al (n 54) 412.

4.4. Pharmacogenomics & Personalised Medicine

A major goal of GWAS is assisting in disease diagnosis and treatment, which is also a key tenet of the emerging field of pharmacogenomics. Pharmacogenomics can show when drugs are ineffective, and can show when drugs are harmful. These are different impacts - a given variant/drug combination will usually affect one but not the other. Pharmacogenomics 'promises to lead to more specific, effective, and personally customized drugs that are designed to complement each person's individual genetic makeup'.[82] Genetic information 'is becoming increasingly important in guiding drug treatment' because the effectiveness of a drug could be 'influenced by a patient's genotype [meaning that] individuals with certain genotypes may be more likely to suffer from adverse drug reactions'.[83] Pharmacogenomics therefore investigates how an individual's genes influence their response to drugs. For instance, 'liver enzymes encoded by the cytochrome *P450* gene family affect the metabolism of many modern drugs, including those used to treat cardiovascular and neurological conditions'.[84] This means 'gene variants that encode inactive forms of the cytochrome P450 enzymes are associated with a patient's inability to break down drugs in the body, leading to drug overdose'.[85]

Another example is Warfarin ('the most common anticoagulant (blood thinner) used worldwide').[86] The precise dose of Warfarin 'is critical: too little, and blood clots are not prevented; too much, and internal bleeding results'.[87] However, individual responses to this drug vary significantly, 'and some of this variation is due to genes'.[88] In particular,

> *CYP2CP9* is a gene that encodes an enzyme that metabolizes warfarin. Over 30 different alleles occur at this locus. People who are homozygous for the *CYP2CP9*1* allele metabolize warfarin normally, but individuals who are homozygous or heterozygous for the *CYP2CP9*2* or *CYP2CP9*3* alleles metabolize warfarin at a much lower rate and therefore require a lower dose. If given the usual dose of warfarin, these people are at greater risk of bleeding. Genetic variation at *CYP2CP* and another locus called *VKORC1* accounts for up to 30% of the variation in response to warfarin dose and risk of bleeding.[89]

As a result of this substantial genetic variation, 'Some hospitals are screening patients for variation at these genes to help determine the proper warfarin dose to administer'.[90] With ever-

[82] Klug et al (n 26) 593.
[83] Pierce (n 21) 166-7.
[84] Klug et al (n 26) 593.
[85] Ibid.
[86] Pierce (n 21) 166-7.
[87] Ibid.
[88] Ibid.
[89] Ibid.
[90] Ibid.

expanding scientific discoveries relating to genetics and disease, pharmacogenomics promises to be a powerful technology in the coming decade.[91]

4.5. Toxicogenomics

Toxicogenomics is a sub-discipline of pharmacology that seeks to shed light on 'gene-environment interactions'.[92] In particular, it investigates 'the application of genomic technologies[93] to study the adverse effects of environmental and pharmaceutical chemicals on human health and the environment'.[94]

In short, toxicogenomics addresses two crucial issues:

1. elucidation of a compound's mode of toxicity, i.e. understanding why it is toxic, and
2. prediction of whether a compound is toxic or not.[95]

This allows for more effective screening of chemicals to:

1. identify hazards;
2. monitor individuals' exposure to toxicants;
3. track cellular responses to different doses;
4. assess mechanisms of action; and
5. predict individual variability in sensitivity to toxicants.[96]

As noted by the Committee on Applications of Toxicogenomic Technologies to Predictive Toxicology and Risk Assessment, 'Toxicogenomics may lead to information that is more discriminating, predictive, and sensitive than that currently used to evaluate exposures to toxicants or to predict effects on human health'.[97] For example, toxicogenomic technologies can be 'adapted and applied for the study of exposure assessment by developing signatures of exposure to individual chemicals and perhaps to chemical mixtures' as well as 'to prospectively identify, understand the mechanisms of, and characterize the extent of genetic

[91] Klug et al (n 26) 595. The power of personalised medicine and pharmacogenomics was recognised by the Obama Administration when Former President Barack Obama signed the bipartisan Precision Medicine Initiative in 2015, see Pamela Sankar and Lisa Parker, 'The Precision Medicine Initiative's All of Us Research Program: An agenda for research on its ethical, legal, and social issues' (2017) 19(7) *Genetics in Medicine* 743.
[92] Committee on Applications of Toxicogenomic Technologies to Predictive Toxicology and Risk Assessment (n 49) 12.
[93] 'for example, genetics, genome sequence analysis, gene expression profiling, proteomics, metabolomics, and related approaches', see ibid.
[94] Ibid.
[95] Benjamin Alexander-Dann et al, 'Developments in toxicogenomics: understanding and predicting compound-induced toxicity from gene expression data' (2018) 14(4) *Molecular Omics* 213, 231.
[96] Committee on Applications of Toxicogenomic Technologies to Predictive Toxicology and Risk Assessment (n 49) 1, 204-212.
[97] Ibid 12.

and epigenetic influences on variations in human susceptibility to the toxic effects of chemicals'.[98] This means that

> Rather than examining the effect of a chemical on one or a few biochemical pathways, the tools of toxicogenomics provide a means to examine the global response of a cell to a chemical stimulus, resulting potentially in a "fingerprint" alteration in expression of thousands of different genes (transcriptomics), proteins (proteomics), or cellular metabolites (metabonomics). The potential exists for such tools to provide convincing proof that a particular disease was related to a specific chemical exposure, through unique changes that potentially can be measured years after the exposure occurred.[99]

However, toxicogenomics still has 'major limitations', including a lack of 'available data resources' where even available data is often 'not entirely the "right" fit for the intended purpose'.[100] Moreover, 'challenges in experimental design, statistical interpretation, and reproducibility need to be addressed before [toxicogenomics] can realize its full potential'.[101] In addition 'Currently, the best model organisms, which provide high-level phenotypic readouts, are mice and rats [but] they do not have exactly the same physiological parameters as humans, e.g. their immune system reacts to compounds differently'.[102] So, like toxicological studies, toxicogenomic studies can also have issues with translating the results of *in vivo* toxicological studies on mice/rats into meaningful conclusions about humans. Despite these limitations, 'the discipline has exceeded expectations of utility in prediction'[103] and 'substantially expanded [the] potential to study and estimate the risks that chemical compounds pose to human health'.[104] In particular, 'toxicogenomics methods are already seeing wider recognition and adoption by the pharmaceutical industry'.[105] As the following chapters will reveal, the impact of toxicogenomics has also extended to the realm of toxic tort cases.

4.6. An Overview of Genetic Markers in Toxic Torts

Since the turn of the century, general population-based epidemiological and toxicological studies have increasingly been supplemented by both general and personalised genetic evidence, providing a potentially valuable tool for litigants to support or refute causation.

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[98] Ibid 204, 206.
[99] David Eaton, 'Scientific Judgment and Toxic Torts – A Primer in Toxicology for Judges and Lawyers' (2003) 12(1) *Journal of Law and Policy* 5, 41.
[100] Benjamin Alexander-Dann et al (n 95) 231.
[101] Zhichao Liu et al, 'Toxicogenomics: A 2020 Vision' (2019) 40(2) *Trends in Pharmacological Sciences* 92, 101-2
[102] Benjamin Alexander-Dann et al (n 95) 231.
[103] Zhichao Liu et al (n 101) 102.
[104] Simone Schmitz-Spanke, 'Toxicogenomics – What added Value Do These Approaches Provide for Carcinogen Risk Assessment?' (2019) 173 *Environmental Research* 157, 163.
[105] Benjamin Alexander-Dann et al (n 95) 232.

Genetic evidence can be adduced for the purposes of establishing a person's identity or predicting a person's health status, susceptibility to environmental exposures, and predisposition to disease (independent of toxic exposures) based on their genetic code. This thesis focuses on the latter, health-related genetic evidence which has received attention from a relatively small minority of predominantly American scholars. Such health-related genetic evidence includes expert evidence relating to family medical history, as well as individual and/or generalised genetic, epigenetic or toxicogenomic data. As Professor Gary Marchant observes, 'Given the potential usefulness of such genetic data for either proving or disproving causation, it is likely that both plaintiffs and defendants will increasingly seek to obtain and introduce such evidence in future toxic tort cases'.[106]

Genetic evidence is potentially vital to proving or disputing causation in toxic tort claims because 'there is almost always some interaction between genetic and environmental factors in the causation of disease'.[107] However, the literature pertaining to genetic evidence contains a multiplicity of claims about the increasing use of this data in the courtroom. Due to the sheer speed of advancements in genetic technology, academic commentary largely falls into three broad areas: descriptive claims about how genetic evidence *is* being used; predictive claims that suggest how genetic evidence *will* be used; and normative claims about how genetic evidence *should* be used. In fact, before the human genome had even been sequenced, legal scholars and bioethicists were already considering how genetic information could be, and should be, used in toxic tort litigation.[108]

It has been said that 'There is no more challenging field of the law for trial lawyers' than toxic torts and 'In genetics as in other fields driving toxic tort law, scientific and technical advances will continue to challenge lawyers, clients, and judges'.[109] These challenges are particularly

[106] Gary Marchant, 'Genetic Data in Toxic Tort Litigation' (2016) 45(2) *The Brief* 22, 23.
[107] Penny Webb and Christopher Bain, *Essential Epidemiology: An Introduction for Students and Health Professionals* (Cambridge University Press, 2nd ed, 2010) 18. As noted by Webb and Bain, the reference to 'environmental factors' in most epidemiological and public health research is taken to mean 'the sum of all non-genetic factors, including psychological, behavioural, social and cultural traits'.
[108] See, eg, Barry Cepelewicz and Eric Wiechmann, 'Genetic injury in toxic tort cases: what science can and cannot prove' (1995) 62(2) *Defense Counsel Journal* 201; Gary Marchant, 'Genetic susceptibility and biomarkers in toxic injury litigation' (2000) 41(1) *Jurimetrics* 67; Susan Poulter, 'Genetic Testing in Toxic Injury Litigation - The Path to Scientific Certainty or Blind Alley?' (2001) 41(2) *Jurimetrics* 211; Gary Marchant, 'Genetics and Toxic Torts' (2001) 31 *Seton Hall Law Review* 949; Christina Callahan, 'Molecular Epidemiology: Future Proof of Toxic Tort Causation' (2001) 8(1) *Environmental Lawyer* 147; Gary Marchant, 'Toxicogenomics and Toxic Torts' (2002) 20(8) *Trends in Biotechnology* 329; John Childs, 'Toxicogenomics: New Chapter in Causation and Exposure in Toxic Tort Litigation' (2002) *Defense Counsel Journal* 441.
[109] L Neals Ellis, Jr, 'Introduction' in D Alan Rudlin (ed), *Toxic Tort Litigation* (American Bar Association, 2007) 10, 15.

evident in the growing use of genetic markers to support or refute causation in Australian and US toxic tort cases. This is because 'reliability and medical significance of biomarkers are likely to be controversial, and litigants may be prone to rely on biomarkers before they have been properly validated'.[110] As a result, courts are likely to have to tackle the challenges of what weight to give this apparently 'objective' evidence given that it will be presented before it is validated.[111]

The use of genetic (and epigenetic) information to support or dispute causation in toxic tort litigation typically involves one or more of the following:

1. Genetic Markers of Exposure;
   (i.e. 'an observable change that occurs with exposure but is otherwise absent'[112])
2. Genetic Markers of Effect; and
   (i.e. 'an observable, *medically significant, harmful* change that occurs with exposure but is otherwise absent' [emphasis added][113])
3. Genetic Markers of Susceptibility
   (i.e. 'an observable genetic variation that alters the extent to which an exposure causes toxic harm'[114])
4. Court-ordered genetic testing.

The remainder of this thesis will critically examine the statute, case law and scholarly literature in each of these distinct areas. The importance of such a study has been explained by a group of American scholars who conducted a similar inquiry into the general use of genetic evidence in American courts:

> …recent trends in the scope and use of genetic tests in litigation are largely generally unknown. If such trends have decreased over time or such tests are infrequently used, this trend would suggest a lower priority or need for systemic reform of evidentiary standards and expert qualifications. On the other hand, clear evidence of rising trends of such contested evidence may suggest the need for more immediate clarification of standards and an evolving discussion of the future of presenting scientific evidence and qualifying scientific evidence experts…Prior scholarly work provides methodological and empirical benchmarks to assess whether genetic tests, and thus their probity and the qualification of experts, have been used at growing rates over time.[115]

This thesis will refer to prior American scholarly work as a comparative benchmark in assessing the Australian position. Following an in-depth examination of the case law, the thesis

[110] Marchant, 'Genetic Susceptibility and Biomarkers in Toxic Injury Litigation' (n 108) 95.
[111] Ibid.
[112] Steve Gold, 'When Certainty Dissolves into Probability – A Legal Vision of Toxic Causation for the Post-Genomic Era' (2013) 70(1) *Washington & Lee Law Review* 237, 261.
[113] Ibid.
[114] Ibid.
[115] Edward Ramos et al, 'Genomic Test Results and the Courtroom: The Roles of Experts and Expert Testimony' (2016) 44 *The Journal of Law, Medicine & Ethics* 205, 221-2.

will conclude with recommendations for practice-oriented instruments (in the form of a Reference Guide) to assist litigants, lawyers, and the courts in understanding the role of genetic evidence.

4.7. Conclusion

This chapter provided a brief introduction to the history and science of genetic information. The scientific information in this chapter forms a crucial component of the reference guide proposed in Chapter 8. As Chapter 8 will show, the proposed guide commences with a clear and comprehensive overview of the science, focusing on all the key terms outlined in this chapter. This includes the discussion in Part 4.1 elucidating the relationship between genetics and human disease, the meaning of genetic information and the role of genetic mutations, gene expression, epigenetics, genetic predisposition and genetic markers of exposure, effect and susceptibility. It will then include the explanation in Part 4.2 highlighting the different types of genetic testing and their purposes, as well as the differences between microarrays, whole exome and whole genome sequencing. The guide will go on to outline the descriptions in Parts 4.3-4.5 emphasising the increasing significance of genome-wide association studies, pharmacogenomics, personalised medicine and toxicogenomics in understanding the interaction between human exposure and disease. The introductory sections of the guide will conclude with an overview of the different types of genetic evidence increasingly being adduced in toxic torts, as outlined in Part 4.6.

Now that this chapter has provided a necessary introduction to the science of genetics, the following chapters will continue this discussion, by analysing the growing role of genetic information in toxic tort litigation. The following chapters will respectively consider the three key concepts of (1) genetic markers of exposure/effect; (2) genetic markers of susceptibility; and, (3) court-ordered genetic testing. Chapter 8 will then highlight how the comprehensive case law analysis in these chapters ultimately form the basis for separate sections of the proposed reference guide.

5. Chapter Five: The Challenge of Proving Causation: Genetic Markers of Exposure/Effect as the Solution?

The previous chapters outlined the toxic tort causation problem, emphasising long-standing concerns of admissibility and sufficiency of causation evidence, and also provided a brief scientific and historical background to genetic information. The balance of the thesis will consider whether genetic evidence typically exacerbates or alleviates the problem of causal indeterminacy in toxic torts. Genetic evidence includes markers of susceptibility, exposure and/or effect. Broadly speaking, genetic markers of exposure and/or effect describe a genetic alteration that leaves a 'mark' indicating exposure to a toxin and/or the effect of such exposure. Genetic markers of susceptibility include genetic variations indicating an individual is more likely to develop illness independently of toxic exposure or more likely to develop illness following exposure. This chapter will focus on markers of exposure and/or effect. The following chapter will go on to consider genetic markers of susceptibility.

This chapter highlights the considerable variability in scientific interpretations of genetic markers of exposure and effect, and the limited utility of insufficiently valid, sensitive or specific markers.[1] Inconsistencies in the case law (concerning the admissibility and/or sufficiency of genetic evidence) suggest there is substantial judicial disagreement, stemming from broader scientific disagreement, regarding the utility and validity of such markers. Ultimately, the tensions highlight that courts require greater guidance in assessing genetic information in the form of a reference guide proposed in Chapter 8.

Part 5.1 of this chapter provides a brief explanation of genetic markers of exposure and/or effect. Parts 5.2 and 5.3 analyse the US and Australian cases involving genetic markers of exposure and/or effect as proof of causation or alternative causation.[2]

[1] For more information on the concepts of sensitivity and specificity, see Steve Gold, 'When Certainty Dissolves into Probability - A Legal Vision of Toxic Causation for the Post-Genomic Era' (2013) 70(1) *Washington & Lee Law Review* 237, 267-277. Even if a marker is sufficiently reliable, specific, and sensitive, plaintiffs could still struggle to show *which* exposure caused their harm where they have experienced multiple exposures to the same substance via different products.

[2] Although the plaintiff almost always bears the legal burden of proof under both Australian and American law (with the key exceptions being the American 'alternative liability' and 'market liability' rules, see *The American Law Institute, Restatement of the Law (Third), Torts: Liability for Physical and Emotional Harm (The American Law Institute, 2010) ('Third Restatement')* § 28(b), the defendant in a toxic tort case is under an evidential burden to produce sufficient evidence to suggest an alternative cause of the injury (i.e., 'alternative causation'). In cases where defendants suggest 'alternative causation', they are suggesting that 'other forces…were the factual cause of the harm *instead of* the defendant's tortious conduct', see ibid § 27, *Comment (e)*. Alternative causes can be distinguished from multiple sufficient causes, as the latter involves a situation where 'the other

5.1. An Overview of Genetic Markers of Exposure and/or Effect

In order to prove exposure to a toxic substance, plaintiffs can adduce evidence of biomarkers existing in their genome that indicate molecular changes occurring to their cells as a result of exposure to a toxic substance.[3] Genetic markers can either indicate exposure to *any* toxic substance or a *specific* substance where a pattern of specific mutations in an individual's genes reveal precisely which toxic substance caused the mutation.[4] In particular, exposure to a toxic substance may result in direct alteration of:

1. Coding DNA sequence;
2. Chromosomal aberrations;
3. Epigenetic factors; and/or
4. Gene expression.[5]

In toxic tort cases, 'Such alterations may serve as biomarkers of exposure, or, if the alterations indicate or accompany clinical manifestations, as biomarkers of effect'.[6] Before continuing with the analysis of exposure biomarkers, it is important to briefly outline the differences between biomarkers of exposure and effect.

Biomarkers of exposure examine exposed and non-exposed biological materials for differences in gene mutations, gene expression, or other indicators such as DNA adducts, which provide evidence of a person's *exposure* to a toxic substance. By contrast, biomarkers of effect 'reflect *occurrences subsequent to* the initial *exposure*-related events and in general, but not always, may be more persistent than exposure biomarkers'.[7] Biomarkers of effect include 'chromosomal alterations, changes in gene expression, altered protein levels (e.g. growth factors, cytokines), and mutations'.[8] Simply put, biomarkers of exposure indicate an individual's level of *exposure* to a substance, while biomarkers of effect indicate the 'medically

forces were operating and sufficient to cause the harm contemporaneously with the defendant's tortious conduct', see ibid.

[3] Steve Gold, 'The More We Know, the Less Intelligent We Are - How Genomic Information Should, and Should Not, Change Toxic Tort Causation Doctrine' (2010) 34(2) *Harvard Environmental Law Review* 369, 390.

[4] Gary Marchant, 'Genetic Data in Toxic Tort Litigation' (2006) 14 *Journal of Law and Policy* 7, 18-19.

[5] Steve Gold, Michael Green and Joseph Sanders, 'Epidemiological Evidence in Toxic Torts' in Michael Freeman and Maurice Zeegers (eds), *Forensic Epidemiology* (Academic Press, 2016) 55.

[6] Ibid.

[7] Christopher Wild, 'Biomarkers of Exposure and Effect' in Timothy Rebbeck, Christine Ambrosone and Peter Shields (eds), *Molecular Epidemiology: Applications in Cancer and Other Human Diseases* (Informa Healthcare, 2008) 82.

[8] Ibid.

significant, harmful *effect'* of that exposure on the individual.[9] However, there is no clear distinction between these two categories of biomarkers because

> there are no sharp boundaries in the continuum leading from exposure to disease. A DNA adduct, for example, is not comfortably forced exclusively into one or other category. In addition, many of the required properties of biomarkers in both categories are common, e.g. sensitivity, specificity, validity, and reliability. Nevertheless, the categorization, if held lightly, can be helpful both for descriptive purposes and to inform discussions of disease mechanisms in the context of what, by definition, is the interdisciplinary research embraced by molecular epidemiology.[10]

Consistently with the above passage and much of the legal scholarly literature in this area[11], this chapter will retain the light distinction between biomarkers of exposure and effect. In particular, the thesis will involve a separate analysis of these two categories while simultaneously acknowledging the similarities between them, including the fact that some biomarkers can indicate both exposure and effect. Although such biomarkers help to identify the causal agent/substance, they still cannot help identify which of a number of exposures to that agent was causal.[12]

5.2. Genetic Markers of Exposure & Effect to Prove or Disprove Causation: US Case Law

US toxic tort litigants have relied on genetic evidence from as early as the 1990s in an attempt to prove or disprove causation.[13] Not only have plaintiffs relied on markers as a method of proof of causation in these cases, but defendants have equally (or perhaps more so) relied on markers to prove alternative causation. Either role, of course, could improve truth-seeking and reduce causal indeterminacy. However, the factual contexts and legal issues in these cases are varied, providing only a limited opportunity for generalisation.

The observed variations in case outcomes are largely attributable to varying judicial opinions on the sensitivity and specificity of the relevant markers. As Professor Steve Gold explains, 'Given the myriad of potentially harmful environmental agents to which we are all exposed, a

[9] Steve Gold, 'When Certainty Dissolves into Probability' (n 1) 261.
[10] Wild (n 7) 82.
[11] See, eg, Gary Marchant, 'Genetic Susceptibility and Biomarkers in Toxic Injury Litigation' (2000) 41(1) *Jurimetrics* 67; Marchant, 'Genetic Data in Toxic Tort Litigation' (n 4); Gold, 'When Certainty Dissolves into Probability' (n 1) Gold, 'The More We Know' (n 3).
[12] For more information, see Part 1.3.2 of this thesis.
[13] See, eg, *Harris v KEM Corp* No. 85 Civ 2127(WK), 1989 WL 200446 (SDNY, 1989); *Harris v Kem Corp*, No. 85 Civ. 2127(WK), 1990 US Dist LEXIS 11150 (SDNY, 1990); *Sutera v Perrier Group of America Inc*, 986 F Supp 655 (D Mass, 1997); *Wells v Shell Oil Co* (DCE Texas, Jury verdict March 2, 1998; *Lavender v Bayer Corp* (W Va Cir, No 93-C-226-K, May 29, 1998); *Edwards v Safety-Kleen Corp* 61 F Supp 2d 1354, 1359-60 (SD Fla, 1999).

biomarker's presence alone will suffice to *prove* a plaintiff's case only if the marker is *specific* to the exposure-disease combination'(emphasis added).[14] On the other hand, 'Given the myriad of metabolic and mutagenic pathways by which some substances can cause illness, a biomarker's absence alone will suffice to *disprove* a plaintiff's case only if the marker is perfectly *sensitive* to the exposure-disease combination' (emphasis added).[15] As the following section will reveal, concepts of specificity and sensitivity explain why evidence of certain markers appear to have more dispositive effect in some contexts, while evidence of other markers in other contexts are inadmissible or unpersuasive.

5.2.1. Genetic Markers of Exposure/Effect to Disprove Causation

Gene expression profiles have proven to be a useful indication of alternative causation in toxic torts where plaintiffs allege exposure to radiation caused their cancer.[16] In *Naomi Guzman v ExxonMobil Corp.*, the plaintiff claimed that her thyroid cancer was caused by exposure to 'naturally occurring radioactive material' ('NORM') 'through her father's work as an oil pipe cleaner'.[17] In particular, the plaintiff alleged that

> The scale in some of the pipes [the majority of those pipes, 'about 95 percent of them', being owned by the defendant, ExxonMobil] contained ionizing-radiation particles, otherwise known as NORM (naturally occurring radioactive material), which became airborne and attached to her father's clothing when he cleaned the pipes. According to [the plaintiff], she herself was exposed to NORM through four routes: while she was in utero, her mother went to the pipe yard to bring her father lunch; post-birth, when she would accompany her mother to the pipe yard to bring her father lunch; whenever her father returned home from the pipe yard, she would inhale and ingest the particles; and while as a toddler, when she was babysat by her aunt and uncle, who also worked at the Intracoastal pipe yard.[18]

The plaintiff's greatest hurdle at trial was proving causation.[19] The plaintiff's expert toxicologist and endocrinologist both suggested that her radiation exposure caused her

[14] Gold, 'When Certainty Dissolves into Probability' (n 1) 267.
[15] Ibid 268.
[16] It is also important to note that in the class action case of *In re TMI Litigation* 193 F 3d 613 (3rd Cir, 1999), genetic markers of exposure were adduced by plaintiffs to attempt to prove that they were exposed to sufficient doses of radiation to cause their cancer. However, this evidence was insufficient to establish causation because the genetic exposure markers were unreliable, as the sample was collected many years after the initial exposure. If the samples were collected much sooner (preferably within a day or two from the initial exposure), the presence or absence of genetic markers would likely have been beneficial in proving or disproving specific causation. For more information, see eg Andrew Askland and Gary Marchant, 'Genetic Data and Toxic Torts: Intimations of Statistical Reductionism' in Richard Sharp, Gary Marchant and Jamie Grodsky (eds), *Genomics and Environmental Regulation* (The John Hopkins University Press, 2008) 86.
[17] *Naomi Guzman v ExxonMobil Corp, ExxonMobil Oil Corp, Humble Inc, and Intracoastal Tubular Services Inc,* No. 693–606 (La Dist Ct, 24th Dist, 2013) Jury Verdicts LEXIS 9774.
[18] Ibid 3.
[19] Ibid 5.

cancer.[20] However, defence experts in pathology and epidemiology testified that the radioactive materials in this case, 'Radium-226 and -228 do not cause thyroid cancer' and that 'Iodine-131…is the only radionuclide that causes thyroid cancer, and [the plaintiff] was not exposed to Iodine-131'.[21]

Interestingly, the defence also obtained permission from the Court to conduct genetic testing on the plaintiff's preserved thyroid tissue. The defendants subsequently engaged a medical toxicology expert who 'relied on the genetic testing, gene-expression testing, and RNA sequencing that were performed on [the plaintiff's] pathology tissue'.[22] The expert's findings were damaging to the plaintiff's causation case:

> The expert explained that a certain number of the population develops cancer randomly without explanation. Since mapping the human genome, however, science is discovering that genomic markers and gene signatures can indicate whether some cancers are sporadic or caused by an agent, the expert said. (Scientists do not have gene signatures for all cancers yet.) According to the expert, [the plaintiff's] tissue did not show the genomic markers/gene signatures to radiation exposure – the genomic markers and genetic signatures show sporadic papillary thyroid cancer.[23]

Therefore, the expert was able to use gene expression profiling to show that the plaintiff's cancer tissue had the 'gene signature' for sporadic thyroid cancer. This meant that the cancer was not induced by radiation, but rather was idiopathic. The expert was able to come to this conclusion because 'messenger RNA gene expression from [the plaintiff's] tissue was found in patterns consistent with non-radiation-induced cancers but inconsistent with cancers from irradiated populations'.[24] In particular,

> scientists were able to rely on a recently published paper that provided a comprehensive overview of gene expression signatures related to radiation-induced thyroid tumors. This published gene list served as the reference point for radiation-induced cancer. The scientists then established the genetic signature for the plaintiff's cancerous tissue. That produced the plaintiff's personal gene expression profile, which was compared to the published gene expression profiles for radiation-induced thyroid tumors to

[20] Ibid.
[21] Ibid.
[22] Ibid.
[23] Ibid. This same expert also testified about the plaintiff's genetic predisposition, see Ibid:

> Additionally, the expert testified, genetic testing demonstrated that Guzman had a fivefold increase in her predisposition to thyroid cancer, with genomic testing showing no gene signature for radiation-induced cancer. Therefore, it could be conclusively ruled out that Guzman's thyroid cancer was in no way caused by her contact with ExxonMobil's drilling pipe, as her thyroid cancer was caused by her genetic predisposition to it, concluded the toxicologist.

[24] Kirk Hartley and David Schwartz, 'A Lawyer's Guide to Genomics in Toxic Tort Cases: Part 1' *Law360* (online at 17 July 2018) < https://www.law360.com/articles/1063736/a-lawyer-s-guide-to-genomics-in-toxic-tort-cases-part-1>. Again, expert testimony of the plaintiff's genetic predisposition was also pivotal to the defence case, see Ibid:

> Additional genetic analysis indicated that Guzman tested positive for inherited mutations in eight genes associated with papillary thyroid cancers. Guzman's family history showed that her mother and aunt both had thyroid cancer. Expert testimony presented these facts and made the case that Guzman's cancer was caused by hereditary gene mutations as opposed to her exposure to NORM.

> determine if any similarities existed. When the results came in, the plaintiff's gene expressions demonstrated a "gene signature" for sporadic thyroid cancer as opposed to radiation-induced thyroid cancer resulting from exposure to NORM.[25]

The defendants were ultimately found not liable by the jury.[26] So, 'It appeared…that the genetics and genomic test results firmly established an alternative causation and may have aided the jury in reaching their verdict'.[27] However, as American jury verdicts are generally opaque, it is difficult to infer the significance a jury gave to this particular evidence. The precise impact of the gene-signature evidence is not entirely clear, especially because other defence expert testimony (such as the aforementioned testimony that Ra-226 and Ra-228 do not cause thyroid cancer) negated general causation and could have sufficed to persuade the jury to reach their verdict. Although it is unclear whether the jury chose to rely on this evidence, the case nevertheless demonstrates that sufficiently sensitive gene-expression profiling can provide decision-makers with an objective basis to reject a plaintiff's causation case.

Exposure biomarkers have also provided proof of alternative causation in cases where plaintiffs allege exposure to benzene caused their leukemia. In *Wells v Shell Oil Co,* the plaintiff alleged occupational exposure to benzene caused his AML (Acute Myeloid Leukemia).[28] The corporate defendant did not dispute general causation, namely that benzene is *capable* of causing AML, but instead disputed specific causation on the basis that benzene only causes types of AML that have specific cytogenetic markers – breaks in the fifth and seventh chromosomes. The jury found the defendant was not liable, after the defence expert testified that these specific genetic markers were not present in the plaintiff's cells.

However, there is judicial disagreement as to the validity of these markers. Only a few weeks after the decision in *Wells,* the court in *Lavender v Bayer Corp* rejected similar evidence as 'nothing more than an untested, unsupported hypothesis cloaked in the aura of scientific knowledge'.[29] The following year, similar evidence was also excluded in *Edwards v Safety-Kleen Corp*.[30] In this case, the defendant attempted to rely on the testimony of an oncologist,

[25] Howard Jarvis, E. Paige Sensenbrenner and Laura Whitmore, 'Genetics and Genomics: Making the Invisible Visible' (2015) *For the Defense* 64, 79.
[26] *Naomi Guzman v. ExxonMobil Corp* (n 17) 13.
[27] Jarvis, Sensenbrenner and Whitmore (n 25) 79.
[28] (DCE Texas, Jury verdict March 2, 1998); Marchant, 'Genetic Susceptibility and Biomarkers in Toxic Injury Litigation' (n 11) 97.
[29] (W Va Cir, No 93-C-226-K, May 29, 1998). See also, Marchant, 'Genetic Susceptibility and Biomarkers in Toxic Injury Litigation' (n 11) 97.
[30] 61 F Supp 2d 1354, 1359-60 (SD Fla, 1999).

who suggested that 'because the decedent's cytogenetic studies indicated a normal karyotype[31] and did not indicate any breakage of chromosomes 5 and 7, his MDS[32] could not have resulted from exposure to benzene'.[33] The Court rejected this testimony because

> By [the defence expert's] own admission, however, the literature he relied upon does not state with any degree of medical certainty that, absent abnormalities in chromosomes 5 or 7, it is very unlikely that the MDS or leukemia was caused by exposure to benzene. Rather, all of the literature in this regard is merely "suggestive" of that conclusion.[34]

Moreover, the expert's hypothesis 'has never been tested' and the 'one recent study' upon which the expert relied 'did not look at any other chromosomes [other than 5 and 7]'.[35] Finally, the defence expert conceded 'that up to 40 percent of people who develop MDS may not have *any* chromosomal abnormalities at all, and some people (albeit a small percentage) exhibit abnormalities in other chromosomes'.[36] The court therefore excluded this testimony on the basis that the expert's theory was 'not scientifically reliable' because it was untested, had not been subject to peer review and was not generally accepted in the relevant scientific community.[37]

The validity of this conclusion arguably still holds true today, especially considering later scientific studies querying an exclusive association between benzene exposure and deletions in chromosomes 5 and 7.[38] These studies show aberrations in these chromosomes are not *perfectly* sensitive markers of benzene-induced leukemia. The lack of perfect sensitivity helps justify rejection of the defence argument that absence of the marker implies absence of causation.[39] On the other hand, these studies also show that the 5/7 aberrations are *fairly*

[31] Chromosome analysis, also known as karyotyping, can be described as 'the original genetic test'. Although karyotyping is still used today, it only 'provides a bird's eye view' and a wide variety of more detailed genetic tests have since been developed, see Edwin Kirk, 'The Genes That Make Us: Human Stories from a Revolution in Medicine' (Scribe Publications, 2020) 11.
[32] Myelodysplastic syndrome – a disease of the bone marrow and blood, which may progress to leukaemia.
[33] 61 F Supp 2d 1354, 1359 (SD Fla, 1999).
[34] Ibid.
[35] Ibid.
[36] Ibid.
[37] Ibid 1360.
[38] See, eg, Luoping Zhang et al, 'The Nature of Chromosomal Aberrations Detected in Humans Exposed to Benzene'(2002) 32(1) *Critical Reviews in Toxicology* 1, 34 ('the loss and long-arm deletion of chromosomes 5 and 7 have been detected frequently in many leukemia patients with likely prior exposure to benzene' but also notes that 'the literature to date does not support the hypothesis that benzene-induced leukemias and preleukemic states are associated exclusively with these changes in chromosomes 5 and 7'); Luoping Zhang et al, 'Chromosome-wide aneuploidy study (CWAS) in workers exposed to an established leukemogen, benzene' (2011) 32(4) *Carcinogenesis* 605, 605 ('Chromosomal aneuploidy, including that of chromosomes 5 and 7, has been detected not only in benzene-related leukemia and preleukemia patients but also in healthy workers with current exposure to benzene'); Kequi Li, 'Increased leukemia-associated gene expression in benzene-exposed workers'(2014) 4(5369) *Scientific Reports* 1, 2-3 (where a deletion in chromosome 7 was found to be related to occupational exposure to benzene).
[39] See also Gold, 'When Certainty Dissolves into Probability' (n 1) 269-270.

sensitive markers of benzene exposure (even in exposed people who are presently healthy). If the marker is also specific to the benzene exposure-disease combination, the presence of the marker could imply causation. However, toxic tort evidence is almost always probabilistic not deterministic. The relevant question is therefore often not perfect sensitivity, but did the evidence help either party meet their burden of proof of more likely than not.

The courts in *Wells, Lavender and Edwards* reached vastly different conclusions depending on the degree to which they were or were not persuaded that the karyotypic marker was sufficiently sensitive. Each court's degree of persuasion could rest on (1) the scientific sophistication of the judges; (2) the precise presentation of evidence by experts for both sides; and (3) the skill of the lawyers. As Professor Marchant observes:

> The absence of aberrations in chromosomes five and seven thus may reduce but not eliminate the possibility that benzene was the causative agent. The attempts by defendants to argue that the absence of these chromosome aberrations positively excludes benzene as the cause of leukemia demonstrates once again that litigants are prone to exaggerate the significance of biomarkers and that at least some courts and juries are likely to be misled by such arguments.[40]

The judicial response to such evidence might also vary over time as researchers collect and publish more data supporting or questioning the marker's sensitivity.[41]

The case of *Henricksen v ConocoPhillips* reveals how an absence of specific genetic markers could undermine a plaintiff's case linking benzene exposure and leukaemia.[42] In this case, the court excluded the plaintiff's causation experts, in part, because they failed to consider whether the cause of the plaintiff's AML could have been *de novo*, i.e. unrelated to the benzene

[40] Marchant, 'Genetic Susceptibility and Biomarkers in Toxic Injury Litigation' (n 11) 98.
[41] For a recent US decision, see the Supreme Court of Pennsylvania decision in *Walsh v BASF Corp* 234 A 3d 446 (Pa, 2020). In that case, the Supreme Court upheld the decision of the Superior Court, which held that the trial court was wrong to dismiss expert 'opinion that medical science, in the form of cytogenetic studies of chromosomal aberrations [abnormalities of the fifth and seventh chromosomes which were identified in cytogenetic testing performed on the plaintiff], was proof of a causal link resulting in AML', see ibid 455. In particular, the Superior Court concluded that 'we find the existence of these studies, together with the differential methodology employed by [the expert], sufficient to pass muster under Frye', see 191 A 3d 838, 848 (Pa Super Ct, 2018). The case was remanded by the Supreme Court and it is currently an open question as to what impact this evidence would have on the final outcome. For an Australian case discussing benzene markers, see Part 5.3 of this chapter discussing *Farley-Smith v Repatriation Commission* [2010] AATA 637.
[42] 605 F Supp 2d 1142 (ED Wash, 2009). See also, Susan Brice and Whitney Christian, 'The Use of Genetic Evidence to Defend Against Toxic Tort Claims—Part II' (2017) 29(10) *Intellectual Property & Technology Law Journal* 9, 12.

exposure[43], as the majority of AML cases (80-90 percent) were *de novo*.[44] In particular, the court noted that

> Either cytogenetic or a distinct pattern of chromosomal aberrations have been considered characteristic findings in nearly ninety percent of all secondary AML, which includes AML caused by exposure to benzene as opposed to gasoline containing benzene. In de novo AML cytogenetic abnormalities are observed only in approximately fifty percent of the time. There was no evidence of chromosomal abnormality in [the plaintiff's] case.[45] [citations omitted.]

In short, the court observed that 90 percent of 'secondary AML' cases (AML caused by environmental factors, including benzene exposure) showed chromosomal abnormalities and were usually preceded by myelodysplastic syndrome. As the plaintiff had neither, the court concluded that the plaintiff's expert opinion was 'unreliable and inadmissible' because the plaintiff's 'presentation is very different from the typical case of chemically induced AML'.[46] Specifically, 'None of the features characteristic or commonly seen in secondary AML have been associated with [the plaintiff's case]' and the expert's methodology was also flawed because it failed to rule in and rule out *de novo* AML as a potential cause.[47] The damaging effect of this evidence on the plaintiff's case is, at least to some extent, reflected in the fact that the court ultimately granted summary judgment in favour of the defendants. The judge's opinion in this case more clearly shows the significance of genetic evidence compared to the aforementioned jury verdicts in *Guzman* and *Wells.*[48]

Genetic markers of effect also undermined the plaintiff's causation case in *Hallquist, ex rel Hallquist v EI Dupont De Nemours*.[49] The plaintiff alleged that exposure to benzene caused their multiple myeloma. The defence expert reviewed the plaintiff's medical records and concluded that they 'did not reveal "the type of biomarkers you would expect to see be altered" if he had been exposed to benzene during this period'.[50] As the plaintiff did not have the

[43] As Professor Steve Gold observes, the court displayed some confusion over the scientific terminology, as 'The court… appeared to equate idiopathic cases ("with no readily identifiable cause") with "endogenous" cases ("onset without external or environmental stimulus"), see 605 F Supp 2d 1142, 1149 (ED Wash, 2009); Gold, 'The More We Know' (n 3) 402.
[44] 605 F Supp 2d 1142, 1149-50 (ED Wash, 2009).
[45] Ibid 1150.
[46] Ibid 1163.
[47] Ibid.
[48] As juries typically do not provide reasons for their conclusion, making it difficult to draw an inference from jury verdicts, unless there is a special verdict form in which the jury expressly makes a finding on the causation element specifically.
[49] No. A-6223-12T2, 2014 NJ Super Unpub LEXIS 2458 (Super Ct App Div, Oct 10, 2014) [6]-[7].
[50] Ibid.

necessary mutations, the defence expert concluded that benzene exposure could not have caused the plaintiff's illness.[51] Ultimately,

> The compensation judge denied the petitioner's claim, finding that the [defence] expert was more credible, and the petitioner had not shown the level of exposure that her expert alleged was necessary to cause the decedent's cancer. The Appellate Division New Jersey Superior Court reviewed the compensation judge's findings and upheld the decision.[52]

Genetic markers of effect therefore seemed to play an influential role in disproving specific causation in this case.

An absence of genetic markers was also 'devastating' to the plaintiff's case in *Tompkin v Philip Morris USA, Inc*.[53] This case involved an allegation that the plaintiff's husband contracted lung cancer and 'died as a result of smoking cigarettes sold by the defendants'.[54] The defendant asserted that exposure to asbestos was the true cause of the plaintiff's cancer, rather than exposure to cigarette smoke.[55] In particular, a defence expert suggested that 'P53 and K-Ras studies [performed on the plaintiff] which test for genetic changes associated with smoking, were negative'.[56] In other words, the plaintiff's sample did not exhibit any genetic mutations consistent with smoking, leading the defence expert to conclude that asbestos exposure was a more likely cause of his cancer.[57] Professor Steve Gold notes that although the expert testified there were no markers of tobacco smoke damage in the plaintiff's tissue, 'The opinion does not make clear whether the expert testified that all tobacco-caused lung cancer displays these cellular or genetic markers'.[58] If the expert did make this testimony, it would have shown the markers were sufficiently sensitive to disprove causation. Ultimately, the jury decided that smoking did not cause the plaintiff's cancer and this decision was affirmed on appeal.[59]

[51] Scott Elder and Anderson Kemp, 'Genomics in the Courtroom: The Current Landscape of DNA Technology in Criminal and Civil Litigation' (2021) 88(1) *Defense Counsel Journal* 1, 9-10.
[52] Ibid.
[53] 362 F 3d 882, 894 (6th Cir, 2004). The 'devastating' quote is from the trial judge who inferred that the jury found the genetic testimony was particularly 'devastating' to the plaintiff's case, see Brice and Christian, 'Part II' (n 42) 12; Gold, 'The More We Know' (n 3) 403. It is also important to note that in the case of *Tompkin v American Tobacco* WL 36113663 (ND, Ohio 2001), a plaintiff alleging tobacco smoke caused his cancer was able to support specific causation by introducing expert evidence that he had specific chromosomal deletions which are more common in cancer victims who have smoked than in cancer victims who have not smoked. Even though the court upheld this evidence as admissible, the federal jury ultimately found in favour of the defendants.
[54] 362 F 3d 882, 882 (6th Cir, 2004).
[55] Ibid 890, footnote no. 5.
[56] Ibid.
[57] Ibid.
[58] See ibid 894; Gold, 'The More We Know' (n 3) 403, footnote no. 217.
[59] 362 F 3d 882, 894 (6th Cir, 2004).

5.2.2. Genetic Markers of Exposure/Effect as Proof of Causation

Genetic markers of exposure/effect have also been used by plaintiffs in an attempt to prove causation. In *Sutera v Perrier Group of America Inc*, the plaintiff's expert asserted that plaintiff's acute promyelocytic leukemia ('APL') was caused by drinking the defendant's sparkling mineral water, which was contaminated with benzene.[60] In particular, the plaintiff argued that evidence of his translocation between chromosomes 15 and 17 supported 'his theory of causation because benzene metabolites are known to cause specific chromosomal translocations, including the 15/17 translocation'.[61] The defendant's experts agreed that 'it's very likely that benzene metabolites could cause a translocation between chromosomes 15 and 17' and that this translocation is 'common in virtually all patients' with the plaintiff's type of leukaemia.[62] However, this acknowledgement was qualified by the assertion that this translocation appears in 'both those who have been exposed to chemical solvents and metals *and those who have not'* [emphasis added].[63]

Even though the defence experts 'agreed that benzene metabolites can cause a chromosomal translocation between chromosomes 15 and 17, both agreed that the mere fact that [the plaintiff] has this translocation is insufficient to prove that it was caused by the exposure to the Perrier water'.[64] This led the court to conclude that 'the translocation of chromosomes is insufficient to support causation'.[65] Therefore, these putative biomarkers of effect are limited by their inability to conclusively illustrate that the plaintiff's chromosomal change was caused by exposure to the defendant's product, as opposed to exposure to *any other* chemicals or metals.[66] So, the issue in *Perrier* ultimately seemed to be about inadequate specificity of the marker. As the putative marker occurs even in sick individuals without benzene exposure, the court found that the presence of the marker did not imply causation.

[60] 986 F Supp 655 (D Mass, 1997).
[61] Ibid 664.
[62] Ibid.
[63] Ibid.
[64] Ibid.
[65] Ibid. Summary judgment was ultimately ordered against the plaintiff for failing to adduce any 'reliable scientific evidence tending to show a causal link between Perrier and Sutera's leukemia', see ibid 668.
[66] The plaintiff's assertions in this case could also be further undermined by later scientific studies, which have returned inconclusive results relating to the effect of benzene exposure on 15/17 translocations, see, eg, Cliona McHale, 'Chromosome Translocations in Workers Exposed to Benzene' (2008) (39) *JCNI Monographs* 74, 74 ('t(15;17) transcripts were detected in two individuals, the result is inconclusive as one was exposed and the other was unexposed.').

By contrast, in *Milward v Acuity Specialty Products Group, Inc* the court did not accept the scientific basis for the plaintiff's expert's opinion that benzene caused the translocation *at all.*[67] This could simply be an extreme case of inadequate specificity (where a marker is so un-specific it is not associated with exposure at all), or it could be based on a distinct issue (such as an inability to demonstrate the particular translocation *in vitro*). The plaintiff's expert toxicologist claimed that 'In almost all cases of APL, there is a characteristic genetic alteration', namely a 15/17 chromosome translocation 'denoted as t(15;17) (q22;q12)'.[68] The expert conceded that

> The t(15;17) translocation is necessary, but not sufficient in itself, to induce APL[69]. In fact, APL occurs in only about ten percent of persons with that chromosomal translocation. In rare cases of APL, the chromosomal translocation is different, but in all cases chromosome 17 is involved.[70]

Despite these limitations, the expert attempted to argue that the plaintiff's exposure to benzene is probably the cause of the plaintiff's 15/17 translocation because benzene is known to cause some chromosomal damage.[71] In other words, the expert made 'the generalization that because…benzene causes damage to some chromosomes, it is "biologically plausible" that it causes damage to other chromosomes'.[72] However, the court initially excluded this expert opinion on the basis that

> general extrapolation is not justified and…there is no direct observational evidence that benzene causes the t(15;17) translocation [so] Dr. Smith's opinion — that because benzene is an agent that can cause some chromosomal mutations, it is "plausible" that it causes the one critical to APL — is simply an hypothesis, not a reliable scientific conclusion.[73]

The first district judge granted summary judgment to the defendants after excluding plaintiff's proffered expert on *general* causation. The court's initial exclusion of this expert testimony, because it was deemed to be scientifically unreliable, was later overturned on appeal. The US Court of Appeals for the First Circuit held that

> The court's analysis repeatedly challenged the factual underpinnings of Dr. Smith's opinion, and took sides on questions that are currently the focus of extensive scientific research and debate-and on which reasonable scientists can clearly disagree. In this, the court overstepped the authorized bounds of its role as gatekeeper.[74]

Ultimately, the '"alleged flaws" [initially] identified by the court go to the weight of [the expert's] opinion, not its admissibility. There is an important difference between what is

[67] 664 F Supp 2d 137 (D Mass, 2009), *rev'd* 639 F 3d 11 (1st Dist, 2011).
[68] *Milward v Acuity Specialty Products Group, Inc* 664 F Supp 2d 137, 143 (D Mass, 2009). See also, Brice and Christian, 'Part II' (n 42) 12.
[69] Acute promyelocytic leukemia – an aggressive type of AML (Acute myeloid leukemia).
[70] *Milward v Acuity Specialty Products Group, Inc* 664 F Supp 2d 137, 143 (D Mass, 2009).
[71] Ibid 147.
[72] Ibid.
[73] Ibid.
[74] *Milward v Acuity Specialty Products Group, Inc* 639 F 3d 11, 22 (1st Dist, 2011).

unreliable support and what a trier of fact may conclude is *insufficient* support for an expert's conclusion'.[75]

Although this evidence was eventually admitted, on remand, the second district judge again granted summary judgment for the defendant but, this time, the district judge held that the plaintiff's evidence of *specific* causation was insufficient.[76] In relation to the genetic evidence, the second district judge noted 'APL is known to be caused in part by a genetic translocation on chromosome 17 but, despite extensive research, there is no scientific consensus as to the causes of the translocation'.[77] As the plaintiff did not argue that the presence of the translocation in Milward's tumour proved specific causation, this comment by the second district judge was *obiter dicta*. This *obiter* comment was arguably contradicted by an Australian court delivering a different judgment in the same year.[78]

In some cases, the presence of exposure/effect markers can be useful to support causation. In *Harris v KEM Corp*, it was alleged that the plaintiff's leukemia was caused by workplace exposure to benzene contained in toxic cleaning products manufactured by the defendants.[79] One of the plaintiff's experts 'analyzed chromosomal tests of [the plaintiff] which showed aberrations indicative of leukemia caused by exposure to benzene, drugs, or radiation'.[80] As the plaintiff 'had not received radiation therapy and…the drug therapy he had received was unlikely to have caused [his] chromosomal aberrations'[81], the expert 'expressed the opinion that, given the factual assumption that [the plaintiff] was exposed to benzene, [his] chronic myelogenous leukemia was caused by that exposure'.[82] Therefore, the expert 'testified that [the plaintiff's] leukemia was evidenced by particular chromosomal aberrations that can be caused by exposure to benzene'.[83] A motion for summary judgment was denied and the case ultimately settled.[84] It is very difficult to know the role this evidence played (if any) in persuading the

[75] Ibid.
[76] *Milward v Acuity Specialty Products Group, Inc* 969 F Supp 2d 101, 116 (D Mass, 2013) ('*Milward*').
[77] Ibid 103.
[78] See Part 5.3.2 of this chapter.
[79] No. 85 Civ 2127(WK), 1989 WL 200446 (SDNY, 1989).
[80] Ibid 16. This expert was 'a specialist in oncology and hematology and [the plaintiff's] treating physician', ibid 2.
[81] Ibid 16.
[82] Ibid 9.
[83] Ibid 8.
[84] *Harris v Kem Corp,* No. 85 Civ. 2127(WK), 1990 US Dist LEXIS 11150 (SDNY, 1990). However, it is also important to note the case of *Hendrian v. Safety-Kleen Systems, Inc*., No. 08-14371, 12-13 (ED, Mich, 2014) where the court observed that the mere presence of chromosomal aberrations characteristic of benzene exposure is insufficient to prove specific causation. A differential diagnosis is still required to rule out 'all potential alternative causes, including, most importantly for purposes for AML, idiopathic origin'.

parties to settle. Presumably, the causation evidence was *supportive enough* to the plaintiff, or *not supportive enough* to the defence, to make the defendant conclude that it would not be worth the risk and expense of trial. The evidence could have been sufficiently ambiguous that the plaintiff, given the defendant's offer, reached the same conclusion and agreed to a settlement.

5.3. Genetic Markers of Exposure & Effect to Prove or Disprove Causation: Australian Case Law

Similarly to the US, Australian toxic tort litigants have been relying on genetic evidence since the 1990s. However, precious few opinions by appellate US or Australian courts have addressed genetic markers of exposure/effect as causation evidence, and none have done so in a general or comprehensive manner.

Many of the Australian cases involving exposure markers relate to gene patenting disputes,[85] criminal law,[86] classification of chemicals[87] and non-genetic markers in asbestos[88] cases.[89] Nevertheless, there is a small number of Australian cases involving genetic markers of exposure/effect in toxic torts.[90] It is notable that the vast majority of these arise in either

[85] See *D'Arcy v Myriad Genetics Inc* [2014] FCAFC 115; *Sequenom, Inc v Ariosa Diagnostics, Inc* [2019] FCA 1011.
[86] See *R v Karger* No SCCRM-98-224 [2001] SASC 64.
[87] *Dow Chemicals (Australia) Ltd v Director, Chemicals Notification and Assessment* [1999] AATA 1023; *Ciba Geigy Australia Ltd and Worksafe Australia Ltd* [1994] AATA 69.
[88] See *Agius v Amaca and Anor* [2007] NSWDDT 13 [2] ('pleural plaques…are a marker of exposure to asbestos); *Lola Merle Evans v Queanbeyan City Council and Anor* [2010] NSWDDT 7 [83] ('diffuse pleural thickening…is a marker of exposure'); *Shaw v Amaca Pty Ltd and Anor* [2008] NSWDDT 3 [7] ('pleural plaques…are markers of exposure to asbestos'); *McDonald v State Rail Authority (NSW) & Others* [1998] NSWDDT 4 [41] ('the presence of pathologically diagnosed asbestosis is a useful marker of exposure'); *Lo Presti v Ford Motor Co of Australia Ltd (No 2)* [2008] WASC 12 [495] ('pleural plaques are a marker of exposure to asbestos'); *McLoughlin and Military Rehabilitation and Compensation Commission, Re* [2006] AATA 825 [19] ('plaque was a marker of exposure to asbestos'); *Sinclair v Resi Corporation and Anor* [2003] NSWDDT 1 [10] ('Pleural plaques are markers of exposure to asbestos'); *D'Argenio v VWA* [2016] VCC 1955 [72] ('Pleural plaques are simply a marker of exposure').
[89] Three cases did not fall into any of these categories but were nevertheless irrelevant for present purposes, see *Plowman v Sisters of St John of God Inc* [2014] NSWSC 333 (medical negligence case concerning compulsion of genetic testing); *Cynthia Bernadette Murray (Legal Personal Representative of James Noel Murray (Decd) and Marcelle Agnes Murray) and Repatriation Commission* [1997] AATA 117 [10] ('skin cancer was used as a "surrogate marker" for exposure to UV light'); *CFMEU v AIG* [2002] QIRComm 5 [34] ('biological markers of exposure to fungi are largely unknown').
[90] *Farley-Smith v Repatriation Commission* [2010] AATA 637; *Farley-Smith v Repatriation Commission* [2005] AATA 968 ('*Farley*'); *Robyn Kathleen Cornish v Repatriation Commission* [1997] AATA 336 ('*Cornish*'); *Evers, Keith Leonard v Racecar Preparation and Management Pty Ltd* [2013] VCC 517 ('*Evers*'). Some cases are not, strictly speaking, toxic tort cases but the facts/judgments can be extrapolated to toxic tort scenarios, see, eg, *Telstra Corporation Ltd v Pine Rivers Shire Council* [2001] QPELR 350 ('*Pine Rivers*'); *Webb v Repatriation Commission* [2001] AATA 633 ('*Webb*').

tribunals or local/specialist courts. This suggests that, similar to the US,[91] such evidence is not being adduced in higher courts and/or that Australian toxic tort cases involving this evidence are typically negotiated, arbitrated, mediated and/or settled.

Despite the varying rules of evidence that apply in Australian lower courts and tribunals, an isolated analysis of the use of genetic evidence to support or refute causation in such cases can still be fruitful. For example, even though the Administrative Appeals Tribunal ('AAT') typically adopts significantly lower standards for admissibility and sufficiency of evidence (e.g. the AAT relies on the 'reasonable hypothesis' standard in *Farley-Smith*[92]), an analysis of these tribunal cases can still provide valuable insight into how litigants are using genetic evidence and the willingness of legal decision-makers to adopt such evidence in determining causation. We now turn to a discussion of Australian cases relating to genetic markers of exposure and/or effect.

5.3.1. Genetic Markers of Exposure/Effect to Disprove Causation

The central issue in *Farley-Smith v Repatriation Commission* was whether a veteran's benzene exposure during service 'precipitated [his] myelofibrosis', or alternatively, whether 'exposure to benzene in service precipitated a myelodysplastic disorder precipitating chronic myeloid leukaemia, which in turn precipitated myeloid fibrosis'.[93] This was complicated by the fact that the 'exposure to benzene occurred some 52 years before the veteran contracted myelofibrosis, and was at best intermittent whilst cleaning guns and machinery over a period of approximately 12 months'.[94]

A defence expert (Professor Fox – a haematologist) advanced the argument that there is no link between benzene exposure and myelofibrosis because the aberrations occur on different chromosomes.[95] In other words, 'it was his opinion that chromosome changes by benzene

[91] In the US, it appears genetic evidence has mainly been adduced in US trial courts with dispositions – such as settlements or jury verdicts – that do not generate judicial opinions.

[92] *Farley-Smith v Repatriation Commission* [2010] AATA 637 [207]:

> Applying what the High Court said in Bushell's case, we must find that the hypothesis raised by [the plaintiff] is reasonable if the material points to some fact or facts which support the hypothesis. In fact, the hypothesis may be reasonable even though an association between the disease and war service is not demonstrated or even if it is shown to be uncommon. A connection need not be proved. Nor is it decisive if the medical or scientific opinion supporting the hypothesis has little support in the medical profession or among scientists. In fact, where a medical practitioner who is eminent in the relevant field of knowledge puts a hypothesis forward, it will be rare where it can be said that such a hypothesis is unreasonable.

[93] [2005] AATA 968 [4]-[5]. The alternative hypothesis was arguably advanced because the potential link between benzene and leukaemia is more established than the link between benzene and myelofibrosis.

[94] *Repatriation Commission v Farley-Smith* [2007] FCA 1058 [17].

[95] *Farley-Smith v Repatriation Commission* [2005] AATA 968 [61].

would produce a different outcome to the chromosome changes to [the veteran as a result of his myelofibrosis]'.[96] Another defence expert (Professor Peach – an epidemiologist) also observed that

> in persons who have suffered myelofibrosis the chromosomes which have changed are numbered 1, 13 and 20. However in diseases caused by benzene exposure for example, acute myeloid leukaemia, the altered chromosomes are numbered 5, 7, 8 and 11. In studies which have been conducted in China, the chromosome changes in persons exposed to benzene have found to have chromosomes numbered 5, 7, 8, 11 and 21. In some laboratory studies where bone marrow has been exposed to benzene, the chromosome changes had been at numbers 5, 7 and 8. It therefore followed on this analysis according to Professor Peach, that the chromosome changes in persons exposed to benzene are different to the chromosome changes to persons who have not been exposed to benzene and who have suffered myelofibrosis. It followed therefore that benzene, on his analysis, did not cause myelofibrosis.[97]

However, this evidence did not appear to persuade the tribunal because the AAT ultimately held that there *was* a link between benzene and myelofibrosis.[98] On appeal, it was held that the Tribunal's decision should be set aside, and the matter be remitted to a differently constituted Tribunal.[99] The differently constituted Tribunal concluded that there was no link between benzene and myelofibrosis and this decision was upheld on appeal to the Federal Court of Australia.[100]

The differently constituted Tribunal also considered genetic evidence. This Tribunal again considered the evidence of the defence expert (Professor Peach) who expressed the opinion that:

> the hypothesis linking benzene exposure with MF [myelofibrosis] is contrary to the type of chromosomal aberrations that have, over recent times, been found to occur in MF…the major metabolite of benzene in the body has only been shown to produce aberrations of chromosomes 5, 7 and 8 in bone marrow. Aberrations of those chromosomes occur in acute myeloid leukaemia and myelodysplastic disorder, both of which are caused by benzene. However, aberrations of these chromosomes do not occur in MF.[101]

This time, the evidence appeared to persuade the Tribunal who concluded that:

> In our opinion, the more recent scientific studies in cytogenetics have clearly distinguished myelodysplastic disorder from MF. The aberrations caused by each disease occur on different chromosomes….As a result, studies linking acute myeloid leukaemia and myelodysplastic disorder with

[96] Ibid [87].
[97] Ibid [61].
[98] Ibid [95-6].
[99] *Repatriation Commission v Farley-Smith* [2007] FCA 1058. The reversal of the first tribunal's decision was based on a denial of procedural fairness, see ibid [47]-[65].
[100] *Farley-Smith v Repatriation Commission* [2010] AATA 637; *Farley-Smith v Repatriation Commission* [2012] FCA 80.
[101] *Farley-Smith v Repatriation Commission* [2010] AATA 637 [226]-[227]. See also [220] 'In his oral evidence, Professor Peach said that no one had actually demonstrated, at the laboratory level, a connection between benzene exposure and MF. He said that at a molecular level, cells have been exposed to substances which have resulted in chromosome aberrations but quite different from the chromosome aberrations that are involved in MF. He said the only evidence of a link between MF and benzene comes from epidemiological studies and from case reports.' At [221], Professor Peach dismissed these epidemiological studies and case reports, describing them as 'low levels of evidence [that have] not been conducted very well'.

> benzene do not constitute scientific evidence which points to a causal link between benzene exposure and MF.[102]

The Tribunal also appeared to be persuaded by Professors Peach and Fox's opinion that the *JAK2* gene mutation distinguishes MF from other blood disorders because this mutation occurs in persons who have MF but not in those who have myelodysplastic syndrome or leukemia.[103] The tribunal concluded that there was no causal link between benzene exposure and myelofibrosis.[104] They held that 'Given the very detailed expert analyses provided by Professor Peach and supported by Professor Fox, we find that the hypothesis relied on by Mrs Farley Smith, that Mr Farley-Smith's MF was connected to exposure to benzene, is not reasonable'.[105] The Tribunal therefore appeared to be strongly persuaded by the genetic evidence of the defence experts.

Evidence of genetic markers was also adduced by defendants in an attempt to show alternative causation in the case of *Webb and Repatriation Commission.*[106] The central issue was whether the plaintiff's death from non-Hodgkin's lymphoma was linked to his exposure to malaria during service or from cigarette smoking.[107] One of the experts, Dr Parkin, noted that translocations in the blood of smokers have 'a very, very high association with follicular lymphoma which in several studies has been shown to be associated with smoking. So, I mean, again, this isn't scientific proof, but it is far from a fanciful relationship'.[108] Another expert, Professor Fox, agreed with the hypothesis linking smoking and non-Hodgkin's lymphoma because 'with follicular lymphoma there is a chromosomal translocation, with respect to T-14 – 18' which he described as 'being associated with genetic abnormality'.[109] Although the tribunal did not directly address this evidence, the tribunal ultimately declined to find that

[102] Ibid [230].
[103] See, eg, ibid [213], [234], [238]. For example, Professor Fox 'referred to the JAK2 gene mutation [a mutation which distinguishes MF from other blood disorders] and noted that benzene has induced changes on different chromosomes. He said that discovery of the JAK2 mutation would suggest that benzene is not involved. Professor Fox said it is recognised that CML results from a quite different mutation, in fact the translocation between chromosomes with activation of a different oncogene to JAK2. Similarly, myelodysplastic syndrome appears to have a different molecular abnormality. On that basis, he said it was inappropriate to consider, on a hypothetical basis, that a factor that would be the cause of CML would also be the cause of MF', see ibid [234].
[104] Ibid [294]. In particular, the Tribunal held that 'the scientific medical research literature and the expert evidence do not establish a causative link between exposure to benzene and PMF'.
[105] Ibid [244].
[106] *Webb and Repatriation Commission* [2001] AATA 633.
[107] Ibid [8]-[9].
[108] Ibid [26].
[109] Ibid [36].

malaria can cause follicular lymphoma (i.e. the tribunal found insufficient evidence of general causation).[110]

The defence experts in *Webb* appeared to testify that a certain translocation is both more frequently found in smokers and in patients with follicular lymphoma.[111] This evidence goes to general causation of lymphoma by *tobacco smoking*, an alleged alternative cause. By itself the genetic evidence sheds no light on the plaintiff's allegation of general causation, namely that malaria can cause follicular lymphoma. If it was also proven that the plaintiff had the translocation, then the genetic evidence would have also been relevant to specific causation by an alternative cause, and therefore also tended to disprove specific causation by malaria (even assuming that general causation by malaria had been proven).

It is particularly interesting that the defence in this case, in an attempt to question whether malaria caused the plaintiff's lymphoma, used genetic evidence to link the lymphoma to smoking. One must wonder whether the genetic evidence also might have sufficed for a plaintiff claiming that tobacco caused their lymphoma.[112]

5.3.2. Genetic Markers of Exposure/Effect as Proof of Causation

The case of *Evers, Keith Leonard v Racecar Preparation and Management Pty Ltd* clearly demonstrates how decision-makers can be effectively persuaded by genetic evidence as a means of proving causation.[113] In this case, a motor racing mechanic alleged that his exposure to benzene in the workplace led to development of acute promyelocytic leukaemia ('APL').[114] The Victorian County Court ultimately held that the plaintiff had discharged the burden of proof, as the court was 'satisfied that the disease suffered by him (APL) is due to the nature of the employment in which he was engaged and that the nature of that employment gave rise to

[110] The tribunal ultimately concluded that 'on the whole of the material before us a reasonable hypothesis has not been raised connecting malaria with nHl [non-Hodgkin's lymphoma]', Ibid [97]. The decision was appealed to the Federal Court, with the conclusion that the decision be set aside and remitted to the AAT, but no reference was made to the evidence of chromosomal translocations on appeal, see *Gloria Webb v Repatriation Commission* [1997] FCA 1130. A subsequent appeal was dismissed, see *Repatriation Commission v Gloria Webb* [1998] FCA 1411.
[111] *Webb and Repatriation Commission* [2001] AATA 633 [26], [36].
[112] For example, in the case of *Tompkin v American Tobacco* WL 36113663 (ND, Ohio 2001), a plaintiff alleging tobacco smoke caused his cancer was able to support specific causation by introducing expert evidence that he had specific chromosomal deletions which are more common in cancer victims who have smoked than in cancer victims who have not smoked. Even though the court upheld this evidence as admissible, the federal jury ultimately found in favour of the defendants.
[113] [2013] VCC 517.
[114] Ibid.

a significantly greater risk of him contracting the disease than had he not been employed in employment of that nature'.[115]

The court accepted evidence adduced by the plaintiff's experts, which relied on 'the conclusion of the IARC[116] that there is sufficient evidence that benzene causes AML and that it probably causes leukaemias with chromosome translocations such as that found in APL'.[117] The 2012 IARC monograph outlined that 'In multiple studies in different occupational populations in many countries over more than three decades, a variety of genotoxic changes, including chromosomal abnormalities, has been found in the lymphocytes of workers exposed to benzene'.[118] This expert testimony 'included a quotation from the monograph to the effect that benzene metabolites can produce multiple genotoxic effects resulting in chromosomal changes in humans, and those changes may include the t15;17 translocation such as that found in the plaintiff'.[119]

The court was 'persuaded generally' by arguments concerning the genotoxic link between benzene and APL.[120] This is notably inconsistent with the above-mentioned US judgment (occurring in the same year) where the court observed that there is no scientific consensus that the 15;17 translocation is causally linked to benzene exposure.[121] This inconsistency suggests that genetic evidence does not alleviate the issue of causal indeterminacy but potentially exacerbates it, particularly where the science is not settled. As the cases have shown, where reasonable scientific minds could differ, reasonable judicial minds could also differ, leading to inconsistent judgments.[122] This is *especially* the case where putative genetic biomarkers have uncertain validity or limited sensitivity or specificity.

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[115] Ibid [140].
[116] International Agency for Research on Cancer, operating under the umbrella of the World Health Organisation.
[117] [2013] VCC 517 [140] (l). It was not disputed that 'APL is a sub-type of AML and involves genotoxic changes, including chromosomal abnormalities', see ibid [140] (i).
[118] Ibid [140] (i).
[119] Ibid [67]. It should be noted that, although this statement related to AML, the IARC review 'referred to benzene as a cause of AML, and APL is a sub-type of AML. There is nothing in the statement contained in the IARC monograph that suggested APL is excluded from the statement concerning AML'; see ibid [69].
[120] Ibid [140] (l).
[121] See *Milward* (n 76); See also *Sutera* (n 60) for another relevant inconsistent case (although not occurring in the same year as *Evers*). It is important to note that a defence expert in *Evers* (Professor Spencer) expressed a similar opinion to the US cases, namely that 'It was not known why the t15;17 translocations occur when they do or, to an extent, why they do…medical science did not know of environmental factors which promote a translocation and the commencement of disease'; see ibid [79]. The other defence expert, Professor Fox, also 'stated that no one knows exactly why, in APL, the t15;17 chromosomal translocation takes place'; see *Evers* (n 113) [99].
[122] It is also notable that (formally at least) in US federal courts and most US state courts, "scientific consensus" is not required for an expert opinion to be admissible, for a case to be submitted to the factfinder, or for a

This issue is also reflected in the case of *Robyn Kathleen Cornish and Repatriation Commission.*[123] In this case, the tribunal explicitly examined the utility of genetic evidence in supporting the plaintiff's causation case.[124] The relevant issue was 'Does exposure to the various chemical defoliants, pesticides and the drug dapsone to which our troops were exposed during their involvement in South Vietnam lead to the development of colon cancer?'[125] The plaintiff adduced evidence of an expert report exploring 'the toxicology of various chemicals to which Vietnam veterans were exposed', where the experts concluded

> As a result of his military service in Vietnam, [the deceased plaintiff] must be regarded to have been exposed to a mixture of chemicals, which have the capacity to induce cytochrome P450 enzymes. The reactions catalysed by these induced enzymes, as well as the actions of transition metal ions and other metabolic processes, tend to produce an excess of reactive oxygen species, and free radicals, leading to oxidative stress. The consequences of oxidative stress lead to membrane damage, cytotoxicity, *mutations, chromosomal aberrations* and carcinogenesis, as well as to other deleterious health effects. It is therefore *more likely than not that there is a causal connection* between the deceased's colon cancer and the chemical mixtures to which he was exposed during his military service in Vietnam.[126] [emphasis added.]

The tribunal was not impressed by this expert opinion. In fact, the tribunal noted that 'This is interesting scientific jargon, but it says nothing about the range of chemicals mentioned being carcinogenic in humans or whether those chemicals have been implicated in colon cancer'.[127] According to the tribunal, the 'fatal flaw' in this opinion was the fact that the authors 'have no special expertise in oncology', leading the tribunal to conclude that their opinion 'adds nothing to the medico-scientific argument in this case'.[128] Taking into account all other evidence, the tribunal determined that the plaintiff's cancer was not 'war-caused'.[129] The decision was overturned on appeal, but no mention was made of this particular expert testimony.[130]

It is unsurprising that the decision was overturned on appeal. The expert's reasoning presented a cogent mechanistic explanation for why the soldier's chemical exposures might cause colon

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factfinder to find in favour of a plaintiff. It is quite plausible that a jury could find causation "more likely than not" even though some part of plaintiff's scientific evidence is not supported by a "consensus".

[123] [1997] AATA 336.

[124] This was a decision of a specialist tribunal named the Veteran's Review Board ('VRB'). The VRB's decision was initially affirmed on appeal to the AAT and the reasons for the VRB's decision was extracted in the AAT's judgment, see ibid [24].

[125] Ibid [1].

[126] Ibid [24].

[127] Ibid.

[128] Ibid.

[129] Ibid. Although both the VRB and the AAT (in the first instance) held the plaintiff's cancer was not war-caused, the AAT relied on the plaintiff's genetic predisposition as proof of alternative causation, see Ibid [142] 'veteran had the misfortune to inherit a genetic predisposition to develop colon cancer from which he died. On the evidence I am satisfied beyond reasonable doubt that his death was unrelated to his operational service'.

[130] The re-hearing made mention of genetic predisposition but no mention of exposure markers or chromosomal aberrations, see *Cornish v Repatriation Commission* [2001] AATA 138.

cancer. This case highlights the importance of decision-makers assessing the overall picture created by all of the evidence, rather than considering each piece of scientific evidence in isolation. The problem in this case seems to be, not that the genetic evidence is unpersuasive, but that it presented a mechanism in the absence of an association. First, the plaintiff's experts did not seem to suggest that any portion of the described mechanism occurred in the decedent. This meant the evidence was of no relevance to proving specific causation. Second, the tribunal's desire for evidence that the chemicals are 'carcinogenic in humans' or 'implicated in colon cancer' seems to imply that epidemiologic[131] evidence of an association between exposure and illness is essential before an explanation of the molecular mechanism of causation will be deemed relevant. This position is similar to the ultimate disposition of *Milward*, but it is less well explained by the tribunal in this case. For example, the fact that the experts are not oncologists seems irrelevant as oncologists are concerned with treating cancer, not finding its causes.

This case signifies that, even at the turn of the century, decision-makers had no issue questioning the quality of genetic evidence and its ability (or lack thereof) to address the issue of causal indeterminacy in toxic torts. Clearly, decision-makers should not reject good genetic evidence and should not accept bad genetic evidence. However, as the science continues to develop, it is becoming increasingly important for decision-makers to better understand the field of genetics in order to accurately assess the utility of the causation evidence in a given case and to effectively articulate the impact of this evidence in their reasoning. Chapter 8 therefore calls for the creation of a Reference Guide to assist courts/tribunals/lawyers/litigants in interpreting this evidence in order to encourage consistency across judgments and across jurisdictions.

[131] The first instance AAT decision also appeared to place emphasis on epidemiologic evidence of an association between exposure and disease, see, eg [1997] AATA 336 [135]: 'all the epidemiologic studies…in which herbicide exposure was known to have been high have failed to reveal any consistent excess of cancers'. However, on re-hearing, the AAT held there was no need for epidemiologic evidence see, eg, *Cornish v Repatriation Commission* [2001] AATA 138 [82]: 'In the case of chemical carcinogenesis there are a number of reasons why the scientific literature may fail to confirm a causal association which does in fact exist. The latency between exposure and clinical presentation of tumor is one obvious example - the statistics may have been gathered before the complication has declared itself.' Ibid [85]: 'In this case the Tribunal concludes that the absence of evidence of a positive statistical correlation between chemical exposure and colonic carcinoma does not render the hypothesis untenable'.

5.4. Conclusion

Although genetic markers of exposure and/or effect can provide probative evidence of causation, the rapidly evolving scientific understanding of genetics has created significant difficulties in persuading a judge or jury of the validity and utility of such markers. Where the US courts view such markers to be sufficiently sensitive, their absence can be fatal to a plaintiff's case linking exposure and disease.[132] Where the courts believe the markers are not sufficiently sensitive, such evidence can be rejected as inadmissible.[133] At the same time, the presence of sufficiently specific markers can be useful to support a plaintiff's causation case.[134]

Australian cases have revealed some consistencies and some remarkable inconsistencies with US judgments occurring over a similar time period. Similar to some US judgments occurring at the turn of the century,[135] Australian cases revealed a level of early scepticism towards the ability of exposure markers to reveal a causal link between the defendant's negligence and the plaintiff's harm.[136] However, later Australian judgments[137] accepting a genotoxic link between exposure and disease were inconsistent with US judgments[138] in the same year, where the court observed in *obiter* that there was no scientific consensus indicating such a causal link. This discrepancy stems from a disagreement relating to the sensitivity and specificity of such markers.

These inconsistencies cannot be addressed through the adoption of different legal tests for factual causation. Without further guidance on the utility of such markers, this evidence will only further confuse and mislead the judge or jury. This could exacerbate the problem of causal indeterminacy, leading to inconsistent case outcomes and posing further obstacles to meritorious claims. As Chapter 8 concludes, inconsistencies in the case law signal that there is a need for further research and the development of practice-oriented instruments[139] in the form of a Reference Guide to assist litigants and legal practitioners in understanding the nature of

[132] See, eg, *Henricksen v ConocoPhillips* (n 42); *Tompkin v Philip Morris USA, Inc* (n 53).
[133] See, eg, *Lavender v Bayer Corp* (n 29); *Edwards v Safety-Kleen Corp* (n 30).
[134] See, eg, *Harris v KEM Corp* (n 79).
[135] See, eg, *Lavender v Bayer Corp* (n 29); *Edwards v Safety-Kleen Corp* (n 30); *Sutera v Perrier Group of America Inc* (n 60).
[136] See, eg, *Cornish* (n 123).
[137] See, eg, *Evers* (n 113).
[138] See, eg, *Milward* (n 76).
[139] Perhaps through a judicial reference manual, such as an addition to the Federal Judicial Center, *Reference Manual on Scientific Evidence* (National Academy of Sciences, 3rd ed, 2011). Planning is currently underway for the next edition of this Manual. In addition, courts could benefit from independent scientific guidance, such as court-appointed experts, assessors (aka 'independent guides of the court'), referees or a 'science panel'. For more information, see Chapter 8.3.

genetic evidence and how such evidence could be used to address the problem of causal indeterminacy in toxic torts. Chapter 8 demonstrates that the section of the reference guide discussing genetic markers of exposure/effect should highlight the importance of ensuring sufficient specificity and sensitivity of genetic markers. The following chapter of this thesis reveals how the reference guide could address notable inconsistencies in cases involving evidence of genetic markers indicating predisposition to disease or susceptibility to toxins.

6. Chapter Six: The Challenge of Proving Causation: Genetic Markers of Susceptibility as the Solution?

The previous chapter examined the utility of genetic markers of exposure/effect in proving causation, or alternative causation, in toxic torts. This chapter will extend the analysis of genetic evidence to encompass genetic markers of susceptibility/predisposition. Defendants could rely on the plaintiff's predisposition to disease as a means to disprove causation, by showing that the plaintiff's condition was caused by their genetic makeup rather than the toxic substance.[1] On the other hand, plaintiffs could argue that they had a genetic susceptibility to the relevant substance and that is why the substance caused their illness, even when other exposed persons (with a different genotype) remain uninjured.[2] In such cases, genetic evidence could help ensure the plaintiff satisfies the balance of probabilities threshold when the remaining evidence is insufficient to reach that threshold. The following chapter will assess the impact of genetic evidence by evaluating the growing practice of court-ordered genetic testing.

This chapter will demonstrate that genetic susceptibility markers can provide probative evidence of causation in a growing number of cases, but 'the statistical evidence in a case should be treated as *one piece of evidence among many*'.[3] Although genetic markers are personal to the plaintiff, they are still statistical in nature. A genetic marker indicating predisposition to disease or susceptibility to a particular toxic substance can typically only show an increased risk, not a certainty.

This chapter will argue that litigants, legal professionals, and courts should be wary of the limitations of predictive genetic test results[4] and only consider such evidence alongside other medical and scientific evidence. This includes, for example, toxicological and epidemiological studies (where available), individual medical records (including lifestyle factors, other co-morbidities, dysmorphology) and family medical history. As the following chapters will reiterate, it is imperative that courts consider the scientific evidence as a whole, rather than

[1] Steve Gold, 'The More We Know, the Less Intelligent We Are - How Genomic Information Should, and Should Not, Change Toxic Tort Causation Doctrine' (2010) 34(2) *Harvard Environmental Law Review* 369, 412-413; Australian Law Reform Commission, *Essentially Yours: The Protection of Human Genetic Information in Australia,* Report No 96 (2003) 1132-3; see also Gary Marchant, 'Genetics and Toxic Torts' (2001) 31 *Seton Hall Law Review* 949.
[2] Ibid.
[3] Susan Haack, *Evidence Matters: Science, Proof and Truth in the Law* (Cambridge University Press, 2014) 71-2.
[4] For more information on the science of genetics and genetic testing, see Chapter 4.

attempting to decide a case on the basis of an isolated piece of evidence. This chapter will begin with an overview of genetic susceptibility markers. Parts 6.2 and 6.3 will then critically examine the US and Australian case law involving genetic susceptibility markers to prove or disprove causation in toxic torts.

6.1. An Overview of Susceptibility Markers

Genetics can help to elucidate the considerable variability in each individual's response to a given toxin. Inherited susceptibility genes can broadly be divided into two groups[5] – those genes that only increase risk when exposed to a toxic substance[6], and those genes that increase risk regardless of exposure.[7] The former can be used by plaintiffs to support causation and the latter can be used by defendants to refute causation. There are several factors that complicate the use of genetic markers as a method of proof of causation. These include (a) penetrance; (b) multiple mutations; (c) statistical estimates; (d) gene-gene and gene-environment interactions; and (e) false positives.

[5] There are also 'protective genes' that can decrease your risk of developing a disease, for example, 'The *APOE* ε4 allele remains the strongest genetic risk factor for sporadic Alzheimer's disease *and the APOE ε2 allele the strongest genetic protective factor* after multiple large scale genome-wide association studies and genome-wide association meta-analyses', see Alberto Serrano-Pozo, Sudeshna Das and Bradley Hyman, 'APOE and Alzheimer's disease: advances in genetics, pathophysiology, and therapeutic approaches' (2021) 20(1) *The Lancet Neurology* 68, 68. It is also 'well established that the faulty allele that leads to sickle cell anaemia also confers resistance to malaria', see Susan Brice and Whitney Christian, 'The Use of Genetic Evidence to Defend Against Toxic Tort Claims—Part I' (2017) 29(9) *Intellectual Property & Technology Law Journal* 3, 8; see also H Franklin Bunn, 'The triumph of good over evil: protection by the sickle gene against malaria' (2013) 121(1) *Blood* 20. The difficulty of causation is 'made exponentially more difficult by the fact that some people have a genetic predisposition to diseases associated with [toxic] exposure, while others have a genetic composition that seems to protect them from the otherwise harmful effects of [toxic substances]', see *McMunn v Babcock & Wilcox Power Generation Group, Inc* (2017) 869 F 3d 246, 280. As the court in *McMunn* observes, 'more than one physician has counselled that the best way to guard against contracting cancer is to "choose your parents carefully"', ibid.

[6] In these situations, 'an interplay occurs between the environment and one's genetic makeup, known as a gene-environment interaction. For instance, genetic variations themselves influence susceptibility to environmental factors. The susceptibility then, in turn, determines whether specific environmental factors increase the risk of acquiring certain diseases. This explains why the human population responds differently to the same environmental factors', see Brice and Christian (n 5) 6. The *Third Restatement* provides the example of a plaintiff who 'has a predisposition to contracting a type of cancer' and 'An environmental exposure triggers the occurrence of cancer in that individual, who would nevertheless have contracted the cancer at some time in the future', The American Law Institute, *Restatement of the Law (Third), Torts: Liability for Physical and Emotional Harm* (The American Law Institute, 2010) *('Third Restatement')* §31, Comment *(c).* It is suggested that 'When this situation obtains, the measure of damage must be adjusted to reflect that the actor has not caused the other person to suffer the harm long-term or until death, but rather for some short period, as indicated by the evidence in the case', ibid §31, Reporter's Note to Comment *(c).*

[7] See, eg, Gary Marchant, 'Genetic Data in Toxic Tort Litigation' (2016) 45(2) *The Brief* 22, 23 ('plaintiffs' genetic traits, which increase susceptibility for a particular toxic substance or create a predisposition to disease without any environmental exposure, can be used to argue for or against causation').

6.1.1. Gene Penetrance

Evidence of susceptibility can take the form of general genetic/molecular epidemiological studies, 'individualised' genetic test results and/or family medical history. The penetrance of a genotype is an important factor in determining causation. Penetrance reveals the likelihood that a genetic variation will result in a disease or disorder.[8] Where the relevant genes are less penetrant, it is more difficult to establish the evidentiary relationship between susceptibility and exposure.[9] However, even though low penetrance genes 'do not invariably produce disease…they [do still] affect the likelihood of developing disease'.[10] For example, individual low penetrance alleles confer low risk, but a person with many low-risk alleles collectively faces a greater risk of disease.[11]

6.1.2 Multiple Mutations

Genetic test results might be definitive for monogenic diseases where the gene is highly penetrant, revealing a precise diagnosis (such as Huntington's disease and cystic fibrosis).[12] However, within the 20-30,000 genes in the human genome, it is estimated that there are greater than 4 million Standard Nucleotide Polymorphisms (SNPs).[13] This complicates the interpretation of even monogenic diseases because thousands of different mutations could each produce the same genetic condition, for example, cystic fibrosis could be produced by over 1,600 different mutations arising in various parts of the *CFTR* gene.[14] The penetrance and expressivity (i.e. the severity of the symptoms) of certain diseases, such as cystic fibrosis, can also vary depending on the type of mutation that is inherited.[15]

[8] Jennifer Champagne, 'Genetic Testing and Testimony in Toxic Tort Litigation: "Admissibility and Evaluation"' (2011) 13(1) *North Carolina Journal of Law & Technology* 1, 17.
[9] Ibid.
[10] Gold, 'The More We Know' (n 1) 385.
[11] To illustrate, GWAS 'identified half a dozen new susceptibility alleles [related to breast cancer]; these occur relatively frequently in the population, but individually confer small increments of risk ranging from seven to twenty-six percent', see Steve Gold, 'When Certainty Dissolves into Probability - A Legal Vision of Toxic Causation for the Post-Genomic Era' (2013) 70(1) *Washington & Lee Law Review* 237, 256.
[12] Huntington's Disease and Cystic Fibrosis are both monogenic disorders that are near 100% penetrant - meaning all affected individuals will develop the disease.
[13] See, eg, William Gahl et al, 'Genetic Approaches to Rare and Undiagnosed Diseases' in Robert Kliegman and Joseph St Geme (eds), *Nelson Textbook of Pediatrics* (Elsevier, 2020) 683.
[14] Gold, 'When Certainty Dissolves into Probability' (n 11) 255; see also Gold, 'The More We Know' (n 1) 385.
[15] Gold, 'When Certainty Dissolves into Probability' (n 11) 255 ('The mutations, located in various parts of the gene, affect the protein in various ways that produce disease of varying severity').

The predictive value of an individual susceptibility allele is complicated by the fact that there is typically more than one gene that could produce a given disease. For example, some *APOE* alleles are known to increase the risk of Alzheimer's disease[16], but other genes also seem to influence the risk of Alzheimer's.[17] This means that 'There is no one "Alzheimer's disease gene"'.[18] More generally, the ever-growing number of 'disease genes' creates additional difficulties in interpreting genetic test results for a given disease.[19]

Matters are further complicated by the fact that some mutations can only be indicative of susceptibility if they are identified in non-cancerous tissues. For example, 'studies have shown that certain mutations in the *BAP1* gene (a tumor suppressor gene) that render its protein product inactive are associated with increased risk of mesothelioma and several other cancers'.[20] As Dr Lisa Bailey and Dr Robyn Prueitt explain:

> because *BAP1* mutations have been observed as both somatic mutations in tumor tissue (i.e., they were acquired during the process of tumor development) and as inherited germline mutations in all non-cancerous tissues of susceptible individuals, the *BAP1* mutations must be identified in normal cells to prove inherent susceptibility of an individual.[21]

It is therefore crucial that only non-cancerous tissue is tested, but 'It is not always possible to gain access to non-cancerous tissue, particularly if the patient has passed away'.[22]

6.1.3 Statistical Estimates

The complexity of genetic susceptibility is further exacerbated by the fact that genetic test results could only be mildly predictive of a genetic condition, simply revealing a pre-symptomatic, predictive diagnosis (such as a *BRCA1* mutation indicating a 40-70% increased risk in breast cancer).[23] These susceptibility markers can only provide a statistical estimate of

[16] See, eg, Serrano-Pozo, Das and Hyman (n 5).
[17] Gold, 'When Certainty Dissolves into Probability' (n 11) 255-6.
[18] Ibid.
[19] According to the genetics database 'GeneCards', as at 10 January 2022, over 18,870 'disease genes' have been identified, see Weitzmann Institute, *GeneCards* (Webpage) <https://www.genecards.org/>; see also Brice and Christian, (Part I) (n 5) 5.
[20] Lisa Bailey and Robyn Prueitt, 'Case Law Highlights SouthEast: Genomics in Toxic Tort Litigation - Are We There Yet?' (2016) 17 *Environmental Litigation and Toxic Torts Committee Newsletter* 26, 27.
[21] Ibid 28.
[22] Ibid.
[23] Although there is considerable variability in the estimated penetrance of *BRCA1* mutations, most studies suggest it ranges from 40-70%, see, eg, Sining Chen and Giovanni Parmigiani, 'Meta-analysis of BRCA1 and BRCA2 Penetrance' (2007) 25(11) *Journal of Clinical Oncology* 1329; Karoline Kuchenbaecker, 'Risks of Breast, Ovarian, and Contralateral Breast Cancer for *BRCA1* and *BRCA2* Mutation Carriers' (2017) 317(23)

an increased risk. As Professor Edwin Kirk explains, 'The risks of people with *BRCA1* and *BRCA2* mutations are greatly increased compared with the general population, but there are no certainties. Some carriers live their lives unaffected by cancer, while others with the same genetic make-up die young'.[24] In other words, there are many people who will inherit a susceptibility allele but suffer no ill-effects.

6.1.4 Gene-Gene and Gene-Environment Interactions

In addition, for many genetic polymorphisms, whether high-risk alleles lead to disease also depends on other factors (such as other genes, environmental, toxicokinetic and epigenetic factors), which modify the extent to which a particular genotype confers risk.[25] In the context of toxic injury, 'if both toxic exposure and genetics are risk factors for disease, to properly

Journal of the American Medical Association 2402. However, some studies suggest it could be as high as 87%, see, eg, Roger Milne and Antonis Antoniou, 'Modifiers of Breast and Ovarian Cancer Risks for *BRCA1* and *BRCA2* mutation carriers' (2016) 23(10) *Endocrine-Related Cancer* T69.

[24] Edwin Kirk, 'The Genes That Make Us: Human Stories from a Revolution in Medicine' (Scribe Publications, 2020) 58. See also Gold, 'When Certainty Dissolves into Probability' (n 11) 277: 'susceptibility genes do not determine that an individual of a particular genotype will contract a specified illness if subjected to a given exposure. Rather, "[t]hey modify risk." So, for example, even though a particular genotype of the NAT2 gene makes it much more likely that a woman smoker will develop breast cancer, not all women of that genotype who smoke end up with breast cancer; some women who smoke develop breast cancer even though they do not have that genotype; some women develop breast cancer even though they neither smoke nor have that genotype. And multiple studies of toxic susceptibility genes are unlikely to give identical results because of the influence of other factors and of random chance' (footnotes omitted). See also Gold, 'The More We Know' (n 1) 415: 'In the same way that classical epidemiologic studies have implicitly assumed the genetic homogeneity of the exposed and unexposed populations, studies that look for and find susceptibility alleles implicitly assume that the populations with and without the gene are homogeneous with respect to toxic exposures. Not everybody who has the BRCA1 susceptibility allele develops breast cancer. Studies estimating the degree to which the gene increases risk have produced varying results. What if some or all of the variance is explained by toxic exposures, or by the interaction of toxic exposures with epigenetic factors? Some evidence already suggests this may be the case for the relatively large risks imparted by certain BRCA alleles that appear to increase breast cancer risk in general but also may act like toxic susceptibility genes with respect to cigarette smoke.' (citations omitted); see also *Booth v Fourmeninapub Pty Ltd* [2020] NSWCA 57 [55] 'The person may have a test for the BRCA2 gene, but if it is confirmed that he or she has that gene, it still does not mean he or she has the disease. Nor did the person have breast cancer when he or she was born, even though almost certainly the person had from before birth a genetic predisposition to breast cancer'.

[25] Gold, 'When Certainty Dissolves into Probability' (n 11) 264-5, 277; see also ibid 27 ('not all individuals with a BAP1 mutation who are exposed to asbestos will develop mesothelioma. Other genes…and other environmental factors, such as ionizing radiation…may also affect risk, but may be hard to identify'); Gold, 'The More We Know' (n 1) 410-411 ('much variation in susceptibility to toxin-produced disease may be multigenic, but gene-gene interactions are difficult to assess. Epigenetic differences, perhaps only from an earlier stage of a patient's life, may affect susceptibility. A welter of personal factors - nutrition and diet, for example - may promote differential susceptibility to toxic exposures, even in genetically similar people. Some of the apparent heterogeneity in susceptibility to toxic substance exposure may itself result from toxic substance exposure! And even if a genetic variation affects susceptibility to a substance's disease-producing effects, the heightened susceptibility may be elusive if it manifests only when exposure exceeds a threshold dose. These difficulties suggest that although molecular epidemiology will sharpen the picture, it may not provide quite as high definition as hoped' (footnotes omitted)); David Adelman, 'The False Promise of the Genomics Revolution for Environmental Law' (2005) 29 *Harvard Environmental Law Review* 117, 122, 141.

analyze their causal effects would require knowing, both qualitatively and quantitatively, how they affect risk jointly as compared to separately: are their effects additive[26], synergistic[27], or antagonistic[28]?'[29] Ultimately, there is 'a staggering amount of variability' in determining whether a genetic variation increases susceptibility to a toxin.[30] As Gold explains, 'Because of gene-gene or gene-environment interactions, individual genetic variants do not typically determine the occurrence of disease, either alone or in combination with exposure to toxic substances'.[31] Jennifer Champagne also maintains that 'The type and quality of mothering an individual receives, the genes an individual possesses, and the environment in which an individual is raised are all factors affecting the characteristics of that individual. However, no one factor alone is typically deterministic.'[32] The interpretation of genetic test results can become further distorted by the fact that 'the same genetic variation can have a different impact on susceptibility within different populations and ethnic groups'.[33] The difficulty of interpretation can also be increased by differing biological arguments (such as genetic exceptionalism/determinism).[34] Ultimately, 'determining and quantifying' the interaction of risk factors 'is difficult and controversial even as a scientific matter, much less as a matter of law'.[35]

[26] The effects are additive where causal agents operate independently to increase risk, e.g. total risk = tobacco *plus* asbestos.
[27] The effects are synergistic when the sum of the effects is greater than the product of the individual effects combined, e.g., total risk = tobacco *plus* asbestos *plus* further contribution from positive synergistic interaction.
[28] The effects are antagonistic when the 'joint effect is less than the sum of each [risk factor] separately in an additive model or less than the product of each separately in a multiplicative model', Joseph Sanders et al, 'Differential Etiology: Inferring Specific Causation in the Law from Group Data in Science' (2021) 63 Arizona Law Review 851, 901-2.
[29] Gold, 'The More We Know' (n 1) 394 explaining arguments of Susan Poulter. Susan Poulter, 'Genetic Testing in Toxic Injury Litigation - The Path to Scientific Certainty or Blind Alley?' (2001) 41(2) *Jurimetrics* 211, 222.
[30] Gold, 'When Certainty Dissolves into Probability' (n 11) 274.
[31] Ibid 274. In an earlier paper, Gold explains that there is a 'fundamental problem with treating genetic predisposition as an alternate cause. The very derivation of the relative risk of a particular genetic variant is unlikely to be independent of toxic exposure, because toxic exposure almost certainly will not be a controlled variable in the study', see Gold, 'The More We Know' (n 1) 415.
[32] Jennifer Champagne, 'Genetic Testing and Testimony in Toxic Tort Litigation: "Admissibility and Evaluation"' (2011) 13(1) *North Carolina Journal of Law & Technology* 1, 20.
[33] Ibid 19; Kirk (n 24) 174. As Kirk explains, 'There is an unfortunate oversupply of studies done in people with European ancestry, unfortunate because of the serious lack of similar studies in people from other populations', Kirk (n 24) 174.
[34] Champagne (n 32) 16. For more information on the role of genetic exceptionalism, see Chapter 7.3.
[35] Gold, 'The Holy Grail' (n 51) 61.

6.1.5 False Positives

Another layer of complexity lies in the fact that many genetic associations are false positive or valid but overstated.[36] As Kirk explains, 'in the early days of GWAS [genome-wide association studies][37], there were numerous GWAS "hits" that turned out to be statistical blips with no relationship to reality'.[38] Even if the study is valid, it is possible that 'the genetic difference does not, of itself, have any direct bearing on the risk of [illness]'.[39] Gold also highlights the role of random chance in GWAS where 'false positive results are easy to obtain and difficult to exclude'.[40] He suggests that 'many of the processes associated with toxicity and disease are simply random'.[41] This creates unique difficulties for the field of toxicogenomics due to the added uncertainty that plagues much of genetics, as 'Over the past decade, it has become uncomfortably obvious that it is very easy to get it wrong in genetics…Population data alone aren't the whole solution, unfortunately, because there is variation that is harmless but rare, as well as variation that is harmless and common'.[42] Due to this inevitable uncertainty, genetic variants can easily be wrongly classified as disease-causing.[43] This uncertainty arises not only from the quality of the studies, but also from the reliability of the whole enterprise of genetic testing, as genetics is an emerging field.

Geneticists must grapple with the fact that 'not only are some *variants* wrongly reported as disease-causing, there are plenty of *genes* that have been wrongly associated with conditions'.[44] To illustrate, 'the genes *CACNB2* and *KCNQ1* are both commonly included in panels of genes

[36] Gold, 'The More We Know' (n 1) 387; Gold, 'When Certainty Dissolves into Probability' (n 11) 264.
[37] Genome-wide association studies (GWAS) are the primary means of identifying genetic influences on genetic disease, see, eg, Kirk (n 24) 173. These studies 'examine large numbers of genes in persons with and without a disease to determine if particular DNA variations are statistically associated with higher disease incidence', see Gold, 'When Certainty Dissolves into Probability' (n 11) 256.
[38] Kirk (n 24) 174.
[39] Ibid.
[40] Gold, 'When Certainty Dissolves into Probability' (n 11) 264. For more on sources of error in study designs, see Chapter 2.1.4.
[41] Ibid 280. 'Experiments have shown that even genetically identical cells exposed to the same environmental conditions can display random variations in gene expression, leading to significant differences in the chemical and phenotypic characteristics of the cells… "Nowadays it is commonly stated that disease is either genetic or environmental, when in reality stochastic events are equally important', see Gold, 'When Certainty Dissolves into Probability' (n 11) 280. Gold concludes that 'It does not matter whether the connection between exposure and disease is really random or whether it only looks random because a truly deterministic pathway is too complex to be fully specified. What matters is that for the foreseeable future, science will not be able to give law a deterministic answer. Look closely enough, and certainty dissolves into probability', see Gold, 'When Certainty Dissolves into Probability' (n 11) 280-1.
[42] Kirk (n 24) 91.
[43] Ibid.
[44] Ibid 92.

for testing people with hypertrophic cardiomyopathy, despite there being only a tenuous link between these genes and this condition'.[45] As a result, there is a real risk that individuals will be informed that a variant in one of these genes could cause a heart condition.[46] This means that tested individuals could wrongly be reassured that they are not at risk or wrongly informed that they are at risk of the relevant condition.[47]

Kirk explains that 'uncertainty is a constant in clinical genetics, and it comes in various forms…All too often, we do a test and find ourselves uncertain about whether the result means anything at all'.[48] This uncertainty means that the mere absence of genetic markers will often be insufficient to disprove causation and the mere existence of such markers will often be insufficient to prove causation.[49] Genetic markers alone will rarely provide conclusive evidence. Genetic data is still population-based so it does not fit with the traditional deterministic model of but for causation.[50] This means that genetic markers are most useful at the population level and are not determinative of individual causation because these markers could be present even without causation.[51] An individual who inherited a susceptibility allele might never develop the relevant disease. However, genetic data can often provide probabilistic evidence that increases or decreases the likelihood of causation, which can be useful if it helps either party meet the more likely than not burden of proof.

[45] Ibid.
[46] Ibid.
[47] Ibid.
[48] Ibid 77.
[49] Bailey and Prueitt (n 20) ('While one can envision different scenarios as to how this information may be used by both plaintiffs and defendants, the state of the science for either side of the argument has many uncertainties that need to be resolved, indicating that genomic information alone does not provide definitive evidence for or against causation').
[50] Gold, 'When Certainty Dissolves into Probability' (n 11). See also Gold, 'The More We Know' (n 1) 400: 'classical epidemiology has a weakness: "the failure to consider the genetic component of any disease-risk factor association . . . dilute[s] the impact of the risk factor in the population, thereby reducing the ability to detect effects of genotypes and exposures."' But similarly, in a genetic epidemiology study the failure or inability to consider other environmental factors, epigenetic factors, multi-gene interactions, and the like will dilute the impact of both the genotype and the toxin being studied. Thus, even where toxicogenomic information is available, it will not represent a "fixed" toxic susceptibility value for a particular gene, but rather the average of a range of susceptibility values associated with that gene across the range of modifying factors. That average, estimated by a sampling process, will be characterized by a degree of uncertainty. This uncertainty, spawned by random chance and the undetected influence of other factors, helps to explain why toxic susceptibility genes do not determine disease causation - "[t]hey modify risk."' (footnotes omitted).
[51] Steve Gold, 'The Holy Grail? The Potential of Genomics to Shape Toxic Tort Litigation' (2016) 58(4) *DRI For the Defense: Toxic Torts and Environmental Law* 59, 62.

Advances in genetic technologies promise to rapidly produce vast amounts of data, but this will only magnify the difficulties in interpreting the data that is produced.[52] To elaborate, it is a 'safe bet…that genetic testing will become more and more commonplace', for example, 'Exome sequencing has already gone from being an exotic, very expensive test ordered only by clinical geneticists to being a routine test ordered by many different specialists'.[53] However, there remains 'a problem that doesn't have an obvious end in sight: the problem of interpretation…the hardest part isn't generating the data - it's understanding what it means'.[54] For example, 'Even when we're looking at variants in a single gene that are known to be linked to a specific genetic condition, it can be a challenge to be sure if the changes you find are the cause of the [patient's condition] or not'.[55] This will clearly continue to present significant challenges to toxic tort litigants who rely on genetic evidence as a means of proving or disproving causation, and courts who are being asked to try to interpret the data.

6.2 Genetic Markers of Susceptibility to Prove or Disprove Causation: US Case Law

Despite the persistent uncertainty clouding the field of genetics, toxic tort litigants have increasingly suggested that genetics could explain the difference in individual susceptibility to disease.[56] In particular, genetic markers could indicate a plaintiff's increased genetic susceptibility to the particular toxic substance or genetic predisposition to the related disease.[57]

Courts have generally been receptive to defence evidence revealing a genetic predisposition, and this evidence has sometimes been detrimental to a plaintiff's case.[58] The strongest defence case would rely on individual genetic test results evidencing the presence of sufficiently sensitive[59] markers in the plaintiff's genome, combined with expert testimony indicating a strong family history of the relevant disease. A plaintiff's genetic predisposition, in and of itself, will typically be insufficient to disprove causation. Such an argument requires 'that the

[52] Ibid 64.
[53] Kirk (n 24) 240.
[54] Ibid 241.
[55] Ibid.
[56] Jamie Grodsky, 'Genomics and Toxic Torts: Dismantling the Risk-Injury Divide' (2007) 59(6) *Stanford Law Review* 1671, 1688-89; Gold, 'The More We Know' (n 1) 389.
[57] Gold, 'The More We Know' (n 1) 407.
[58] See, eg, *Harris v Secretary of HHS*, 2014 WL 3159377 (Not reported in Fed Cl)*; Snyder v Secretary of Department of HHS,* 2009 WL 332044 (Fed Cl, Feb 12, 2009)*; Godfrey v Secretary of HHS,* 2014 WL 3058353 (Not reported in Fed Cl) ('*Godfrey*').
[59] See, eg, Gold, 'When Certainty Dissolves into Probability' (n 11) 267-277. For more information, see discussion in Chapter 5.

toxic and genetic risk factors are additive', rather than synergistic.[60] If the risks factors are synergistic, they interact so the toxic risk cannot be excluded as a cause. It is therefore crucial that courts consider evidence of a plaintiff's genetic predisposition alongside all the other available evidence, including any toxicological/epidemiological studies, individual medical records, lifestyle factors, and/or testimony as to differential aetiology.

A growing number of plaintiffs are countering the defendant's argument of genetic predisposition, by instead suggesting their genetic predisposition made them more susceptible to the defendant's product.[61] This is the modern equivalent of the 'eggshell' plaintiff whose genetic makeup makes other factors (such as chemical exposures) more likely to increase their risk of injury.[62] Although this evidence can be helpful in supporting a plaintiff's causation case, it is wrong to assume 'that a genetically based susceptibility to toxic exposure [constitutes] specific—that is, individualized or "particularistic"—causation evidence'.[63] This is because the 'genetic subpopulations studied by molecular epidemiology are still populations, not individual cases of disease' and the outcome of such studies is 'still a probabilistic relative risk that exposure poses to a person of a given genotype as compared to the risk faced by a person of the same genotype in the absence of exposure'.[64] So, genetic susceptibility evidence inevitably carries similar issues to other population-derived data.

Both defendants and plaintiffs should avoid making the assumption that genetic evidence constitutes 'an entirely unequivocal, definitive, "scientific" statement of the "truth", particularly with respect to specific causation'.[65] Litigants, legal professionals, and courts should acknowledge the limitations of this evidence and avoid 'overselling' it.[66] Otherwise,

[60] Gold, 'The Holy Grail?' (n 51) 61.
[61] See, eg, *Dwyer ex rel Dwyer v Secretary of HHS* 2010 WL 892250; *Rite Aid Corp v LevyGray*, 876 A 2d 115, 140 (Md App, 2005), aff'd, 894 A 2d 563 (Md, 2006); Beck (n 79) 35-6; *RK, on behalf of AK v Secretary of HHS* 2015 WL 10936124; *Murphy v Secretary of HHS* 2016 US Claims LEXIS 677; *Godfrey* (n 58); *Durden v Secretary of Dept of HHS* 2007 WL 4962000, 18.
[62] A defendant will remain liable for the plaintiff's total harm even where the plaintiff has a pre-existing condition or unusual characteristic/s resulting in harm of a greater magnitude or different type than might be reasonably foreseeable, see, eg, The American Law Institute, *Restatement of the Law (Third), Torts: Liability for Physical and Emotional Harm* (The American Law Institute, 2010) §31; *Smith v Leech Brain & Co Ltd* [1962] 2 QB 405. This is not strictly relevant to factual causation but is relevant to proximate cause/scope of liability/remoteness. Although this thesis largely confines its scope to a discussion of factual cause as identified in Chapter 1.3, it is necessary to briefly discuss the eggshell skull rule in order to provide a robust analysis of genetic susceptibility evidence.
[63] Gold, 'The Holy Grail' (n 51) 62.
[64] Ibid. ('This simple truth is easily overlooked when considering the technological achievements of toxicogenomics, but it is central to consideration of how courts likely will respond, as well as how they should respond, to the output of this technology').
[65] Gold, 'The Holy Grail?' (n 51) 65.
[66] Ibid 65. For more information on the limitations of genetic evidence, see Chapter 7.1.

this evidence will only add further complexity to the litigation. Chapter 8 emphasises the need for a framework to avoid the misuse of genetic evidence in civil litigation.

The following section will first consider how defendants have used genetic predisposition to establish alternative causation. It will then go on to examine how plaintiffs have adduced evidence of a genetic susceptibility to support their causation case.

6.2.1 Genetic Markers of Susceptibility to Disprove Causation

A growing number of defendants have sought to argue an inherited genetic defect caused the plaintiff's disease as opposed to toxic exposure.[67] Where genetic testing was unavailable, defendants have been able to request a plaintiff's individual and familial medical history of disease to argue that genetic predisposition was a cause of plaintiff's illness.[68] Even before the human genome was sequenced, defendants attempted to rely on a plaintiff's genetic background (in the form of family medical history) to support an alternative causation defence.[69] This shows that the use of genetic evidence is not a new idea in proof of causation, but what is changing is the accuracy/detail of this evidence (although there undoubtedly remain questions about what the genetic evidence actually indicates in a given case).

The US Secretary of Health and Human Services, in defending claims in the vaccine court[70], 'has been by far the most prominent advocate' of using genetic predisposition as an alternative cause.[71] To illustrate, there have been several cases where plaintiffs allege their injury was caused by the diphtheria and tetanus toxoids and acellular pertussis vaccine ("DTaP").[72]

[67] Marchant, 'Genetic Data in Toxic Tort Litigation' (n 7) 23.
[68] Champagne (n 32) 12.
[69] See, eg, Gary Marchant, 'Genetic Susceptibility and Biomarkers in Toxic Injury Litigation' (2000) 41(1) *Jurimetrics* 67, 98.
[70] This is the Office of Special Masters of the US Court of Federal Claims. Also known as the National Vaccine Injury Compensation Program. This no-fault compensation program was established in 1988 for resolving vaccine injury claims. It was designed to remove vaccine injury cases from the civil courts.
[71] As Professor Gold explains, 'Defendants have argued that a plaintiff's genetic endowment, rather than an accused exposure, is the actual cause of the plaintiff's condition. The United States government, in claims under the Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§300aa-1-300aa-34, has been by far the most prominent advocate of this position', see, eg, Gold, 'The Holy Grail?' (n 51) 60; *Simanski v Secretary of HHS* 115 Fed Cl 407 (2014) *aff'd*, 601 Fed Appx 982 (Fed Cir, Feb 26, 2015) ('*Simanski*'); *Hopkins v Secretary of HHS* 84 Fed Cl 530 (2008); *Godfrey* (n 58) 23 ('Simply put, respondent's experts proffered opinions that I find more reliable and persuasive than those of [plaintiff's expert]. Genetics alone is a sufficient and "but for" cause for Ms. Godfrey's condition.'); *Wintz v Northrop Corp* 110 F 3d 508, 511-514 (7th Cir, 1997); *Chapman v Procter & Gamble Distributing* 766 F 3d 1296, 1310 (11th Cir, 2014).
[72] See, eg, *Waters v Secretary of HHS* 2014 WL 300936 (Fed Cl, Jan 7, 2014) ('*Waters*'); *Sucher v Secretary of HHS* 2010 WL 1370627 (Fed Cl, Mar 15, 2010); *Snyder v Secretary of HHS* 553 Fed Appx 994 (Fed Cl, Jan 28, 2014) ('*Snyder*').

Evidence of genetic predisposition has been successful in disproving causation in these cases, so long as the plaintiff tests positive for the relevant mutation.[73] The key mutation in a number of cases involved the *SCN1A* gene, 'although not definitive, variant SCN1A genes have been *associated* with, depending on the range of symptoms, familial hemiplegic migraines, generalized epilepsy with febrile seizures plus ("GEFS+"), and SMEI [Severe Myoclonic Epilepsy of Infancy]' (emphasis added).[74]

It has been more difficult for defendants to maintain an alternative causation argument where the plaintiff does not have the relevant gene mutation. For example, in *Sucher,* the plaintiff tested negative for a mutation of the *SCN1A* gene.[75] Despite the fact that the defence experts 'did not view as dispositive the fact that [plaintiff's] SCN1A testing found no genetic link'[76], the court ultimately held the DTaP vaccine caused the plaintiff's condition and was not superseded by any possible genetic predisposition.[77]

By contrast, in *Snyder,* the plaintiffs' genetic test results revealed variants in the *SCN1A* gene, leading the court to conclude that the *SCN1A* gene mutations were, more likely than not, the sole cause of the plaintiffs' seizure disorders.[78] In other similar cases, the court also concluded that the plaintiff's condition was caused by their *SCN1A* mutation, as opposed to vaccine-related causation.[79] In such cases, it is imperative that the courts do not treat genetic evidence as determinative of causation, but instead view this evidence as part of the bigger picture, especially because association is not causation. Simply because *SCN1A* is associated with seizure disorders, this does not mean it *causes* such disorders. Moreover, as noted earlier, genetic evidence is still statistical/population-level data, which means it carries many of the problems associated with other forms of statistical data.[80] The different outcomes of the testing

[73] Ibid.
[74] *Snyder* (n 72) 996. Plaintiffs have also suggested the *SCN1A* gene mutation makes them more susceptible to environmental triggers (eg vaccines), see, eg, *Faoro v Secretary of HHS* 2016 WL 675491 (Fed Cl, Jan, 29, 2016).
[75] See *Sucher* (n 72) 15.
[76] For example, one of the defence experts suggested 'there's other reasons why you can have epilepsy. It's not just SCN1A, there's SCN1B, there's SCN2A', see ibid 49. The expert also explained that 'when [plaintiff] was tested for genetic mutations that could be associated with a predisposition for seizures, there were not then available the plethora of tests that now abound', see ibid 50. The plaintiff in this case also had a strong family history of febrile seizures, see, eg, ibid 51.
[77] By contrast, the plaintiff's expert appeared to argue there was a genetic susceptibility, see, eg, ibid 112. The court seemed to prefer the plaintiff's expert testimony, see, eg, ibid 116-122.
[78] *Snyder* (n 72) 999, 1004.
[79] *Waters* (n 72) 23; *Deribeaux v. Sec'y of HHS* 717 F 3d 1363, 1368 (Fed Cir, 2013). See also James Beck, 'The Coming Ubiquity: Product Liability Implications of Pharmacogenomic Advances' (2015) 57(9) *DRI For The Defense: Drug and Medical Device* 33, 37.
[80] For more information, see Chapter 6.1. Certainly, if the relevant mutation is a highly penetrant, highly specific mutation that causes the disease at issue, the fact that the genetic data are population-based is reduced to

in *Sucher* and *Snyder* at least partly explains the very different outcomes of these two cases. In *Sucher*, there was no alternative causation because the plaintiff did not test positive for the variation and, in *Snyder*, the defendants were able to prove alternative causation where the plaintiff had the relevant *SCN1A* variation. It is therefore appropriate they came to the opposite outcome. That simply shows that the genetic evidence was relevant and outcome-determinative.

In addition to the different outcomes of the genetic tests in these cases, it is interesting that the court in *Sucher* appeared to accept the plaintiff's expert testimony but the court in *Snyder* dismissed the same expert.[81] The Court in *Snyder* observed that '[i]n his entire career, [plaintiff's expert] has not focused on genetics or seizure disorders. The basis of [his] opinions comes from his interpretation of medical articles about genetic epilepsies. This research was done for the purpose of presenting an opinion in this case'.[82] By contrast, the Court explained the defence experts 'study neurologic problems associated with genetic abnormalities as a regular part of their full-time careers, and they counsel patients with genetic mutations that cause neurological problems….[t]heir professional duties give them a depth of knowledge that is not matched by [plaintiff's expert]'.[83] Changes in scientific understanding or methods seem to go a long way toward reconciling these apparently conflicting holdings. These cases ultimately reveal the importance of using experienced experts who are aware of the most recent scientific advancements.[84]

The tension between *Sucher* and *Snyder* highlights one of the fundamental issues with genetic test results. The science of genetics is ever-evolving, more and more mutations are being identified as causes of a given disease, and the scope and precision of genetic test results is vastly improving. A defence expert in *Sucher* explained that 'there's other reasons why you can have epilepsy. It's not just SCN1A, there's SCN1B, there's SCN2A' and the plaintiff had a strong family history of febrile seizures but 'when [plaintiff] was tested for genetic mutations that could be associated with a predisposition for seizures, there were not then available the

a triviality, i.e., 100% of mutation carriers develop the disease and 100% of non-carriers do not. In regards to *SCN1A*, 'penetrance varies by phenotype', e.g., the penetrance is estimated 'to be 70% for the GEFS+ phenotype [but] 90% for the familial simple febrile seizure phenotype', see Ian Miller and Marcio Sotero de Menezes, '*SCN1A Seizure Disorders*' in Adam Ardinger et al (eds), *Gene Reviews* (US National Library of Medicine, 2007-2022).

[81] The same defence and plaintiff experts were used in both cases, except for one additional defence expert in *Snyder*.

[82] *Snyder* (n 72) 1001-2.

[83] Ibid 1002.

[84] Ibid 1000-1003.

plethora of tests that now abound'.[85] So, adopting the defence expert's logic, the genetic test results were not definitive proof that there is no possible genetic predisposition. The expert seems to be relying on the cliché that 'Absence of evidence is not evidence of absence'. However, the expert's assertions would have been far more persuasive if they were supported by scientific literature suggesting a causal link between these other mutations (e.g., SCN1B and SCN2A) and epilepsy, as well as genetic test results evidencing the presence of the relevant mutations in the plaintiff's genome.

Genetic test results are becoming an increasingly crucial component of a defendant's alternative causation case. In some cases, expert opinion on possible genetic causes has been totally excluded where the expert is unable to produce a genetic test result showing the plaintiff in fact possesses the relevant predisposition.[86] For example, in *BNSF,* the court excluded 'general evidence that genetics and heredity could play a role in degenerative spinal conditions', due to 'the absence of any evidence that [plaintiff] had a genetic predisposition to such injuries'.[87] This seems entirely as it should be – such evidence would have no bearing on the case if the plaintiff did not have the relevant genetic predisposition. Given that courts have previously used evidence of family medical history as evidence of genetic predisposition, courts should still give weight to such evidence but they should also insist on having the actual genetic test results, so long as the test is sufficiently directed to causation of the plaintiff's injury as described in Chapter 7.

Interestingly, in another case occurring in the same year as *BNSF,* the plaintiff's causation case was actually undermined by their refusal to obtain genetic testing to confirm or reject the defence theory of alternative causation.[88] In that case, compensation was denied partly because the plaintiff's 'have done very little to refute these conclusions [that their injury was not vaccination-related but was caused by an inherited genetic condition], including allowing genetic testing'.[89] This case suggests there is an interaction with the burden of proof depending upon which party is seeking to rely on the genetic evidence. Of course, if genetic susceptibility forms part of the plaintiff's case, then they need to undergo genetic testing to adduce evidence of that. However, defendants should not be allowed to raise a general wide-ranging suggestion of genetic causes and thereby tip the balance of the evidence unless the plaintiff agrees to

[85] *Sucher* (n 72) 49-51.
[86] See, eg, *BNSF Ry Co v Phillips* 434 SW 3d 675 (Tex App Fort Worth, May 22, 2014).
[87] Ibid 682, 703.
[88] *Simanski* (n 71) 427.
[89] Ibid.

genetic testing. As argued in Chapter 7, defendants should raise a specific genetic condition or trait, rather than fish for evidence.

Where a sufficiently strong genetic explanation exists for the plaintiff's symptoms, their claim may be denied if they fail to obtain genetic testing. However, if the possible genetic explanation advanced by the defence is weak, the expert testimony should be entirely excluded if it is unsupported by evidence of the plaintiff's genetic predisposition. As James Beck explains, 'Unsurprisingly, defense-side pharmacogenomics alternative cause evidence also needs to be supported adequately by both known facts and expert testimony. Otherwise, a defendant's assertion of a genetically based alternative cause runs the risk of failing'.[90]

Some courts have suggested experts are not required to rule out genetics as a potential cause of the plaintiff's illness.[91] On the face of it, this seems like a reasonable approach, it cannot be for the plaintiff to actively rule out genetic conditions unless the defendant has identified specific relevant potential conditions or traits. For example, in *Kirk,* the court held that experts are not required to rule out all possible causes when conducting a differential aetiology.[92] Similarly, the court in *Bettisworth* observed that a differential aetiology opinion 'can be reliable with less than full information' so the relevant expert in this case was not required to 'sufficiently investigate [plaintiff's] possible…genetic predisposition'.[93]

However, several other courts have required genetic predisposition be considered as part of an expert's differential aetiology.[94] These courts have refused to admit causation testimony that does not rule out genetics as an alternative cause of the relevant disease.[95] For instance, in *Blackwell,* the court observed that '[the trial judge] did not err in finding that "a gene or series

[90] Beck (n 79) 37.
[91] See, eg, *Bettisworth v BNSF Railway Co* 2020 WL 3498139 (D Neb, June 29, 2020) ('*Bettisworth*'); *Kirk v Schaeffler Group USA* 2014 WL 2807681 (WD Mo, June 20, 2014) 3.
[92] *Kirk v Schaeffler Group US* 887 F 3d 376, 392 (8th Cir, 2018).
[93] *Bettisworth* (n 91) 8-9.
[94] See, eg, *Blackwell v Wyeth* 408 Md 575, 616-8 (Md, 2009) ('*Blackwell*'); *Doe v Ortho-Clinical Diagnostics* 440 F Supp 2d 465, 477-8 (MDNC, 2006) ('*Doe*').
[95] Ibid; *Schenk v Novartis Pharmaceuticals Corp* 2014 WL 3656904 (D Ariz, July 23, 2014) 4-5; *Henricksen v Conoco Phillips Co* 605 F Supp 2d 1142, 1162 (ED Wash, 2009); *Perry v. Novartis Pharms. Corp* 564 F Supp 2d 452 (ED Pa, 2008); *Blackmon v American Home Products Corp*, 346 F Supp 2d 907, 919 (SD Tex, 2004); *Soldo v. Sandoz Pharms Corp* 244 F Supp 2d 434, 517 (WD Pa, 2003); *Medalen v Tiger Drylac USA, Inc,* 269 F Supp 2d 1118, 1139 (D Minn, 2003); *Kane v Motorola, Inc*, 779 NE 2d 302, 309 (Ill App, 2002). See also Beck (n 79) 37-8; Joseph Eaton, Kara Kapke, and Apryl Underwood, 'Medical Genetics in Chemical Exposure Cases: Genetic Testing of a Plaintiff – The Pros and Cons' (2012) 54(1) *DRI: For the Defense* 58, 65: 'Likewise, courts have excluded medical causation testimony when the expert ruled out a limited portion of genetic causes but ignored other known and unknown genetic causes', see, eg, *Hendrix v Evenflo Co,* 255 FRD 568, 598 (ND Fla, 2009) aff'd, 609 F 3d 1183 (11th Cir, 2010); *Doe* (n 94) 447-48; *DeLuca v Merrell Dow Pharms, Inc,* 791 F Supp 1042, 1044, 1054 (DNJ, 1992) ('*DeLuca*').

of interacting genes that have not yet been identified" is the "most prevalent alleged cause of autism," based upon our review of the record. We agree that [plaintiff's expert] did not sufficiently consider genetics in his differential diagnosis equation'.[96] Such cases are however open to doubt because, just as in any plaintiff's attempt to prove causation by differential aetiology, proper doctrine would require some evidence to 'rule in' genetics as a cause before requiring a plaintiff to 'rule out' genetics.

Similarly, in *Doe v Ortho-Clinical Diagnostics, Inc*, the court refused to admit the plaintiff's expert testimony on specific causation partly on the basis that his differential diagnosis was not properly performed because he failed to consider the 'high probability that an unknown genetic cause cannot be ruled out as the specific cause of [the plaintiff's] autism'.[97] In other words, the expert's 'differential diagnosis failed to acknowledge the one conclusion that is generally accepted in the medical community with respect to the causation of autism, which is, that its cause is genetic, but that the exact genetic sequence of autism is unknown'.[98] So, the court in *Doe* emphasised that there was a scientific consensus that a genetic cause exists, even if it cannot be ruled out. The court also appears to suggest the expert's differential aetiology was deficient, not because they failed to rule out an *unknown* cause, but because their opinion was *inconsistent* with the scientific consensus and did not appear to take any account of that consensus. However, if generalised beyond the context of autism, it seems inappropriate to require plaintiffs to prove a negative (e.g., that genetics did not cause the plaintiff's disease), absent sufficient evidence of the positive (e.g., that genetics might have caused the plaintiff's disease).

As a result of advancements in genetics, experts are increasingly relying on individualised genetic test results to bolster their testimony. As Joseph Eaton, Kara Kapke and Apryl Underwood explain, a reliable differential aetiology 'cannot simply dismiss genetics as a possible alternative cause without providing a scientifically valid basis for doing so'.[99] For example, a plaintiff's expert is likely to sufficiently rule out genetics where the plaintiff (and potentially also their parents) have undergone 'a full battery of all genetic testing, and the test results showed there was no known genetic cause for [their] injury'.[100] On the other hand,

[96] *Blackwell* (n 94) 616.
[97] 440 F Supp 2d 465 (MDNC, 2006).
[98] Ibid 477-8.
[99] Eaton, Kapke and Underwood (n 95) 65.
[100] *Castillo v EI DuPont de Nemours & Co* 854 So 2d 1264 (Fla, 2003) where the court held an expert sufficiently ruled out genetics after the plaintiff's parents were genetically tested and the results showed no known genetic cause for plaintiff's injury; see also ibid.

simply inquiring into the plaintiff's family history is unlikely to be sufficient for ruling out genetics as an alternative cause.[101] So, there seems to be some support in the US courts for the inclusion of genetic test results in a differential aetiology analysis. However, it should be emphasised that this conclusion is derived from only a fairly small number of cases in a very limited set of factual contexts. Also, in evaluating the utility of this evidence, courts should remember that genetic evidence 'will simply provide an increasingly detailed description of probabilistic associations--population-based frequencies rather than deterministic certainties'.[102]

6.2.2 Genetic Markers of Susceptibility as Proof of Causation

While a plaintiff's genetic predisposition can be used to disprove causation, the lack of such predisposition can be used to support a plaintiff's causation case 'by ruling out other potential causes'.[103] The absence of a predisposition might strengthen the plaintiff's case that it was the exposure that caused their illness.[104] Even at the turn of the century, courts were willing to permit expert testimony indicating an absence of the relevant illness in a plaintiff's family history in order to strengthen the case that exposure caused the plaintiff's illness.[105] This creates some tension with the aforementioned cases where courts held the absence of family history was insufficient to rule out genetics as an alternative cause.[106] This tension reveals that, while some courts are willing to accept an absence of family history as a method of supporting causation, other courts may also require genetic testing and/or accompanying expert testimony of geneticists before accepting that there is no genetic predisposition. Surely with the increased accuracy, efficiency and affordability of genetic testing, the latter requirement would, in a growing number of cases, be a more effective means of ensuring there is no genetic predisposition.[107]

[101] Experts have been excluded where they only inquire into the plaintiff's family history to rule out genetics as an alternative cause, see, eg, *National Bank Commerce v Dow Chemical Co* 965 F Supp 1490, 1522 (ED Ark, 1996); *DeLuca* (n 95) 1044.
[102] Gold, 'The Holy Grail' (n 51) 65.
[103] Champagne (n 32) 9.
[104] On the other hand, the presence of a susceptibility to toxic triggers could support the plaintiff's causation case by making them an eggshell plaintiff.
[105] See, eg, *Landrigan v Celotex Corp* 605 A 2d 1079, 1082 (NJ Supp Ct, 1992); Champagne (n 32) 9-10.
[106] See *National Bank Commerce v Dow Chemical Co* 965 F Supp 1490, 1522 (ED Ark, 1996); *DeLuca* (n 95) 1044.
[107] For more on genetic testing, see Chapter 7.

With the advent of genetic testing, negative genetic test results have been used (in addition to an absence of relevant family history) to strengthen the plaintiff's causation case. In *Village of Buffalo Grove*, the court considered evidence that the plaintiff's genetic test results 'showed no deleterious mutation', and this 'genetic test lowers the likelihood that [plaintiff's] cancer was due to a hereditary cause, however, not all mutations are detectable and, not all genes were tested' but '[g]iven the negative test results…and the lack of a strong family history of cancer, an underlying gene mutation cause of his cancer is unlikely'.[108] The court concluded that evidence of the plaintiff's 'exposure to noxious and carcinogenic substances, as well as genetic and other medical evidence show[ed] a decreased likelihood that [plaintiff's] cancer arose independent of his service as a firefighter'.[109]

Similarly, the case of *In re Prempro* also reveals how an absence of relevant genetic mutations, and the presence of certain exposure, could support a plaintiff's causation analysis.[110] In this case, the plaintiff alleged that her use of hormone replacement therapies caused her breast cancer. The defence appealed the trial court's decision, arguing that a plaintiff's expert failed to consider how genetic predisposition (such as a relevant *BRCA1 or BRCA2* mutations or family history) could be alternative causes of the plaintiff's breast cancer.[111] However, the court affirmed the trial decision because the plaintiff had already submitted to all available genetic tests and all results were negative for the most common breast cancer genetic mutations.[112] Although the defence experts maintained that genetics caused the plaintiff's illness, the jury decided exposure to hormones caused her cancer.[113]

Plaintiffs have sought to rely on the eggshell principle to explain why their exposure caused their illness. The 'eggshell principle' traditionally refers to a doctrine holding a defendant liable for all harm caused to a particularly vulnerable plaintiff even though the degree of harm caused to the plaintiff was unforeseeably greater than that which a normal plaintiff would have suffered. That is not really an issue of factual causation. This chapter uses 'eggshell' to refer to the rather different situation in which an exposure causes harm to the plaintiff even though the same exposure would not be sufficient to induce harm in a person with a different genetic endowment. As Professor Gary Marchant explains, 'Even if epidemiology studies show that

[108] *Village of Buffalo Grove v Board of Trustees of the Buffalo Grove Firefighters' Pension Fund* 141 NE 3d 1200, 1203, 1207 (Ill Appell Ct, Jan 17, 2020).
[109] Ibid 1218.
[110] *In re Prempro Products Liab Litig* 586 F 3d 547 (8th Cir, 2009).
[111] Ibid 566.
[112] Ibid.
[113] Ibid.

the relative risk in the general population is less than 2.0, genetically susceptible ["eggshell"] plaintiffs could argue that their individual risk is higher than the general population due to their unique susceptibility, and indeed may exceed the twofold legal threshold'.[114] For example, plaintiffs in *In Re TMI Litigation* alleged that they developed thyroid cancer as a result of exposure to radioactive waste emanating from the defendant's facility.[115] They suggested that even if the general population would not have developed cancer as a result of this exposure, the plaintiffs had a genetic susceptibility to ionising radiation which increased their risk of illness.[116] However, this argument failed because the plaintiffs did not adduce evidence to show they in fact carried the relevant susceptibility gene/s.[117] Genetic susceptibility arguments also failed in *Hall v Baxter* where the court rejected expert testimony of susceptibility to silicone because the plaintiffs offered no proof that they carried any gene variants conferring susceptibility.[118]

In *In Re Bendectin,* the plaintiffs asserted that 'there was a genetic susceptibility to Bendectin that varied among individuals'.[119] However, this argument was undermined by the fact that 'all their witnesses testified only that there were individual susceptibilities to drugs in general. No one testified that there was such a susceptibility to Bendectin'.[120] The court subsequently concluded that the trial judge was correct to advise counsel 'that if the plaintiffs argued to the jury that there was such an individual susceptibility to Bendectin, he would have to instruct the jury that there was no evidence to that effect'.[121] The evidence in *In Re Bendectin* was clearly even more generalised than the evidence in *In Re TMI* and *Hall.* Due to the state of the science at the time these cases were heard, it was particularly difficult for plaintiffs in these cases to adduce sufficiently specific genetic evidence.

[114] Marchant, 'Genetic Data in Toxic Tort Litigation' (n 7) 23.
[115] *In re TMI Litigation* 193 F 3d 613, 622 (3d Cir, 1999); ibid.
[116] Ibid.
[117] Ibid.
[118] *Hall v Baxter* 947 F Supp 1387, 1456 (D Or, 1996); See also Champagne (n 32) 10; Marchant, 'Genetic Data in Toxic Tort Litigation' (n 7) 23.
[119] *In Re Bendectin Litigation* 857 F 2d 290, 317 (6th Cir, 1988). For more information on *In Re Bendectin,* see Chapters 2.2.1 and 2.2.4. The failure of proof in the Bendectin cases did not result simply from the lack of tools for assessing gene-toxin-disease associations. As Chapter 2.2.1 of this thesis highlights, the plaintiffs' problem in Bendectin was the failure of large epidemiologic studies to discern any association at all between exposure and birth defects in the population at large. The plaintiffs' failure did not arise simply because they could not prove heightened toxic susceptibility among people with certain genotypes. Nevertheless, this case is important in showing that, even in the 1980s, plaintiffs attempted to argue they were genetically susceptible to toxins.
[120] Ibid.
[121] Ibid.

Even as the science has continued to improve, plaintiffs have still struggled to show they have the genetic variation that confers susceptibility.[122] For instance, in *Kolakowski,* the plaintiff could not prove their claim because 'even if medical literature had identified a genetic predisposition for enhanced sensitivity to mercury toxicity, no genetic analysis was done in this case to test [plaintiff]] for such a gene expression'.[123] Similarly, in *Easter,* expert testimony that 'some children are genetically susceptible to mercury poisoning' was precluded where the plaintiff did 'not meet th[at] genetic profile'.[124]

These cases all demonstrate that plaintiffs raising a genetic susceptibility argument will struggle to prove their claim without test results showing the plaintiff carries the relevant susceptibility gene/s. Genetic susceptibility evidence will only be relevant to a plaintiff's causation case if they can show not only the mere possibility of susceptibility, but also that the plaintiff has the genetic variation that confers such susceptibility.[125] As the court in *Mills* explained, 'when a plaintiff asserts a claim based on something in his or her own genome, he or she is responsible for producing the evidence to prove it'.[126] Mills involved a motion to dismiss at the pleadings stage. The plaintiff's complaint in Mills acknowledged that factual causation depended on whether plaintiff possessed a susceptibility allele, but rather than test in advance of filing (which would have made the filing unethical had the test turned out "wrong" for the plaintiff), the plaintiff alleged the presence of the allele only on '[u]pon information and belief'. [127] As the plaintiff could not really have 'believed' any 'information' about the allele, but could easily have obtained that information, dismissal of the case made sense. However, this is different from a case in which a plaintiff argued, for example, that an unknown genetic variation increased the plaintiff's particular risk from exposure-related disease above the overall relative risk reported in an epidemiologic study. Professor Marchant suggests that 'To prevail on such arguments in the future, plaintiffs will likely need to undergo genetic testing to substantiate their claims of genetic susceptibility'.[128] This approach is surely correct because liability depends upon specific causation not merely general causation.

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[122] See, eg, *Trainer v Secretary of HHS* 2013 WL 4505803, 7 (Fed Cl, July 24, 2013); *Kolakowski v Secretary of HHS* 2010 WL 5672753, 43 (Fed Cl, Nov 23, 2010) ('*Kolakowski*'); *Easter v Aventis Pasteur* 358 F Supp 2d 574, 575 (ED Tex, 2005) ('*Easter*'); *Agee v. Purdue Pharmaceuticals* 2004 WL 5352989, 3 (WD Okla, Nov 22, 2004), aff'd, 242 F Appx 512 (10th Cir, 2007); *Rimbert v Eli Lilly & Co* 2009 WL 2208570, 19 (DNM, July 21, 2009), aff'd, 647 F 3d 1247 (10th Cir, 2011); *Mills v. Bristol-Myers Squibb Co* 2011 WL 4708850, 2 (D Ariz, Oct 7, 2011) ('*Mills*').

[123] *Kolakowski* (n 122) 43.

[124] *Easter* (n 122) 575; Marchant, 'Genetic Data in Toxic Tort Litigation' (n 7) 23.

[125] Champagne (n 32) 12.

[126] *Mills* (n 122) 2.

[127] Ibid 3.

[128] Marchant, 'Genetic Data in Toxic Tort Litigation' (n 7) 23.

In the recent talcum powder litigation, counsel for the plaintiffs was able to effectively rely on the eggshell principle to suggest plaintiffs whose genetic test results showed a *BRCA1* or *BRCA2* mutation were 'move[d]…closer to the edge of the cliff [and were] in especially precarious situations for being exposed to significant levels of asbestos that might give [them] a shove'.[129] The plaintiff's expert testified that 'The last person you'd want to expose to asbestos with the most potent carcinogens is somebody who had any defect in their ability to repair DNA'.[130] The plaintiffs could therefore effectively present the case that their genotype heightens their risk of developing ovarian cancer after exposure to talcum powder. It is likely that, as genetic testing becomes more routine, these arguments will become increasingly common. In response, defendants could argue the alleged exposure to talcum powder could not have a synergistic effect, and the plaintiffs would have developed this ovarian cancer regardless of toxic exposure. However, the success of this argument depends largely on the ability to adduce sufficient scientific evidence, and expert testimony, in support.

The vaccine courts have considered the role of genetic predisposition as a potential superseding cause of the plaintiff's injury.[131] In *Byers,* the defence proffered arguments that the plaintiff's genetic predisposition was a superseding cause, but the court concluded that the plaintiff's injuries 'would not have occurred *but for* her vaccination' and observed that

> I]f the administration of the vaccine(s) to [plaintiff] "creates or increases the foreseeable risk of harm" that preexisted and coexisted in [her] genetic predisposition..., and the vaccine is found to be a substantial factor in causing her injury, then…the genetic predisposition [cannot] constitute a superseding cause.[132]

This position has been upheld in several other cases where the court concluded that any genetic predisposition did not overbear the effect of the vaccine as a cause of the plaintiff's injury.[133] As the court noted in *Byers,* 'a causative factor unrelated to the vaccine may only be accounted as superseding (*i.e.*, negating the vaccine's causative impact) where its operation is "extraordinary" *and* where the resulting harm therefrom is qualitatively distinct from the risk

[129] *Gail Lucille Ingham et al v Johnson & Johnson et al* (Trial Transcript, Cir Ct of the City of St Louis, vol 18A, 26 June 2018) 3573, (vol 18B) 3658-9. The author thanks Kirk Hartley for drawing this transcript to the author's attention.
[130] Ibid. The expert explained that 'severe errors in cell division were unlikely to be the sole cause of a Plaintiff's ovarian cancer because such genetic mutation is "not something that generally happens unless you've done something that makes it much more likely to happen. Like a carcinogen."' *Robert Ingham et al v Johnson & Johnson et al* 608 SW3d 663, 711(Mo Ct App, No ED107476, 23 June 2020).
[131] See, eg, Beck (n 79) 36.
[132] *Byers v Secretary of HHS* 2010 WL 5663019, 26 (Fed Cl, Nov 30, 2010) ('*Byers*').
[133] See other cases with a similar rationale, eg, *Zeller v Secretary of HHS* 2008 WL 3845155, 26 (Fed Cl, July 30, 2008); *Sucher* (n 72) 43.

posed by the vaccine'.[134] It should be noted that the concept of a 'superseding' cause relates to proximate/legal causation and has little relevance in determining factual causation. If the plaintiff's genes and the defendant's vaccine combined to cause the harm, both are factual causes. If the plaintiff's genes would have caused the harm even absent the defendant's vaccine, the vaccine is simply not a factual cause. It is unclear how a plaintiff's genes could ever 'supersede' the causal role of the defendant's vaccine, if that causal role were proven.

Some US courts have readily dismissed the genetic susceptibility testimony of plaintiffs' experts on the basis that they are simply speculative. For example, in *In Re Downing Corporation,* plaintiff's expert suggested that 'silicone played a role in triggering their diseases specifically in these individuals who probably have genetic predisposition to autoimmune disease'.[135] The court excluded this testimony because the expert 'cites no support for this opinion'.[136] Also, in *Young,* the plaintiff's expert argued there was a 'genetic basis for "mold illness"' which could 'explain how plaintiffs' extensive symptoms can arise from a brief or mild exposure'.[137] This opinion was excluded after the defendant's expert rebutted that '"[t]here are no accepted genetic markers for susceptibility to mold…induced diseases."', leading the court to conclude 'Thus, the inclusion of a diagnostic criteria based on genetics is entirely without merit'.[138] The courts are undoubtedly correct to suggest that experts should only be allowed to assert genetic predisposition as an alternative cause if they are able to cite medical or scientific support for their opinion. However, the reasoning of the courts sometimes reveals a potential lack of understanding of the nuances of genetic evidence. For example, in *Tamraz,* a plaintiff's expert opined that the plaintiff 'likely had a genetic predisposition to Parkinson's Disease and that exposure to manganese triggered his Parkinson's to develop'.[139] This opinion was ruled inadmissible because it was based on speculation about an undiagnosed 'genetic predisposition', 'even though [plaintiff] has no family history of Parkinson's Disease'.[140] The court's reasoning here is questionable to the extent that it implies a lack of

[134] *Byers* (n 132).
[135] *In Re Dow Corning Corporation* 541 BR 643, 651 (ED Mich, 2015).
[136] Ibid 652.
[137] *Young v Burton* 567 F Supp 2d 121, 137 (DDC, 2008).
[138] Ibid. See also *Munro v Regents of University of California* 263 Cal Rptr 878, 882-83 (Cal App, 1989) where a genetic susceptibility claim was excluded due to the absence of expert testimony.
[139] *Tamraz v Lincoln Elec. Co.* 620 F 3d 665, 670-71 (6th Cir, 2010).
[140] Ibid. The court observed that the plaintiff's expert made several 'speculative jumps' in his explanation of the causal chain – for example, 'he described the literature hypothesizing a link between environmental toxins and latent genetic Parkinson's Disease as "all theoretical"…he conceded he knew of no studies finding a link between manganese and Parkinson's Disease and that "studies that have looked at that . . . have not found a very strong correlation."…he conceded that "speculation" led him to guess that Tamraz had "an underlying predisposition to Parkinson's disease,"…even though Tamraz has no family history of Parkinson's Disease... A

family history is dispositive or even relevant when the expert is in fact arguing that a genetic variation plus an exposure trigger were required to cause disease.

Genetic susceptibility can also have an impact on class certification, by indicating there are no common issues where there is genetic heterogeneity among the class.[141] This suggests plaintiffs with differing genotypes cannot form a single class, and instead an individualised assessment of risk and cause is required.[142] For instance, in *Sheridan*, the plaintiffs sought medical monitoring for their increased risk to chronic beryllium disease (CBD) as a result of exposure to beryllium.[143] It was established that only individuals who have a particular genetic marker will develop CBD as a result of exposure to the defendant's product.[144] The defendant alleged only 1-3% of the population have this susceptibility marker, but the plaintiff suggested this number was far greater, amounting to as much as 30-40% of the population.[145] The class-wide monitoring claim failed because '[P]laintiffs did not prove they were at a significantly increased risk of developing [the disease] and thus did not present sufficient evidence to make out a prima facie cause of action for medical monitoring'.[146] Differing genetic susceptibility was also a barrier to class certification in *Pohl*, where the court held:

> An overwhelming consideration to the court here is that in attempting to decide whether the plaintiffs as a class have a significantly increased risk of contracting CBD as a result of exposure is not an issue common to the class. The testimony indicated a need for genetic predisposition to beryllium sensitization. Since only susceptible persons can develop CBD at a given dose, because of their own immunological response to particles of beryllium the issue of increased risk is not common to the class.[147]

The court affirmed summary judgment against the medical monitoring claim.[148] These CBD cases all ultimately demonstrate how class certification can be denied due to differing genetic makeup among a class of plaintiffs. This argument extends beyond CBD cases, and could apply to many other mass torts where courts will be able to deny class certification on the basis of

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negative answer at any one of these steps would defeat his overall theory of causation. The reality that all of them were speculative makes the theory speculative three times over', ibid. For a criticism of the decision in *Tamraz*, see, eg, Ellen Melville, 'Gating the Gatekeeper: *Tamraz v. Lincoln Electric Co.* and the Expansion of Daubert' (2012) 53(6) *Boston College Law Review* 195.

[141] Marchant, 'Genetic Data in Toxic Tort Litigation' (n 7) 24.

[142] Ibid.

[143] *Sheridan v NGK Metals Corp* 609 F 3d 239, 244 (3d Cir, 2010).

[144] Ibid.

[145] See, eg, ibid 252.

[146] Ibid 252.

[147] *Pohl v NGK Metals Corp* 2006 Phila Ct Com Pl LEXIS 472, 41-2.

[148] *Pohl v NGK Metals Corp* 936 A 2d 43, 51 (Pa Super, 2007); For another case where a defendant was awarded summary judgment against a plaintiff seeking medical monitoring as a result of exposure to beryllium, see *Anthony v Small Tube Mfg Corp* 580 F Supp 2d 409 (ED Penn, 2008).

genetic heterogeneity.[149] This presents a setback to plaintiffs who will be unable to obtain the strategic advantage of a class action.

6.3 Genetic Markers of Susceptibility to Prove or Disprove Causation: Australian Case Law

In stark contrast to the small but steadily rising number of litigants introducing genetic test results in US toxic tort cases, the vast majority of Australian cases have merely hypothesised as to a plaintiff's genetic profile, by relying on experts to analyse a plaintiff's family history or explore the genetic nature of the plaintiff's condition.[150] Australian litigants could learn from the US approach to use genetic information more effectively. It could be beneficial for Australian litigants to rely on robust evidence of the plaintiff's genotype (identifying a specific genetic variation or marker) as proof of specific causation or alternative causation. Yet, as the following section will reveal, this evidence could exacerbate problems of causal indeterminacy where there are conflicting interpretations of the genetic test results.

The following section uses an array of cases as examples which are not in the nature of 'toxic torts' but rather involve statutory compensation schemes (e.g., military pensions, worker's compensation) or tribunals which operate under statutes which relax causation requirements (e.g., dust diseases). There are different statutory provisions about causative link that apply in these cases and the nature of these provisions very much impact how the courts would receive and evaluate the genetic evidence. For example, there is a reverse onus approach in the repatriation commission cases about whether disease is connected to war service.[151] This makes it difficult to draw conclusions from those cases and apply them to more classic 'tort' cases.

Despite the varying rules of evidence that apply in Australian lower courts and tribunals, an analysis of the use of genetic evidence to support or refute causation in such cases can still be

[149] See, eg, Marchant, 'Genetic Data in Toxic Tort Litigation' (n 7) 24.
[150] However, there has been at least one Australian case where the defence was able to rely on the plaintiff's genetic test results to prove the plaintiff's illness was genetic, see *Hunt v Repatriation Commission* [2016] AATA 554 discussed in Chapter 6.3.1.
[151] See, eg, the Tribunal in *Cornish v Repatriation Commission* [2001] AATA 138 adopts the lower standard of proof in the *Veterans' Entitlements Act 1986* (Cth) s 120 - namely that the injury/death/disease will be war-caused unless the decision-maker 'is satisfied, beyond reasonable doubt, that there is no sufficient ground for making that determination'.

useful. For example, even though the Administrative Appeals Tribunal ('AAT') typically adopts significantly lower standards for admissibility and sufficiency of evidence, an analysis of these tribunal cases can still provide valuable insight into how litigants are using genetic evidence and the willingness of legal decision-makers to adopt such evidence in determining causation. We now turn to a discussion of Australian cases relating to genetic markers of susceptibility.

6.3.1 Genetic Markers of Susceptibility to Disprove Causation

Hunt is a notable Australian vase where the defence was able to rely on the plaintiff's genetic test results to prove the plaintiff's illness was genetic. In that case, the plaintiff's genetic test results were used to show his illness, 'hereditary neuropathy with liability to pressure palsies (HNPP)', was genetic, rather than war-caused.[152] The Tribunal observed that genetic testing of the plaintiff was 'positive' for HNPP and an expert recorded the 'deletion of the peripheral myelin protein 22 gene (PMP22) is most probably the case of [HNPP] in this patient. This mutation is inherited as an autosomal dominant trait'.[153] This evidence prompted the Tribunal to conclude that plaintiff's HNPP was not war-caused because his 'HNPP was congenital, inherited and present at birth. There is no material that points to the condition arising out of or being attributable to [plaintiff's] operational service'.[154]

The plaintiff appealed to the Federal Court of Australia which ordered the Tribunal's decision be set aside and remitted the matter to the same Tribunal member for re-hearing.[155] On remittal, the Tribunal re-heard the application on the papers and held that the illness (HNPP) was war-caused, on the basis that it was aggravated by his 'wearing of webbing and the use of an old style adding machine' but not 'from his ingestion of Dapsone'.[156] The Tribunal reconsidered earlier medical evidence, including expert opinions that plaintiff's HNPP, although congenital, was 'brought on and worsened by his service in the Army'.[157] On re-reviewing the evidence, the Tribunal was 'satisfied that these expressions connote more than a *mere possibility*…the

[152] *Hunt v Repatriation Commission* [2016] AATA 554.
[153] Ibid [68].
[154] Ibid [70]. See also ibid [94] 'I have no material that points to the hypothesis that [plaintiff's] HNPP was contributed to, or aggravated by, his operational service. I am satisfied that the material does not raise a reasonable hypothesis connecting [plaintiff's] HNPP with his operational service'.
[155] *Hunt v Repatriation Commission* [2019] FCA 1191.
[156] *Hunt v Repatriation Commission* [2017] AATA 697 [61].
[157] Ibid [28]; *Hunt v Repatriation Commission* [2016] AATA 554 [68].

material does raise a reasonable hypothesis'[158] in relation to the webbing and use of an adding machine.[159] However, the Tribunal still refused to accept the arguments of the plaintiff's expert that his HNPP made him genetically susceptible to the effects of Dapsone.[160] This case ultimately demonstrates how scientific advancements (such as the advent of genetic testing) can exacerbate the problem of causal indeterminacy, by providing the courts with more evidence but little means of resolving conflicting expert interpretations of that evidence.

Australian defendants have also successfully relied on evidence of a plaintiff's family history to disprove their causation case.[161] In 1997, the case of *Cornish* considered whether there was a causal connection between colon cancer and the plaintiff's 'exposure to…various chemical defoliants, pesticides and the drug dapsone' during the Vietnam War.[162] A defence expert suggested that the plaintiff was predisposed to colon cancer because 'his father died of bowel cancer and he has a brother who has colonic polyps'.[163] This prompted the Veterans' Review Board to conclude that

> The most likely 'cause' of the deceased's cancer was his familial predisposition to the disease. Whilst it cannot be stated definitely that a family history was the cause of disease development, this hypothesis can be assessed at the level of "more probable than not". By comparison, there are no data directly implicating herbicides, pesticides, etc as causing colon cancer. The possibility that Vietnam service contributed to disease cannot be excluded. However, this supposition cannot be deemed a reasonable hypothesis.[164]

On reviewing the Board's decision, the tribunal considered 'whether, given the veteran's family history, the exposure to herbicides/pesticides/dapsone increased the likelihood of the development of his cancer or accelerated its onset'.[165] An expert called on behalf of the plaintiff

> testified that the question is not one of causation, but that the veteran was exposed to a combination of factors which statistically gave him a higher risk of contracting the condition from which he died. Rather than saying that the exposure to those substances gave rise to an increased risk that augmented the genetic contributor, the veteran is said to have started out with a higher base line risk than other individuals who did not have a family history of cancer of the colon. This additional risk, according to [plaintiff's expert], was "additive" - that is any further risks, such as exposure to herbicides, would add

[158] The Administrative Appeals Tribunal ('AAT') typically adopts significantly lower standards for admissibility and sufficiency of evidence (e.g. the 'reasonable hypothesis' standard). For more information, see Chapter 5.3.
[159] *Hunt v Repatriation Commission* [2017] AATA 697 [29]-[30].
[160] Ibid [36], [44].
[161] *Robyn Kathleen Cornish v Repatriation Commission* [1997] AATA 336 (7 September 1997). This case, like most other Australian cases discussed in this chapter, is a tribunal decision. Tribunals typically adopt significantly lower standards for admissibility and sufficiency of evidence (e.g. the 'reasonable hypothesis' standard). It should also be noted that, because tribunals review administrative determinations, tribunals might uphold administrative agency decisions that the tribunal would not itself have reached in the first instance.
[162] Ibid [1].
[163] Ibid [24].
[164] Ibid.
[165] Ibid [108].

> to the risk that the veteran, given his family history, would contract colon cancer. This theory assumes either that these herbicides were carcinogenic (as to which no evidence was submitted), or else that these chemicals - whatever they were - acted as tumour promoters in combination with dapsone in some kind of catalytic reaction.[166]

In short, the plaintiff's expert maintained that the pesticides interacted with the plaintiff's family history 'to confer a [additive] risk in excess of that attaching to any one of the factors in isolation'.[167] In response, the defence expert argued that 'since we don't know that any single pesticide causes colon cancer, there is no way that anyone can speculate, in my view, about interaction between pesticides…there's just no data there'[168] and it is simply 'a vague generalisation, lacking any support by reference to scientific theory, let alone the medical literature'.[169] This led the tribunal to reject the proposition of the plaintiff's expert 'that exposure to dapsone on its own, or in conjunction with herbicides and/or pesticides constituted an added risk in the development of colon cancer in persons with a familial predisposition to develop the condition'.[170] The tribunal observed this proposition was 'based on intuition rather than science and cannot survive as a reasonable hypothesis connecting this veteran's colon cancer with his operational service'.[171] The tribunal concluded that 'This veteran had the misfortune to inherit a genetic predisposition to develop colon cancer from which he died…his death was unrelated to his operational service'.[172] This decision was ultimately overturned on appeal, with the appeal court revisiting the question of whether the plaintiff might have been genetically susceptible (rather than predisposed).[173]

[166] Ibid [109].
[167] Ibid [114].
[168] Ibid [110].
[169] Ibid [112]-[113].
[170] Ibid [117].
[171] Ibid.
[172] Ibid [142].
[173] For more information, see Chapter 6.3.2 discussing *Cornish v Repatriation Commission* [2001] AATA 138 (23 February 2001).

Several defendants in workers' compensation cases[174] and motor vehicle accident cases[175] have also successfully relied on genetic predisposition to prove alternative causation. These cases do not rely on genetic test results, instead they rely on expert testimony relating to the plaintiff's family medical history or the genetic aetiology of the plaintiff's condition. Although these cases are not toxic torts, they are helpful in showing the willingness of courts to allow a defendant to escape liability if they offer rebuttal proof that the plaintiff's injury was caused by a genetic predisposition.

Non-toxic-tort cases are also instructive in revealing whether family history is sufficient to prove a genetic predisposition. In *Hawker*, the plaintiff appealed on a number of grounds, including that the trial judge erred in concluding the plaintiff had a genetic predisposition to schizophrenia.[176] The court held the trial judge did not err in finding 'that the plaintiff was predisposed to a psychiatric illness because of his family background'.[177] The plaintiff was injured when his bike collided with a stationary van driven by the defendant. The appeal was

[174] See, eg, *Hartog v Comcare* [2017] AATA 1164 [64]-[70] (where the Tribunal held the plaintiff suffered from a genetic disorder which caused their hearing loss condition, so it was unrelated to his employment); *Leslie Hubbard v Military Rehabilitation and Compensation Commission* [2009] AATA 363 [93]-[94]; [102] ('Accordingly, I find that [plaintiff's] hypertension was not contributed to in a material degree by his employment... In fact, the probable explanation is that [plaintiff] was genetically predisposed to developing hypertension and the most that can be said about his employment is that it may have accelerated his development of hypertension…that does not satisfy the test required by the SRC Act.'); *Michelle Anne Vasiliu v Comcare* [2009] AATA 719 [39], [50] ('the Tribunal finds that [plaintiff's] employment…did not aggravate or contribute in a material way to her bipolar disorder….This finding is consistent with… [expert's] finding that biological and genetic factors contributed to the condition'); *John Bolton Humphreys v Repatriation Commission* [2005] AATA 610 [31] ('The Tribunal considers that based on the medical evidence before it, the osteoarthritis suffered by the Applicant has a constitutional pathology and is the product of a genetic predisposition towards osteoarthritis and that the specific traumas that the Applicant suffered when the crank handle struck him three times on each wrist were insufficient to trigger or cause osteoarthritis.'); *Wojcik v General Carrying Pty Ltd* [2021] VSC 233 [117] (The Panel considered the worker's family history, her concurrent medical conditions and unrelated smoking history and concluded that the worker was likely to develop symptomatic heart disease at some stage irrespective of the psychological distress being present due to any accepted workplace injury….[135] I agree with the employer's submissions to the effect that the Panel's reasons clearly explain that Ms Wojcik's impairment had developed over time largely as a result of causes other than psychological injury).

[175] See, eg, *De Groot v The Nominal Defendant* [2005] NSWCA 61 [192] ('The Trial Judge also found…that the defendant has demonstrated its thesis that [plaintiff] suffers from a learning disorder and Attention Deficit Disorder, each of which is genetic or congenital in origin and not causally related to the motor vehicle accident… The basis for the Trial Judge's finding that the appellant suffers from a learning disorder and an Attention Deficit Disorder each of which is genetic or congenital…is supported by evidence.). Evidence of genetic predisposition is not always successful in proving alternative causation, see, eg, *Foxley v TAC* [2021] VCC 1222 [64] ('it was submitted that there was a genetic predisposition to the psychiatric injury complained of. The Defendant relied on the fact that there was family history of psychiatric injury and [plaintiff] had begun presenting psychiatrically because of this naturally occurring predisposition. I do not accept that argument. Dr Strauss [expert] makes clear that the motor vehicle accident continues to be a significant factor in his psychiatric presentation. Dr Strauss' opinion is limited in value to some degree because he only saw [plaintiff] once, but he had access to the full range of background materials and this placed him in a sound position to opine').

[176] *Hawker and Ors v Miller* [2011] SASCFC 76 [99].

[177] Ibid.

dismissed on all grounds, with the court holding there was 'Ample evidence from which it was open to the trial judge to conclude as he did', such as a number of medical reports and expert evidence supporting 'the conclusion that the plaintiff was disposed to suffer from psychosis or a schizoaffective disorder'.[178] This case suggests that family history can be sufficient to prove genetic predisposition as an alternative cause, even in the absence of genetic test results, so long as other medical evidence also supports the alternative causation defence. This difference in US and Australian approaches could exist because US litigants have been more prone to adducing genetic test results as proof of alternative causation. However, Australian litigants are only recently relying on this type of evidence, and have been more accustomed to relying on evidence of family history.

The more recent case of *East Metropolitan Health Service v Ellis* is an example where the court demanded genetic testing to provide a plausible alternative cause.[179] In this medical negligence case, an expert 'commented, almost in passing, that the [plaintiff's] global developmental delay "may be accounted for by subtle underlying genetic abnormality"'.[180] However, the trial judge held 'In the absence of any evidence that any testing had occurred in relation to the suggestion…this comment [was not] a plausible alternative hypothesis for [plaintiff's] Developmental and Cognitive Impairments'.[181] As the science improves, courts might be more inclined to require genetic test results to prove alternative causation. However, it should also be noted that there was no mention of family history in this case, so it is unclear whether, in the absence of genetic testing, family history would have sufficed here to prove genetic predisposition.

In *Alder v Khoo,* the Court implied that a plaintiff might be required to submit to genetic testing in order to rebut a defence allegation that their injury was a genetic disorder.[182] It is unclear in this case how specific the defendant's allegation of predisposition would need to be before the plaintiff would be required to submit to testing. If the plaintiff needs to provide evidence of family history/genetic testing in order to establish genetic susceptibility, surely the defendant should not be allowed to raise a broad allegation of predisposition. The

[178] Ibid [100].
[179] *East Metropolitan Health Service v Ellis (by his next friend Ellis*) [2020] WASCA 147.
[180] Ibid [237].
[181] Ibid.
[182] *Alder (as litigation guardian for Alder) v Khoo* [2013] QSC 312 [5] (If the plaintiff 'was serious about rebutting the allegation in the proceeding that his son suffers from the genetic disorder, one would have thought this [genetic testing] to be an obvious piece of evidence to be obtained by the [plaintiff]').

defendant should be required to point to at least evidence of relevant family history. As Chapter 8 highlights, there is a need for further guidance to ensure fairness and consistency.

Other non-toxic-tort cases are helpful in showing that even if a plaintiff submits to genetic testing and their results are negative, the defendant could arguably still rely on the hypothesis that genetic predisposition is an alternative cause. In a medical negligence case, *X v Sydney Children's Hospitals,* the Court held 'Because of the confined nature[183] of the tests ordered (and, as I understand it, conducted), it is not possible from the results of those tests to exclude any and every genetic cause. Nor did the Defendants, by their conduct, estop themselves from raising genetic causes'.[184] As a result, the defendants were not precluded 'from raising other alternative causes, including ones with a genetic basis'.[185] This is inconsistent with the approach of the US court in *Sucher* where the court appeared to disregard the defence experts' views that the plaintiff's limited *SCN1A* testing was insufficient to rule out an alternative genetic cause.[186] The approach in *X v Sydney Children's Hospitals* is arguably more appropriate than the approach in *Sucher* to the extent that the Australian court at least recognised that the results of very limited genetic testing rarely provides definitive proof of causation, or alternative causation.

The cases of *East Metropolitan Health Service v Ellis* and *X v Sydney Children's Hospitals* reveal, on the one hand, the growing inclination of courts to require genetic test results and, on the other hand, the courts' growing appreciation of the limitations of such results. This seemingly paradoxical approach to genetic testing data is justified to the extent that such test results can help to eliminate some genetic causes, but, due to the state of the science, they cannot rule out all genetic causes. As Chapter 8 explains, litigants, legal professionals, and courts should be careful to consider these limitations and the potential for conflicting expert interpretations of the genetic data. Evidence of a plaintiff's genotype, family history, and medical records will all collectively help to illuminate the plaintiff's disease aetiology.

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[183] *X v Sydney Children's Hospitals Specialty Network and Anor (No 4)* [2011] NSWSC 1310 [25] (The testing involved a. genetic analysis of ABCC8 and KCNJ11 genes; b. serum transferrin isoforms; and c. high density SNP array comparative genomic hybridisation, for the purposes of ascertaining: 1.whether the CHI diagnosed in the Plaintiff has an identifiable genetic basis; 2.whether the diagnosed CHI is connected to a genetic disorder such as congenital disorders of glycosylation or "CDG"; and 3.whether the plaintiff suffers from genomic disorders which may explain her developmental and language disorder'). For more information on the different types of genetic tests and their purposes, see Chapter 7.

[184] Ibid [28].

[185] Ibid [29].

[186] See discussion of *Sucher* (n 72).

6.3.2 Genetic Markers of Susceptibility as Proof of Causation

Due to the complexity of genetic susceptibility arguments, courts have generally been less inclined to accept a plaintiff's argument relating to their genetic vulnerability to the relevant toxin. However, there has been at least one toxic tort case, the case of *Hazeal*, where the plaintiff successfully argued that they had a genetic susceptibility that was triggered by exposure to a herbicide.[187] In that case, the court considered an expert report where a specialist dermatologist commented that the aetiology of the plaintiff's condition is unknown but 'The present theory is that it is a genetically determined disorder of the immune system. It is proposed that some external (environmental) factor may then precipitate the onset of the disease'.[188] The expert went on to explain that 'Chemical injury to the skin caused by excessive exposure to unknown toxic chemical, Tordon…has, by some unknown mechanism, precipitated the onset of [plaintiff's] connective tissue disease'.[189] So, 'notwithstanding a genetic predisposition, there has to be a trigger to set off the reaction'.[190] Another expert also testified that 'The temporal evidence suggested to her that the factor of being sprayed was sufficient, in the deceased's case, to trigger off that chain of events'.[191] The medical evidence led the Tribunal to conclude that the plaintiff 'was a genetically vulnerable person and that the exposure to Tordon 50D [herbicide] set in train the development of [the plaintiff's] ultimate condition'.[192] Evidence of genetic susceptibility was therefore pivotal to the plaintiff's case. This case differs from the above-mentioned US cases where plaintiffs failed to prove they were genetically susceptible.[193] Those US cases involved uncertainty as to whether the plaintiff had the relevant genetic susceptibility, so the evidence was relevant to specific causation. However, this Australian case differs from the US cases because the evidence here seems to involve uncertainty as to the general causal mechanism.

Evidence of genetic susceptibility was useful in proving causation in *Ergon Energy v Rice-McDonald.* The plaintiff alleged that exposure 'to carbon tetrachloride and cigarette smoke in

[187] *Hazeal v Local Government Association Workers Compensation Schemes (Corporation of the City of Whyalla)* [2006] SAWCT 36.
[188] Ibid [56].
[189] Ibid [57]. The expert also considered the illness could have been caused by 'Exposure to ultraviolet light over a long period of time whilst working outdoors without adequate protection'.
[190] Ibid [61].
[191] Ibid [77]. This expert also testified that 'UV exposure may also have been an early aggravating factor (tr 120). She said that such exposure may precipitate the onset of or exacerbate the course of systemic lupus'.
[192] Ibid [222].
[193] See Part 6.2.2 discussing e.g., *Tamraz* (n 139).

the workplace' caused his lung cancer.[194] The Tribunal noted 'the possibility that all of the above exposures may have taken on a greater degree of significance by virtue of a possible genetic predisposition to developing lung cancer by virtue of [plaintiff's] father having developed lung cancer'.[195] The Tribunal accepted expert opinion that this susceptibility 'increased the likelihood that exposure…was causative. So the fact that the relative risk from passive smoking was less than 2.0 did not mean that the evidence, taken as a whole, did not establish causal connection'.[196] This is the equivalent of the aforementioned modern eggshell plaintiff argument. The Tribunal agreed that individuals with a genetic susceptibility could be more vulnerable to the harmful effects of toxic exposure, compared to the general population.[197] On appeal, the Court dismissed the application for review and held 'The present question is not whether the Tribunal's conclusion was correct. It is whether the Tribunal has explained the means by which it has reached its conclusion…In my view the reasons…were sufficient…having regard to the evidence and the clear terms of the respective medical opinions'.[198] This case demonstrates that where the medical opinions are based on a plaintiff's family history, genetic susceptibility can provide probative evidence of causation.

Where the expert evidence is not sufficiently detailed, genetic susceptibility arguments will be dismissed by the courts. A number of cases have highlighted the importance of expert testimony. For example, the case of *Hodge* had similar facts to *Hazeal* but a vastly different outcome.[199] The court considered whether exposure to an insecticide, or UV exposure, could trigger a genetically susceptible plaintiff to develop lupus.[200] Experts expressed the opinion that the plaintiff's 'prolonged exposure' to the insecticide 'and resulting severe cutaneous burns could well be the triggering event to the development of a previously dormant genetically mediated condition of SLE [lupus]'.[201] The court was not persuaded by this evidence, holding that 'Whilst I accept there is a strong possibility of these burns being implicated the evidence

[194] *Ergon Energy Corporation Ltd v Rice-McDonald & Ors* [2009] QSC 213 [3]-[4].
[195] Ibid [7].
[196] Ibid [22].
[197] Ibid.
[198] Ibid [24].
[199] See also *Hodge v WorkCover* [2008] SAWCT 21.
[200] Ibid [2] ('While Mr Hodge was working as a jackaroo he experienced a significant episode of skin exposure to a synthetic pyrethroid insecticide, which caused him a sensation of burning, severe pain and skin redness. Mr Hodge also experienced exposure to solar radiation during the period of his employment.'); [3] ('Mr Hodge has asserted that his underlying genetic susceptibility to contracting SLE was likely to have been triggered by one or more of three circumstances he experienced in his employment. They included: absorption of insecticide through his skin; a chemical burn to his skin caused by insecticide contamination; and an exposure to ultraviolet radiation during the course of his employment. In rejecting the claim, the compensating authority has denied the validity of each claimed causal factor.').
[201] Ibid [32]-[33].

falls short of the degree of persuasion required before I can find on the balance of probability it was a valid causal factor'.[202] The court was reluctant to accept the expert's testimony due to the 'absence of any medical literature to support [the expert's] theory'.[203] Perhaps more detailed expert testimony, or an additional expert supporting this opinion, would have persuaded the court to reach a conclusion similar to *Hazeal*.

Evidence of genetic susceptibility was also unsuccessful in proving causation in the case of *Lilley.*[204] The plaintiff alleged he developed motor peripheral neuropathy as a result of exposure to pesticides in the course of employment. The plaintiff's expert 'conducted a liver detoxification profile' and concluded that the plaintiff is genetically 'much more sensitive to toxic exposure than the average person' so his 'ability to eliminate toxins…is significantly impaired'.[205] As a result, the plaintiff's 'exposure to [insecticides] (even at supposedly safe levels) would have led to much greater build up of the same in his body' such that 'his current problem was undoubtedly caused by his exposure to neurotoxins'.[206] However, the Tribunal was not persuaded by this evidence, ultimately holding that the medical expert evidence can only indicate a possibility that the plaintiff's condition was caused by exposure

[202] Ibid [89]. Instead, the Court was persuaded that the UV exposure was sufficient to cause the plaintiff's illness, ibid [99] ('In my opinion, the strength of the expert evidence of the ability of UV exposure to cause a flare of SLE, together with Mr Hodge's actual exposure during the period of his employment and the timing between this exposure and the onset of symptoms, and notwithstanding Dr Awerbuch's reservations about Mr Hodge's vulnerability, leads persuasively to the conclusion that the SLE that Mr Hodge suffered in March 2004 was probably triggered by his work related UV exposure.').

[203] Ibid [82]:
'Against this submission is the lack of any recognition in the relevant medical literature of direct exposure to this type of chemical as triggering or causing a flare of SLE. Given the relative commonality of the chemicals one would expect there to be some epidemiological evidence of association if it is a valid cause and effect association. The nature of potentially relevant occupational or environmental triggers appears to have been studied to some significant degree. This is not a case where the relevant causal theory has not been tested by reference to any epidemiological evidence. I recognise of course the limits of medical science and particularly in relation to the developing field of knowledge of the pathogenesis and etiology of SLE.'
Ibid [83]:
'In my view the absence of any medical literature to support Dr Odger's theory, which on its own has some attractive logic and plausibility, counts against acceptance of that theory. Accordingly I reject the contention that Mr Hodge's primary chemical exposure to the pyrethroids caused or triggered a flare of his condition.'
Ibid [89]:
'However for the same reasons as above I am particularly influenced by the lack of any medical evidence to support this theory, even though Dr Odgers explanation of a likely autoimmune process seems plausible. Again burns to the skin from this chemical or other chemicals, or episodes of sunburn of either a mild or severe nature are relatively common and if such a causal relationship existed it is likely to have been medically observed and reported. Whilst I accept there is a strong possibility of these burns being implicated the evidence falls short of the degree of persuasion required before I can find on the balance of probability it was a valid causal factor.'

[204] *Lilley v Comcare* [2003] AATA 738.

[205] Ibid [25].

[206] Ibid. A defence expert also considered plaintiff's 'condition had been caused or aggravated by his service on the basis that his type of peripheral neuropathy could have been caused by toxic exposure. He has been exposed to DDT and Malathion over an extended period and he has an inherited metabolic abnormality which would make him abnormally susceptible to the effects of these chemicals', see ibid [74].

to insecticides.[207] The expert opinion in this case might have been more persuasive if it were supported by other experts, or expert testimony exploring whether there was also a family history of the relevant disease.

Some cases have implied that evidence in the form of family history may be required to support an argument of genetic susceptibility.[208] For example, in *Mitchell v Repatriation Commission,* the Court considered whether the plaintiff's exposure to Dapsone and herbicides/pesticides during the Vietnam War caused his chronic lymphocytic leukemia.[209] Plaintiff's counsel proposed that the plaintiff 'might have been genetically susceptible to the haematological side effects of Dapsone and that in that way the administration of Dapsone to him might have been causally related to his developing chronic lymphocytic leukaemia'.[210] However, this opinion was rebutted by a defence expert who confirmed 'that it would be necessary to define what was meant by genetic susceptibility, for instance that members of the veteran's family had suffered particular medical problems' and 'Certainly, in the absence of any evidence of leukaemia in his family, the fact that the veteran suffered from it did not afford any support for the hypothesis'.[211] It seems the plaintiff's expert did not make clear what they meant by 'genetic susceptibility', so the defence expert simply assumed they meant family history and concluded that the plaintiff would need to adduce evidence of their family history in order to support their susceptibility argument. This expert also testified that, 'although there had been considerable investigation into the possible relationship between [substance exposures by Vietnam veterans] and various types of cancer, no evidence had been found of a connection between either Dapsone or any of the herbicides or pesticides used in Vietnam and leukemia'.[212] The Tribunal concluded that, on the basis of this expert's evidence, the plaintiff's condition was not war-caused.[213]

The aforementioned case of *Cornish* had similar facts to *Mitchell,* but a different outcome. The Tribunal in *Cornish* was again required to consider whether the plaintiff's exposure to pesticides, chemical defoliants and Dapsone caused plaintiff's colon cancer, either singly, or in combination with one another.[214] An expert maintained that 'mild dapsone-induced

[207] Ibid [123].
[208] *Paulette Rosina Mitchell v Repatriation Commission* [1991] AAT 446.
[209] Ibid [5].
[210] Ibid [9].
[211] Ibid.
[212] Ibid [6].
[213] Ibid [12].
[214] *Cornish v Repatriation Commission* [2001] AATA 138 [48].

immunosuppression, combined with a genetic predisposition to colonic cancer and exposure to carcinogenic herbicides, together caused the Veteran's cancer'.[215] Another expert rebutted that there is no cumulative effect, 'at least between dapsone and chemical carcinogens', but this expert was 'less dogmatic' about whether there is a 'cumulative risk from genetic and environmental factors'.[216] This expert conceded 'his doubts about the hypothesis linking herbicides and colon cancer arose from a paucity of evidence'[217] but 'he did not think it was a ridiculous hypothesis'.[218] The Tribunal reasoned that:

> 80. It is significant that the *Veteran belonged to a subset of herbicide-exposed patients, those with a family history of colonic cancer. It is common ground that this subset has not been studied separately*. The research papers which failed to find correlation between herbicides and colonic cancer were not examining this group of high-risk patients…
> 82. The Tribunal *notes the paucity of evidence linking herbicide exposure to colonic carcinoma. Of itself however, that lack of evidence does not mean inevitably that an hypothesis linking the two is "contrary to proved scientific facts".* To use the philosopher's analogy, the counting of any number of white swans does of itself disprove the existence of black swans. The fact that white swans abound is not a proved scientific fact of the kind which would make the hypothetical existence of a black swan untenable. *In the case of chemical carcinogenesis there are a number of reasons why the scientific literature may fail to confirm a causal association which does in fact exist. The latency between exposure and clinical presentation of tumor is one obvious example - the statistics may have been gathered before the complication has declared itself.*
> ….
> 84. Is the absence of evidence of a positive statistical correlation between chemical exposure and colonic carcinoma decisive in this case? Does it render untenable the hypothesis linking the Veteran's operational service with his death? The Tribunal answers each of these questions in the negative. Its reasoning is as follows:
>
> (a) A distinction must be drawn between the general proposition and the particular circumstances of the Veteran's case.
> (b) There is good evidence that components of one or more of the chlorphenoxy herbicides are multi-site carcinogens causing lymphoma, soft tissue sarcoma and, in experimental animals, liver tumors and cancers of the oro-pharynx, lung and endocrine system.
> (c) At least one scientific paper (the Alavanja paper) raises the possibility specifically of a positive causal association between herbicides and colon cancer. Its authors and Professor Stewart both stress that this is no more than inferential - there are other explanations of the association which may not be causal. Nevertheless, the findings cannot be dismissed and must be judged alongside those studies which do not find any association.
> (d) Dr McCullagh, one of the two experts who gave oral evidence in this case, is of the view that the Veteran's exposure to dioxin and his ingestion of dapsone were both significant risk factors for bowel cancer.
> (e) *The Veteran belonged to a sub-group of the general population with a familial predisposition to carcinoma of the colon. While chlorphenoxy herbicides have been widely studied, their carcinogenic effects for this sub-group has not specifically been studied. Such a study would be very difficult to undertake.*
> (f) On all of the expert evidence in this case, it is at the very least possible that dioxin causes bowel cancer. The dispute between the experts goes largely to the order of likelihood of that being the case.
> (g) *The hypothesis that chlorphenoxy herbicides increase the risk of carcinoma of the colon specifically in people with a familial predisposition to the disease is proposed by one expert and is not rejected by the other.*

[215] Ibid [45].
[216] Ibid [47].
[217] Ibid; [transcript: 16 May 2000 p55, line 19, p56 line 5, p57 line 36].
[218] Ibid [63].

> 85. In this case the Tribunal concludes that the absence of evidence of a positive statistical correlation between chemical exposure and colonic carcinoma does not render the hypothesis untenable. *The Tribunal finds that the hypothesis put forward by the Applicant in this case is a reasonable hypothesis*…[219] [emphases added]

The Tribunal concluded that 'The question [of causation] is left open by a notable and, in the circumstances, understandable paucity of research into the effects of dioxin in persons who, like the [plaintiff], have a genetic predisposition to carcinoma of the colon'.[220] The Tribunal found the plaintiff was entitled to compensation because the Tribunal was not convinced beyond a reasonable doubt that the plaintiff's death was not war-caused.[221] As the plaintiff in this case was able to rely on expert testimony explaining the interaction between the plaintiff's genetic predisposition and substance exposure, their genetic susceptibility argument was more effective than the plaintiff in *Mitchell*. Nevertheless, it is difficult to understand how a plaintiff with a family history of cancer (*Cornish*) is allowed to recover compensation but a plaintiff lacking evidence of such family history is denied compensation (*Mitchell*). Chapter 8 of this thesis proposes a Reference Guide to assist litigants/lawyers/courts in understanding genetic evidence and to promote greater consistency across judgments in order to avoid unfairness.

In addition to these pivotal toxic tort cases, courts adjudicating dust disease cases have indicated their willingness to consider genetic information. These courts have specifically identified a lack of evidence of genetic information in toxic tort cases. For example, in *Amaca v Ellis*, the High court indicated that they were open to hearing submissions on genetic predisposition.[222] The transcript states:

> GUMMOW J: Is there any evidence of the role of genetics in this?
> MR ABBOTT: Do you mean predisposition via genetic, or the effect of these carcinogens on a gene?
> GUMMOW J: No, predisposition.
> MR ABBOTT: There is a mention, and I cannot bring it to mind, about it is yet unknown as to what the cause is or the likely cause of why people - - -
> FRENCH CJ: The family history in this particular case did not figure in the evidence?
> GUMMOW J: It did, did it not?
> FRENCH CJ: It was mentioned, but - - -
> MR ABBOTT: Not that we are aware of. Some of experts proffered genetic predisposition as one possible factor which might impinge on the impact of why some people got lung cancer when exposed to more than one carcinogen, and why some people did not get cancer when exposed to the same amount of carcinogens over the same time.
> GUMMOW J: What is page 257 talking about?
> MR ABBOTT: Page 257?

[219] Ibid [80]-[85].
[220] Ibid [88].
[221] Ibid [89]-[90]. This tribunal adopts a lower standard of proof compared to the balance of probabilities standard usually adopted in civil litigation (see e.g., *Civil Liability Act 2002* (NSW) s 5E).
[222] *Amaca Pty Ltd v Ellis & Ors* [2009] HCATrans 296 (4 November 2009).

> GUMMOW J: Yes, the first two paragraphs.
> MR ABBOTT: The passage I have just read from, Dr Leigh being asked about multiplicative effect?
> GUMMOW J: No, page 257, the top of the page.
> MR ABBOTT: I assume it is a reference to Mr Cotton's family history and the possibility of some genetic - - -
> FRENCH CJ: He refers on the previous page to having noted that family history.
> MR ABBOTT: Yes, the report. I must say, I have not read that report.
> GUMMOW J: Do these epidemiological studies take this sort of thing into account - - -
> MR ABBOTT: Yes, I think it is a question of which epidemiological - - -
> GUMMOW J: - - - as a matter of scientific method when they are looking at populations?
> MR ABBOTT: I cannot answer that, I am sorry. Having said that I cannot answer that, is my last answer. I have finished my submissions, if the Court pleases.[223]

The court was clearly open to considering genetic evidence and the parties could have bolstered their case by adducing evidence of family history or even genetic test results.

Several other cases have raised the issue of genetic susceptibility to dust diseases.[224] This argument was successful in at least one case.[225] In *Briggs v RTL Mining,* several experts suggested the plaintiff's condition was genetic but required an environmental trigger, that could have been anything from UV light to an infectious agent to occupational dust exposure.[226] This led the Court to conclude that there is a causal link between occupational exposure to ash, coal dust and smoke and the plaintiff's condition.[227] In *Booth v Amaca and Amaba*, the Court observed that 'Because most people exposed to asbestos fibres do not contract mesothelioma, it is thought that persons contracting the disease suffer from some underlying genetic susceptibility'.[228] Similarly, in *BHP Billiton,* the court observed that:

> Mesothelioma is a rare condition: it is likely that its incidence depends on genetic susceptibility of particular individuals, although the circumstances of that susceptibility are not presently known. It is nevertheless accepted that some individuals may suffer mesothelioma after exposure to far lower levels of asbestos dust than would be required for other asbestos caused conditions.[229]

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[223] Ibid 2580-2630.
[224] See, eg, *Pryde v Telstra Corporation Limited (Compensation)* [2016] AATA 811 [193] (An expert 'said that why some individuals who are exposed to asbestos developed lung cancer while most do not is not an entirely answered question, but he suggested it must have something to do with genetic susceptibility to cancer in the first place.'); *Lola Merle Evans v Queanbeyan City Council and Anor* [2010] NSWDDT 7 (A genetically susceptible person may contract lung cancer because of exposure to asbestos at a concentration that reflected minimal risk, however that is not the case advanced for [plaintiff].); *Van Soest v BHP Billiton Limited* [2013] SADC 81 [369] (expert suggested 'other probable explanations for the induction of mesothelioma in only a small percentage of people exposed to asbestos. Genetic susceptibility to the carcinogenic effects of asbestos being one'); *Shaw v BHP Billiton Ltd* [2015] SADC 3 [700] ('theoretically, if each individual forming a worker population was exposed to 'precisely the same inhaled dose of asbestos' some would develop asbestos-related cancer and some (the majority) would not. Genetic susceptibility and resistance would play a part').
[225] *Briggs v RTL Mining & Earthworks* [2019] VMC004.
[226] Ibid [28], [43], [56], [67]-[73].
[227] Ibid [104]-[105].
[228] *John William Booth v Amaca Pty Limited and Amaba Pty Limited* [2010] NSWDDT 8 (10 May 2010) [56].
[229] *BHP Billiton Ltd v Dunning* [2015] NSWCA 55 [26].

The court therefore rightly implies that genetic variability explains why some people get sick despite low exposures that would not sicken others – substantially changing how the evidence weighs in the case. This genetic explanation could be harnessed by plaintiffs to support their causation case, but it could also be used by defendants who could treat the genetic explanation as an alternative cause. As genetic testing continues to become faster and cheaper, litigants will be better placed to adduce evidence of genetic test results to support or refute their causation case.[230]

Experts are already testifying in relation to the *BAP1* gene in some Australian mesothelioma cases. In *Amaca v CSR,* an expert observed that mesothelioma can be attributed 'to an underlying innate susceptibility factor such as the BAPI [sic] Tumour Predisposition Syndrome'.[231] More recently, in *Gough v Comcare,* an expert explained 'We do not know about [plaintiff's genetic predisposition, such as germline BAPI [sic] status, and our current knowledge with regard to (other) factors determining genetic predisposition to mesothelioma is in general incomplete'.[232] Australian litigants could potentially benefit from adopting a similar approach to the US where plaintiffs are increasingly genetically tested to determine their *BAP1* status.[233] However, it should be noted that the more common issue with mesothelioma is identifying which asbestos exposure was causal, and genetic evidence provides no assistance in these situations. This is because genetic markers cannot show *which* exposure caused the plaintiff's illness.

6.4 Conclusion

Genetics can help to illuminate the variability in individuals' responses to toxic exposures. A fortunate genetic endowment could protect some individuals from developing disease as a result of exposure to a toxic substance, while a genetic misfortune could induce disease in some who have never been exposed to the relevant toxin. Litigants are increasingly relying on genetics as a method of proof of causation, or alternative causation, in toxic torts. A growing number of defendants have argued, sometimes successfully, that inherited genetic mutation/s

[230] For more information on genetic testing and toxic torts, see Chapter 7.
[231] *Amaca Pty Ltd v CSR Ltd & Anor* [2015] VSC 582 (21 October 2015) [727]; see also *CSR Limited v Amaca Pty Ltd* [2016] VSCA 320 (16 December 2016) [151].
[232] *Gough v Comcare (Compensation)* [2020] AATA 4669 [37].
[233] *Ortwein v CertainTeed Corp, et al., Alameda County Superior Court* No. RG13701633 (12 December, 2014) (Lee J)*; Joseph Thrash, et al v The Boeing Co* 2018 WL 2573097*; Dustin W. Holsten, et al. v Amalgamated Sugar Co. LLC, et al.,* No. 18-L-1664, Ill. Cir., Madison Co*; Cynthia B. Cowger v Qualitex Co.,* No. 2018-L-012099, Ill. Cir., Cook Co; *Jessica Blackford-Cleeton and Brandon Cleeton v. AK Steel Corp.*, No. 15-L-17 (Richland County Circuit Court, IL).

caused the plaintiff's injury independent of any toxic exposure. On the other hand, a growing number of plaintiffs have argued their genetic makeup makes them more vulnerable to the effects of exposure. The success or failure of both plaintiff and defence arguments have largely depended on whether the plaintiff tested positive for the relevant genetic markers and whether the plaintiff had a strong family medical history of the disease.

As Chapter 8 explains, the case law analysis has indicated a strong need for a Reference Guide to assist litigants/lawyers/courts in understanding, e.g., the difference between predisposition and susceptibility, the distinction between family history and genetic test results, the role of gene-gene and gene-environment interactions, and the importance of gene penetrance. The proposed guide will emphasise that, while genetic evidence can alleviate the issue of causal uncertainty, it does not provide a complete picture. More traditional methods, such as toxicology, epidemiology, and analysis of plaintiff's medical records, will continue to play a significant role in illuminating toxic tort causation.

We will only see a more complete picture of the plaintiff's disease causation after all relevant medical and scientific evidence have been considered as a whole. The following chapter will build on this argument, by suggesting that plaintiffs should be required to undergo genetic testing that is specifically directed towards causation of their injury. This thesis ultimately suggests that, despite its challenges, genetic evidence still has an important role to play in toxic tort litigation but further guidance (in the form of a reference guide proposed in Chapter 8) is required to ensure consistency and fairness across judgments and across jurisdictions.

7. Chapter Seven: Court-Ordered Genetic Testing: The Defendant's Right to Examine the Plaintiff's Genome?

The previous chapters examined genetic markers of exposure, effect, and susceptibility as methods of proof of causation in toxic torts. This chapter will build on this analysis, by arguing that toxic tort defendants should have a right to examine the plaintiff's genome for the purpose of determining the presence or absence of genetic markers. It analyses the small but growing number of Australian and US personal injury cases where defendants have sought to compel genetic testing of plaintiffs in order to identify potential alternative causes of their injury. It finds that, despite the concerns of some scholars, courts continue to show a willingness to order genetic testing on the basis that possible benefits of the test results outweigh any risks to the plaintiff's privacy and autonomy. It concludes that genetic testing should be ordered so long as the test is directed towards causation of the plaintiff's injury and the defendant has identified a sufficient prospect that the findings of the proposed testing may reveal an underlying genetic trait or condition as an alternative cause. This is not to suggest that this evidence should be determinative of causation, this chapter simply asserts that genetic evidence should be collected in the form of court-ordered genetic testing – it will be for the trial court to determine what weight to give to that evidence and what conclusions can actually be drawn from this evidence. The following chapter proposes a Reference Guide to assist the courts/litigants/lawyers in assessing the strengths and limitations of genetic evidence in a given case.

This chapter will begin with an investigation of how courts manage requests to compel genetic testing in toxic tort cases. It will then consider the broader societal implications of compelling genetic testing for the purpose of disputing medical causation. As noted by Professor Gary Marchant, 'genetic data will present courts with both great opportunities and serious challenges to ensure that such information is used in a sound, effective, and ethical manner'.[1] The 'collateral consequences' include individual and familial privacy violations, stigmatisation, discrimination, psychological trauma, as well as increased 'delay, confusion and risk' due to unreliable test results.[2] Part 7.1 will explain the relevant legal framework governing court-

[1] Gary Marchant, 'Genetic Data in Toxic Tort Litigation' (2016) 45(2) *The Brief* 22, 28.
[2] Diane Hoffmann and Karen Rothenberg, 'Judging Genes: Implications of the Second Generation of Genetic Tests in the Courtroom' (2007) 66 *Maryland Law Review* 858; David Hirsch and David Amor, 'Exome and genome sequencing in litigation' (2020)(156) *Precedent* 15, 18-19.

ordered genetic testing in US and Australian tort litigation. Parts 7.2-7.5 will examine the socio-economic ramifications of court-ordered genetic testing, including reliability (Part 7.2), privacy (Part 7.3), stigma/trauma (Part 7.4) and efficiency (Part 7.5).

7.1. The Legal Framework

7.1.1. US Law – An Overview

Several US courts have shown a willingness to grant motions to compel genetic testing in toxic torts and, in some cases, the results of the test have been fatal to the plaintiff's case.[3] For example, in *Bowen v EI Dupont,* the plaintiff alleged that her 'retarded foetal growth and cell development' (birth defects) were caused by exposure to Benlate (fungicide) *in utero* while her mother was spraying houseplants in the early stages of pregnancy.[4] The defendant alleged that there were no environmental causes and in fact a specific condition (CHARGE syndrome) and in particular a genetic variation (*CHD7*) was the cause of the plaintiff's harm.[5] The defendant was able to successfully obtain a court order to genetically test the plaintiff for that specific genetic variation and the genetic test revealed the plaintiff had the *CHD7* variation.[6] This evidence was so powerful that it even prompted the plaintiff's expert to switch sides and support the defendant's contention that CHARGE syndrome was the correct diagnosis and the *CHD7* gene 'played a substantial role in bringing about [the plaintiff's] condition'.[7] The Court granted the defendant's motion for summary dismissal and concluded that 'The position advocated by the defense is clear – the mutated CHD7 gene was the sole and proximate cause of [plaintiff's] CHARGE syndrome' and the defence 'theory has substantial support in the record in that it has been tested, peer reviewed and published, apparently without consequential dissent'.[8]

Bowen is a testament to the sheer power of court-ordered genetic testing to disprove medical causation in toxic torts, by providing highly persuasive evidence of alternative causation.

[3] See, eg, *Bowen v. E.I. DuPont de Nemours &. Co*., No 97C 06-194, 2005 WL 1952859 (Del Super Ct, 5 August 2005) ('*Bowen*'); *Naomi Guzman v ExxonMobil Corp, ExxonMobil Oil Corp, Humble Inc, and Intracoastal Tubular Services Inc,* No. 693–606 (La Dist Ct, 24th Dist, 2013) Jury Verdicts LEXIS 9774 ('*Guzman*'); *Ortwein v. CertainTeed Corp., et al., Alameda County Superior Court* No. RG13701633 (Cal Super Ct, 12 December, 2014) (Lee J)*; Richard Ortwein, et al v Certainteed Corporation, et al,* No RG 13701633, 2016 Jury Verdicts LEXIS 67523 (*Ortwein*).
[4] *Bowen* (n 3).
[5] Ibid 19.
[6] Ibid 18-19.
[7] Ibid 20.
[8] Ibid 41.

However, it is important to note that '*Bowen* represents an extreme case because, according to the court, everyone with the mutated gene ultimately suffers from the syndrome. It is rare for any single genetic defect to inevitably cause a specific injury'.[9] Nevertheless, as Sanders et al explain, 'genetic information has become more important in narrowing the possible causes of an individual's ailment'.[10] So, even though it is rare for diseases to be caused by a single genetic defect, genetic data is nevertheless an increasingly important aspect of any causal analysis in toxic torts.[11]

Similarly, in *Naomi Guzman v ExxonMobil Corp.*, the Court granted the defendant's request for genetic testing of a sample of the plaintiff's preserved thyroid tissue.[12] The plaintiff in this case claimed that her thyroid cancer was caused by exposure to 'naturally occurring radioactive material' ('NORM') 'through her father's work as an oil pipe cleaner'.[13] The results of the tests indicated that the plaintiff had the genetic markers/gene signatures for sporadic papillary thyroid cancer, and did not have the gene signature for radiation-induced cancer.[14] It also revealed that the plaintiff had a number of hereditary gene mutations predisposing her to thyroid cancer, leading the defendant's expert toxicologist to conclude that the plaintiff's cancer 'was in no way caused by her contact with [defendant's] drilling pipe, as her thyroid cancer was caused by her genetic predisposition to it'.[15] In particular, the plaintiff 'tested positive for inherited mutations in eight genes associated with papillary thyroid cancers [and her] family history showed that her mother and aunt both had thyroid cancer'.[16] The impact of this evidence, in combination with all other defence evidence, can be inferred from the fact that the defendants were ultimately found not liable by the jury.[17] As this case is a jury verdict, the precise impact of the evidence is unclear. However, the expert testimony of the plaintiff's

[9] Joseph Sanders et al, 'Differential Etiology: Inferring Specific Causation in the Law from Group Data in Science' (2021) 63 *Arizona Law Review* 851, 863. See also, eg, Steve Gold, 'The Holy Grail? The Potential of Genomics to Shape Toxic Tort Litigation' (2016) 58(4) *DRI For the Defense: Toxic Torts and Environmental Law* 59, 61.
[10] Sanders et al (n 9) 863.
[11] As Sanders et al explain, the *Bowen* diagnosis 'not only specified the disease, but it also indicated that a genetic defect was the overwhelmingly most-likely cause of the injury…the most useful biomarker would be one that would allow us to define signature diseases. That is, the marker would be able to differentiate injuries with known multiple causes into subsets within which everyone with the injury and the marker is known to have been exposed to the same putative cause. This does not guarantee there are no other potential causes of this effect, but it would almost certainly be admissible evidence on specific causation', see Sanders et al (n 9) 900.
[12] *Guzman* (n 3).
[13] Ibid 3.
[14] Ibid.
[15] Ibid.
[16] Kirk Hartley and David Schwartz, 'A Lawyer's Guide to Genomics in Toxic Tort Cases: Part 1' *Law360* (online at 17 July 2018) < https://www.law360.com/articles/1063736/a-lawyer-s-guide-to-genomics-in-toxic-tort-cases-part-1>.
[17] Ibid.

genetic predisposition was seemingly noteworthy, as 'It appeared…that the genetics and genomic test results firmly established an alternative causation and may have aided the jury in reaching their verdict'.[18]

There have also been several other US personal injury cases where genetic testing has been compelled to determine the issue of medical causation.[19] These cases primarily involved birth-related (or early-childhood) medical negligence claims where the alleged injury typically involved a form of brain damage.[20] Although these cases are not toxic torts, they reveal the issues that courts consider when determining whether to order a genetic test and are often cited in toxic tort cases to reveal the willingness (or reticence) of courts to order genetic testing as a method of proof of causation or alternative causation.

There have been at least twenty-three personal injury cases in the US involving court-ordered genetic testing.[21] Eleven of these cases arose in the Federal Courts, four in the Illinois courts, three in the Californian courts, three in the courts of Delaware and two in New York. Eight of these cases involved toxic tort claims, primarily asbestos exposure.[22] The rest of the cases are primarily birth-related medical negligence claims.[23] In almost all these personal injury cases, the court compelled the plaintiff to submit to genetic testing. In only three of these twenty-

[18] Howard Jarvis, E. Paige Sensenbrenner and Laura Whitmore, 'Genetics and Genomics: Making the Invisible Visible' (2015) *For the Defense* 64, 79.

[19] *Bennett v. Fieser*, 1994 WL 542089 (D Kan, 25 February 1994) 2*; Dodd-Anderson v. Stevens*, 1993 WL 273373 (D Kan, 4 May 1993) 1; *Harris v Mercy Hospital* 596 N E 2d 160, 163 (Ill App, 1992); *Cruz v Superior Court* 17 Cal Rptr 3d 368, 369 (Cal App, 2004); *Bowen* (n 3); *Cutting v United States*, 2008 WL 5064267 (D Colo, 24 November 2008) 1; *Phillips v Christianacare Health System*, No 06-05-013 (Del Super Ct, 27 June 2008); *Simbolon v North Memorial Health Care,* No 27-CV-09-19205 (D Minn, 18 August 2010); *Guzman* (n 3); *Rogers-Duell v Chen* 974 NYS 2d 769 (NY Sup Ct, 2013); *Young v United States*, 2015 WL 5823025, 311 FRD 117 (D NJ, 2015); *Meyers v Intel Corp,* No D66911 (Del Super Ct, 11 June 2015); *Ortwein* (n 3); *Kaous v Lutheran Medical Center* 30 NYS 3d 663, 665-6 (NY App Div, 2016); *Kriloff v Providence Health & Services*, 2016 WL 11121002 (D Or, 12 January 2016) 1; *Fisher for XSF v Winding Waters Clinic, PC* 2017 WL 574383 (D Or, 13 February 2017) *aff'd* 2017 WL 4780616 (D Or, 22 October 2017); *Mandel v American Int'l Indus,* No BC644175 (LA County, 28 June 2017); *Burt v Winona Health Services*, 2018 WL 11222161 (D Minn, 26 February 2018); *Joseph Thrash v Boeing Co,* 2018 WL 2573097 (ND Cal, 2 March 2018) 3*; Burt v Winona Health*, 2018 WL 3647230 (D Minn, 1 August 2018); *Dustin W. Holsten, and Katlin A Holsten v Amalgamated Sugar Co. LLC, et al.*, No 18-L-1664 (Ill Cir, Madison Co, 2018)*; Kallal v Lyons* No 4-20-0319 (Il App, 4th Dist, 4 May 2021); *Cynthia B Cowger v Qualitex Co.*, No. 2018-L-012099 (Ill. Cir, Cook Co, 2021). A number of these cases appear to have settled (see e.g. *Holsten*).

[20] *Bennett* (n 19)*; Dodd-Anderson* (n 19)*; Harris* (n 19)*; Cruz* (n 19)*; Cutting* (n 19)*; Phillips* (n 19)*; Simbolon* (n 19)*; Young* (n 19)*; Kaous* (n 19)*; Fisher* (n 19)*; Burt* (n 19)*; Kallal* (n 19)*; Rogers* (n 19) involved an alleged delay in diagnosis of the Plaintiff's hydrocephalous when he was approximately 2 years old.

[21] See footnote 19.

[22] *Bowen* (n 19) (exposure to Benlate); *Guzman* (n 3) (exposure to radioactive material); *Meyers* (n 19) (exposure to pollutants); *Ortwein* (n 3) (asbestos exposure); *Thrash* (n 19) (asbestos); *Holsten* (n 19) (asbestos); *Cowger* (n 19) (asbestos); *Mandel* (n 19) (asbestos).

[23] See n 20.

three cases, the court denied the defendant's request for genetic testing.[24] Where the defendant requested testing of the plaintiff's parents, the courts typically denied such testing on the basis that one or both of the parents were not parties to the proceedings.[25]

US federal courts may order a party to submit to genetic testing where there is 'good cause' and the testing involves 'a *party* whose mental or physical condition…is *in controversy*' [emphasis added].[26] Pursuant to r 35(a) of the *Federal Rules of Civil Procedure* ('*FRCP*'),

> (1) *In General.* The court where the action is pending may order a party whose mental or physical condition—including blood group—is in controversy to submit to a physical or mental examination by a suitably licensed or certified examiner. The court has the same authority to order a party to produce for examination a person who is in its custody or under its legal control.
>
> (2) *Motion and Notice; Contents of the Order.* The order:
>
> (A) may be made only on motion for good cause and on notice to all parties and the person to be examined; and
>
> (B) must specify the time, place, manner, conditions, and scope of the examination, as well as the person or persons who will perform it.[27]

In *Schlagenhauf v Holder,*[28] the Supreme Court explained that the requirements of 'in controversy' and 'good cause'

> are not met by mere conclusory allegations of the pleadings nor by mere relevance to the case-but require an affirmative showing by the movant that each condition as to which the examination is sought is really and genuinely in controversy and that good cause exists for ordering each particular examination. Obviously, what may be good cause for one examination may not be so for another. The ability of the movant to obtain the desired information by other means is also relevant.[29]

In essence, mere relevance is insufficient to satisfy the good cause/in controversy requirements and there should be no other means by which the defendant could obtain the desired information.

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[24] *Fisher* (n 19); *Rogers* (n 19); *Cowger* (n 19). Note that the defendants in Cowger submitted a motion to reconsider on 26 January 2021.
[25] See, eg, *Cutting* (n 19) 4; *Young* (n 19) 123; *Meyers* (n 19); *Kallal* (n 19) 11-12. But note *Cruz* (n 19) 652 where the court ordered Plaintiff's mother to be tested even though she was not a party, because she was an 'agent'.
[26] *Federal Rules of Civil Procedure* (US) r 35.
[27] See also ibid r 35(b) pertaining to expert's reports.
[28] 379 US 104 (1964).
[29] Ibid 118.

A number of US states have adopted a version of r 35 of the *FRCP*. For example, §2032 of the *California Code of Civil Procedure* (‘*CCCP*’) maintains the ‘good cause’ and ‘in controversy’ requirements of r 35. In particular, § 2032.020 provides that

> (a) Any party may obtain discovery, subject to the restrictions set forth in Chapter 5 (commencing with Section 2019.010), by means of a physical or mental examination of (1) a party to the action, (2) an agent of any party, or (3) a natural person in the custody or under the legal control of a party, in any action in which the mental or physical condition (including the blood group) of that party or other person is *in controversy* in the action. [emphasis added].

Section 2032.320 provides the further requirement that

> (a) The court shall grant a motion for a physical or mental examination under Section 2032.310 only for *good cause* shown….
>
> (d) An order granting a physical or mental examination shall specify the person or persons who may perform the examination, as well as the time, place, manner, diagnostic tests and procedures, conditions, scope, and nature of the examination. [emphasis added].[30]

There is an additional condition in Californian personal injury cases that any examination of the plaintiff must ‘not include any diagnostic test or procedure that is painful, protracted, or intrusive’.[31] This is consistent with the approach of courts in other Australian and US jurisdictions where the invasiveness of medical examinations is also considered.[32]

In contrast to California, other US states have only adopted aspects of r 35 of the FRCP. For example, r 215(a) of the *Illinois Supreme Court Rules* provides that

> In any action in which the physical or mental condition of a party or of a person in the party's custody or legal control is *in controversy*, the court, upon notice and on motion made within a reasonable time before the trial, may order such party to submit to a physical or mental examination by a licensed professional in a discipline related to the physical or mental condition which is involved… The order shall fix the time, place, conditions, and scope of the examination and designate the examiner. [emphasis added].

[30] See also *Cal Code Civ Proc* § 2032.310.
[31] See ibid § 2302.220.
[32] See, eg, *Fisher* (n 19)*; Harris* (n 19)*; Cruz* (n 19); *PL by her tutor TL v Dunstan* [2020] NSWSC 297; *Pederson v Northern NSW Local Health District* [2020] NSWSC 741; *KF By Her Tutor RF v Royal Alexandra Hospital for Children known as the Children’s Hospital Westmead and Anor* [2010] NSWSC 891*; Wells by his tutor McGuffog v Hunter New England Local Health District* [2018] NSWSC 1877; *Plowman v Sisters of St John of God Inc* [2014] NSWSC 333. For more information, see Part 7.4 of this chapter.

Therefore, the plaintiff's condition should be 'in controversy' but there is no longer a requirement for 'good cause' under Illinois law.[33]

7.1.2. Australian Law – An Overview

Although there have not yet been any Australian toxic tort cases involving court-ordered genetic testing, there have been a small but growing number of Australian cases where personal injury plaintiffs refused to comply with the defendant's request for genetic testing and were subsequently ordered to submit to the testing.[34] These cases have all arisen in the New South Wales Supreme Court. Most of these cases involved plaintiffs alleging that their disabilities (typically involving cerebral palsy[35] or autism[36]) were due to birth-related injuries, such as hypoxia-induced brain damage, caused by the defendant's negligence. At least two of the cases involved a motor vehicle accident claim.[37]

The defendants in all these personal injury cases requested that the plaintiffs undergo genetic testing to determine whether genetic predisposition was a cause of their injury.[38] In other words, defendants sought to explore whether the plaintiffs could have been genetically predisposed to their disabilities. In each of these cases, the court ultimately granted the

[33] *Illinois Supreme Court Rules*, r 215 Committee Comments.
[34] *KF By Her Tutor RF v Royal Alexandra Hospital for Children known as the Children's Hospital Westmead and Anor* [2010] NSWSC 891; *Plowman v Sisters of St John of God Inc* [2014] NSWSC 333; *Prudence McDonald v Dr Ng;; Matthew McDonald by his tutor Prudence McDonald v Dr Ng* [2018] NSWSC 1050; *Sharif Zraika by his tutor Halima Zraika v Walsh* [2014] NSWSC 1774; *Wells by his tutor McGuffog v Hunter New England Local Health District* [2018] NSWSC 1877; *PL by her tutor TL v Dunstan* [2020] NSWSC 297; *Pederson v Northern NSW Local Health District* [2020] NSWSC 741. See also, David Hirsch, 'Important Cases in Medical Negligence' [2019] 153 *Precedent* 4.
[35] *KF* (n 34); *Plowman* (n 34); *Sharif* (n 34); *Prudence* (n 34).
[36] *PL* (n 34); *Pederson* (n 34); *Wells* (n 34).
[37] *Sharif* (n 34). One of the other cases also involved a motor vehicle accident claim, that was heard together with the medical negligence claim, *Wells* (n 34).
[38] The types of genetic testing requested/ordered in these cases typically involved WGS, WES and microarrays: *Sharif* (n 34); *Pederson* (n 34); *PL* (n 34); *Wells* (n 34); *Prudence* (n 34). *KF* (n 34) is the oldest case (2010) so the order only involved microarrays and single-gene analysis. *Plowman* (n 34) only involved microarray (array CGH). Some defendants also requested a range of other tests, including trio sequencing (*Sharif* (n 34)) or testing for a specific condition, e.g. Fragile X (*PL* (n 34)) testing. In some cases, the requested testing included a very broad provision allowing for 'any other tests relevant to [or 'appropriate for'] the investigations of the genetic cause of the plaintiff's condition' but this 'wide-ranging' part of the defendant's request was ultimately dismissed by the court: *Sharif* (n 34) [22], [51] (Defendants agreed that testing would not extend to 'any other tests appropriate for the investigation of a genetic cause of the plaintiff's condition'); *PL* (n 34) [3], [87], [91] (Court held that that the request for 'any other tests relevant to the investigations of the genetic cause of the plaintiff's condition' was 'too wide-ranging'). In a few of these cases, the plaintiff had already undergone some genetic testing (such as karyotype testing (*Prudence* (n 34) [15][18]); and/or testing for a specific syndrome/s[38]) prior to the court ordering further testing: *Prudence* (n 34) [17] (Plaintiff had already undergone testing for Rett and Angelman Syndrome, Smith-Lemi-Opitz Syndrome and Fragile X syndrome); *PL* (n 34) [63] (Plaintiff had already undergone testing for VACTERL syndrome).

defendant's motion to compel genetic testing of the plaintiff. Although these cases are primarily medical negligence claims, the principles can easily be extrapolated to toxic tort cases, especially by revealing how courts respond to requests for genetic testing in personal injury cases.

The law in NSW provides that courts may order a party to submit to a medical examination, including genetic testing, where that party's 'physical or mental condition is relevant to a matter in question'.[39] This order may be made pursuant to pt 23, div 1 of the *Uniform Civil Procedure Rules 2005* (NSW) ('*UCPR*').[40] An order for medical examination encompasses 'orders for tests including blood tests, x-rays, CAT scans and MRIs'.[41] It is 'common ground' that medical examinations extend to genetic testing.[42] In particular, r 23.4 stipulates that:

> (1) The court may make orders for medical examination, including an order that the person concerned submit to examination by a specified medical expert at a specified time and place.
>
> (2) If the court orders that the person concerned submit to examination by a medical expert, the person must do all things reasonably requested, and answer all questions reasonably asked, by the medical expert for the purposes of the examination.

The term 'medical examination' is defined as 'any examination by a medical expert'[43], excluding rehabilitation assessments.[44]

If an individual does not submit to a court-ordered medical examination, the court is provided the broad discretion to make any 'judgment or…order as it thinks fit'.[45] Rule 23.9 provides that:

> (1) If a party makes default in compliance with this Part, or a notice or order under this Part, the court may give or make such judgment or such order as it thinks fit, including--
>
> > (a) if the party in default is a plaintiff, an order that the proceedings be dismissed as to the whole or any part of the relief claimed by the party in the proceedings, or

[39] *Uniform Civil Procedure Rules 2005* (NSW) ('*UCPR*') rr 23.1, 23.4.
[40] For equivalent rules in other Australian states, see, eg, *Supreme Court (General Civil Procedure) Rules 2005* (Vic) rr 33.01-33.12; *Uniform Civil Rules 2020* (SA) rr 112.9-112.10; *Supreme Court Rules 1987* (NT) rr 33.01-33.13. Note that the courts retain the discretion to dispense with procedural rules, see, eg, *Civil Procedure Act 2005* (NSW) r 14.
[41] *Wells* (n 34) [37]; *Rowlands v State of New South Wales* (2009) 74 NSWLR 715, 726, 730.
[42] *PL* (n 34) [37].
[43] Where a 'medical expert' is defined as including a 'dentist, medical practitioner, occupational therapist, optometrist, physiotherapist and psychologist'.
[44] *UCPR* (n 39) r 23.1(2).
[45] Ibid r 23.9(1).

> (b) if the proceedings were commenced by statement of claim and the party in default is a defendant, an order that the party's defence be struck out and that judgment be given accordingly.
>
> (2) If a person for whose benefit relief is being claimed, not being a party, makes default in compliance with this Part, or an order under this Part, the court may give such judgment, or make such order, as it thinks fit, including an order that the proceedings be dismissed as to the relief so claimed.
>
> (3) This rule does not limit the powers of the court to punish for contempt.

Therefore, if a plaintiff refuses to submit to a medical examination, their case could be stayed or dismissed and they could also be punished for contempt.[46]

Before requesting a court-ordered medical examination, defendants will typically serve a notice on the plaintiff requiring them to attend for medical examination.[47] The notice must 'be in the form of a request that the person concerned submit to examination by a specified medical expert at a specified time and place'.[48] Moreover, the defendant must pay to the plaintiff 'a reasonable sum to meet the travelling and other expenses…of and incidental to the medical examination, including the expenses of having a medical expert chosen by the person [to] attend the examination'.[49] If the plaintiff defaults in compliance with the notice, this will trigger r 23.9 of the *UCPR* and the court is able to make 'such order as it thinks fit' including an order compelling the medical examination.[50]

Regardless of jurisdiction, there are several commonalities among the approaches of courts requested to compel genetic testing. In determining whether the 'good cause' and/or 'in controversy' requirements have been met, US courts have considered a range of issues including privacy, personal inviolability, the purpose and reliability of the requested tests, the safety of the proposed tests and whether the requested tests involve only a 'party' to the instant litigation. Similarly, NSW courts have considered these issues when determining whether the proposed testing 'sheds light on the issue of causation'.

As a result of the steady rise in the number of cases involving genetic evidence, it is hardly surprising that several scholars have emphasised the importance of legal practitioners and litigators familiarising themselves with genetic testing. For example, as early as 1999, Weiss

[46] Prior to the promulgation of these rules, NSW courts 'had no power to order a person to submit to a medical examination, but could [only] direct that an action be stayed unless the plaintiff submitted to examination by doctors nominated by the defendant', see *Kurnell Passenger and Transport Service Pty Limited v Randwick City Council* (2009) 230 FLR 336, 354-355; [2009] NSWCA 59 [79] quoted in *Wells* (n 34) [33].
[47] *UCPR* (n 39) r 23.2.
[48] Ibid.
[49] Ibid r 23.3.
[50] Ibid r 23.9.

et al maintained that 'the litigator must be familiar with the types of tests that are appropriate to address the issues in each case and he or she must be comfortable discussing, in the courtroom, the methods used, their strengths and weaknesses, and the implications of the results generated from them'.[51] Almost twenty years later, Marchant also concluded that 'plaintiffs attorneys may soon have an ethical duty to notify their clients whose health is at issue that they may be required to submit to genetic testing in pursuing their claims'.[52] Likewise, in 2020, Hirsch and Amor observed that 'one can now expect defendants to require the plaintiff to submit to [genetic] testing', particularly in cases involving conditions with unknown aetiology, such as cerebral palsy.[53] It is likely that genetic testing will become routine in personal injury cases (including toxic torts) in the near future.

The increasing reliance on genetic testing generates several ethical, legal and social implications ('ELSI').[54] In order to unpack these issues in more detail, the remainder of this chapter will analyse how courts have managed requests for genetic testing in toxic tort cases and consider whether the approaches of the courts align with the concerns of scholars relating to reliability, privacy, stigma, and efficiency.

7.2. Reliability

7.2.1. Literature

The varying reliability of genetic testing has been a source of significant contention among legal scholars. As Ramos et al explain, 'Because much of the science of genetic and particularly genomic evidence is still unsettled, it is particularly difficult for judges to evaluate when and how such evidence will prove relevant to the courtroom'.[55] Marchant observes that,

[51] Randi Weiss et al, 'The Use of Genetic Testing in the Courtroom' (1999) 34(3) *Wake Forest Law Review* 889, 913.
[52] Marchant (n 1) 22. He goes on to highlight that 'Given the potential usefulness of such genetic data for either proving or disproving causation, it is likely that both plaintiffs and defendants will increasingly seek to obtain and introduce such evidence... One expert has even suggested that it should become "standard practice" for defendants to seek genetic testing of plaintiffs in order to identify potential alternative causes', ibid 23.
[53] David Hirsch and David Amor, 'Exome and Genome Sequencing in Litigation' (2020) (156) *Precedent* 15, 18.
[54] See, eg, Sarah Vallance and Margaret Brain, 'The Appropriateness of Genetic Testing in Cerebral Palsy Cases' (2016) (133) *Precedent* 4, 5.
[55] Edward Ramos et al, 'Genomic Test Results and the Courtroom: The Roles of Experts and Expert Testimony' (2016) 44 *The Journal of Law, Medicine & Ethics* 205, 211-12. As Allison Hite explains, 'trial court judges share a long history of evaluating scientific evidence for admissibility purposes, and the Federal Rules of Evidence require that they "ensure that any and all scientific testimony or evidence admitted is not only relevant, but reliable"', Allison Hite, 'Who's to Blame: How Genetic Information Will Lead to More Accurate Decisions in Toxic Tort Litigation' (2012) 63(4) *South Carolina Law Review* 1031, 1048.

despite this uncertainty, 'Given the often substantial stakes and one-time nature of toxic tort litigation, litigants will likely seek to use potentially helpful data even if its significance is not yet adequately understood'.[56] Hoffman and Rothenberg add that there is a real risk that courts 'may give these genetic test results more weight than they deserve because the tests appear definitive when, in actuality, they may be only mildly predictive of a genetic condition'.[57] In other words, although genetic testing could reveal a precise diagnosis, it could also simply reveal a pre-symptomatic, predictive diagnosis.

Kording and DuMontelle go one step further and suggest that 'because the results of genetic testing are predictive in nature, they are speculative, and, as such, not relevant',[58] 'inherently unreliable'[59] and should be inadmissible.[60] They elaborate that, due to the predictive nature of genetic testing, 'there is a colossal difference between the existence of an expressed condition, either diagnosed or in full-blown stages, and a possibility, a maybe or a potential disease'.[61] They therefore maintain that courts should not be afforded the broad discretion to order genetic testing simply because 'the plaintiff has a family history of any genetic-based affliction'.[62]

While it is true that defendants should not be allowed to embark on a fishing expedition, this does not warrant a ban on all genetic testing. Defendants should clearly not be allowed to

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[56] Marchant (n 1) 26.

[57] Hoffman (n 2) 873. Although it should be noted that, in their survey, Hoffman and Rothenberg discovered that 'Where…the tests were to be used for predictive purposes, the judges seemed skeptical and concerned about their potential power and persuasiveness. In final comments about the survey and about genetic testing generally, one judge said: "we're scared of it because it's a new technology"', see ibid, 912-913.

[58] Niccol Kording and Janine DuMontelle, 'An Overview of Admissibility of Genetic Test Results in Federal Civil Actions: An Uncertain Destiny' (1998) 19(4) *Whittier Law Review* 681, 683. Similarly, Professor Steve Gold highlights that:

> The numbers alone are daunting: within the 30,000 to 40,000 genes in the human genome, researchers have identified more than ten million single nucleotide polymorphisms ("SNPs"), and millions more may exist. But the difficulties go beyond the sheer numbers of genes, alleles, diseases, and combinations thereof. Even with technological advances, it has been argued that "[m]ost reported genetic associations have been false positive results,"' and others have been valid but overstated. For many genetic polymorphisms, whether the high-risk allele leads to disease depends on other genes… To the extent that genetic factors themselves confer risk of disease, they may help to explain a paradox that has plagued the assessment of causation in toxic tort cases: the existence of "background" risk, or the incidence of disease absent known exposure. Genetic factors, however, "by themselves are thought to explain only about 5%" of the incidence of cancer. Beyond the interaction of susceptibility genes with an individual's other genes and epigenetics, a further interaction, exogenous to the individual, is also critical: interaction with the environment,"' which affects both genes"' and epigenetic factors. [citations omitted]

Steve Gold, 'The More We Know, the Less Intelligent We Are – How Genomic Information Should, and Should Not, Change Toxic Tort Causation Doctrine' (2010) 34(2) *Harvard Environmental Law Review* 369, 387-8.

[59] Kording and DuMontelle (n 58) 698.

[60] Ibid 699.

[61] Ibid 691. See also ibid 699.

[62] Ibid 693.

probe a plaintiff's genome without a clear indication of the condition or gene mutation they expect to find. However, specific and scientifically justified[63] genetic testing could help the truth-seeking mission of the court. As both Professors Anthony Niedwicki and Gary Marchant explain, the courts should always consider 'the specifics of the tests'[64] to avoid ordering tests that are 'overly intrusive', 'inexact in their results and are open to several interpretations'. [65]

The accuracy and reliability of genetic tests inevitably varies depending on the genetic condition at issue.[66] Some genetic test results could cause more harm than good, by simply confusing the court. As genetic testing has a predictive function, it is not necessarily well matched with the demands of the causation inquiry because causation is a retrospective inquiry not a predictive inquiry. For example, it is particularly difficult to attempt to predict the probability of the plaintiff developing a multifactorial disorder. Multifactorial disorders are caused by gene-environment interactions, so they are by their very nature much harder to predict compared to a monogenic (single gene) disorder or even a polygenic (multiple genes) disorder.[67] Genetic testing is usually more accurate in determining the probability of developing monogenic or polygenic disorders because the manifestation of the disorder does not depend on environmental factors. It is caused by genes and genes alone.

Even monogenic and polygenic disorders are problematic. For example, the genetic test might be able to accurately predict the probability of developing a disease, but it will usually be *unable* to account for how severe these symptoms will be and when the symptoms will occur, if at all.[68] As Rothstein explains, 'genetics is not a crystal ball' and 'genetic technology can, at best, assign a broad range of risk. The only true test is the test of time'.[69]

The reliability of health-related genetic tests will continue to be a subject of debate in the courts. Ramos et al explain that genetic testing 'and our ability to interpret genomic data are enabling an extraordinary rate of discovery regarding the relationship between human genetic variation

[63] Testing would satisfy this threshold so long as defendants have provided a clear indication of the condition or genetic trait they expect to discover.
[64] Anthony Niedwicki, 'Science Fact or Science Fiction? The Implications of Court-Ordered Genetic Testing Under Rule 35' (2000) 34 *University of San Francisco Law Review* 295, 309; *Bennet* (n 19); *Dodd-Anderson* (n 19). See also, eg, *Harris* (n 19); *Kaous* (n 19).
[65] Marchant (n 1) 26-7; Niedwicki (n 64) 308. Jennifer Champagne similarly notes that 'even scientific developments are the result of human activity and remain "subject to people's assumptions, preconceptions, and biases"', Jennifer Champagne, 'Genetic Testing and Testimony in Toxic Tort Litigation' (2011) 13(1) *North Carolina Journal of Law & Technology* 1, 19.
[66] Niedwicki (n 64) 313.
[67] Mark Rothstein, 'Preventing the Discovery of Plaintiff Genetic Profiles by Defendants Seeking to Limits Damages in Personal Injury Litigation' (1996) 71(4) *Indiana Law Journal* 877, 882-4.
[68] Niedwicki (n 64) 313, 298, 311-12; Hoffman (n 2) 896-7.
[69] Rothstein (n 67) 882.

and health, but the incorporation of such research into practice, much less trial and evidence, is still in its nascent stages'.[70] Indeed, there are still very many genetic variants of unknown significance where the functional importance of the genetic variant is unknown and/or is unable to be conclusively linked with a disease.[71] So, we know these genes have a variation but we do not know the significance of this variation. It could be pathogenic (disease-causing) or it could be completely benign (having no impact whatsoever on the development of disease). As Hirsch and Amor ask, 'Could [a variant of unknown significance] be enough to persuade a judge that the plaintiff has not made out their case? Will the plaintiff have to negate the possibility of a genetic cause of their [condition]? What if they can't – because nobody can?'[72] These are crucial questions that will continue to pervade the courts in the coming years.

In addition, genetic test results can be subject to a variety of different interpretations, depending on the expert analysing the results. Genetic test results provided to the court could contain both relevant and irrelevant or even misleading information. Courts are faced with the difficult task of not only evaluating the quality of the information but also the qualifications of the expert analysing the results.[73]

Courts inevitably *must* consider the scientific value, validity or utility of the genetic test and the nature of the genetic trait or condition at issue. Plaintiffs have put their health at issue by alleging that the defendant' negligence caused their illness – it is only right that defendants should be allowed to test the plaintiff's case by exploring alternative causes of the plaintiff's condition. If courts admit genetic evidence to support causation, they cannot then refuse defendants the similar right to use genetic evidence to dispute causation. Testing should always be appropriately confined to an examination which is relevant to the issues in the proceedings. For example, sometimes a single gene test, gene panel, microarray or whole exome sequencing would suffice and the greater complexity and heightened privacy and stigma concerns associated with whole genome sequencing would simply be unnecessary. To limit the scope of testing, the plaintiff could only be tested for particular genetic marker/s, rather than testing the whole genome and revealing to the plaintiff and/or defendant genetic information that goes beyond what is strictly relevant to causation in the case.

To ensure consistency and fairness, a framework/guidelines would be a suitable means of guiding the courts in the use of their discretion. Indeed, Ramos et al conclude that 'since the

[70] Ramos et al (n 55) 228.
[71] Ibid 210; Hirsch (n 53) 15.
[72] Hirsch (n 53) 18.
[73] Ramos (n 55) 227.

scope of large-scale genetic and genomic testing can be vast, an overview of key genetic testing frameworks is useful when determining how one might assess their validity and utility when proffered as expert evidence'.[74] In particular, Ramos et al felt that 'it is timely to provide a framework for understanding how uncertainty about genetic and genomic tests influences evidentiary considerations in the court room'.[75] Similarly, Hoffman and Rothenberg concluded that a framework is crucial to ensure that, when evaluating whether to compel genetic testing, 'Judges…consider…the scientific value or utility of the test [and] the nature of the genetic trait or condition'.[76] This thesis supports calls for a framework or Reference Guide, and provides an outline of a proposed framework in Chapter 8.

7.2.2. US Case Law

The US courts have often considered the reliability of genetic testing and reached a variety of different conclusions. In *Rogers,* the court denied the defendant's request for genetic testing partly due to the absence of any argument by the defendant as to the reliability of the proposed testing.[77] This was a case where the plaintiff alleged their condition was the result of a failure to diagnose and treat their hydrocephalous. The court observed that 'defendants have not specified the type of genetic test they wish to employ nor placed any limitation on the information they would collect'.[78] The court went on to conclude that

> While DNA testing for identification purposes is ubiquitous, defendants' proposed testing, to determine the genetic cause of a disability, is uniquely novel… Defendants submit a single hearsay sentence, made by their attorney, to establish their need for genetic testing. He states that the defendants' pediatric neurologist "suspects there is a genetic cause for [plaintiff's] presentation, and he noted that the child has several anatomical dysmorphic features that support his theory that a genetic condition is responsible for the child's overall presentation."…even if accepted for its truth, defendants' attorney offered an insufficient explanation of the test, its scientific reliability or the genetic condition suspected. Moreover, his recitation of what the pediatric neurologist "suspect[ed]" renders his allegations speculative at best.[79]

The court refused to order the testing because the defendants had failed to clearly identify the nature of the proposed testing and the specific genetic condition at issue.

[74] Ibid 210.
[75] Ibid 205.
[76] Hoffman (n 2) 905-6. See also Niedwicki (n 64) 348 where Niedwicki suggests that courts should consider the admissibility of the future test results before determining whether the proposed testing should be ordered.
[77] *Rogers* (n 19).
[78] Ibid 296-7.
[79] Ibid 297-8.

The court in *Fisher* followed a similar line of reasoning when they denied the defendant's request for genetic testing.[80] *Fisher* was a birth-related medical negligence claim where the plaintiff allegedly suffered brain damage, developmental/cognitive delay, learning and physical disabilities. The defendant sought an order compelling the plaintiff to submit to genetic testing to confirm whether their 'impairments are more likely than not the result of a genetic condition unrelated to prenatal care…including by conducting [WES]'.[81] The plaintiff submitted that the defendant's expert 'testimony is deficient for failing to identify specific genetic syndromes or conditions for which defendants seek testing'.[82] The plaintiff's expert suggested WES:

> uncovers vast amounts of genetic information that has nothing to do with the potential genetic syndrome… He characterizes WES technology as "so new and the experience so limited" that many insurers consider it "investigational and experimental" and so do not cover it… He states that WES is "not considered standard-of-care genetic testing in children for whom the remote possibility of a genetic diagnosis has been raised… Accordingly…(WES) is unlikely to determine the cause of [Plaintiff's] brain damage."[83]

The court agreed with the plaintiffs and observed that the defendants 'have not shown that the near entirety of [Plaintiff's] genome, as WES [Whole Exome Sequencing] would assay, is in controversy. WES has the potential to uncover genetic predispositions to numerous conditions unrelated to [P's] known injuries, such as cancer, cardiac arrhythmias, neurologic disorders, and metabolic disorders'.[84] The Court found that the defence expert's 'vague testimony regarding a possible, though unidentified, genetic cause of [Plaintiff's] condition [was] particularly troubling'.[85] The Court maintained that the defence needed to specify 'a particular genetic condition to identify and confirm'.[86] They concluded that the plaintiff's expert was 'more persuasive than' the defendant's expert in relation to the reliability of the proposed test.[87] The court also held that the inability to compel the plaintiff's relatives to submit to genetic testing 'undercut[s] the purported value of WES, and thus weigh[s] against the Court's compelling plaintiff to submit to it'.[88] Although trio sequencing can be more powerful[89] than

[80] *Fisher* (n 19).
[81] Ibid 4.
[82] Ibid 6.
[83] Ibid 7-8.
[84] Ibid 11.
[85] Ibid 15.
[86] Ibid 20; See also ibid 19.
[87] Ibid 16; See also ibid 21.
[88] Ibid 18-19.
[89] See, eg, Michaela Kuhlen, 'Family-based germline sequencing in children with cancer' (2019) 38(9) *Oncogene* 1367, 1367: 'In contrast to sequencing only single index patients, family-based NGS of the germline is a very powerful tool for providing unique insights into inheritance patterns (e.g., DNMs, parental mosaicism) and types of aberrations (e.g., SNV, CNV, indels, SV)'.

individual sequencing, courts should not decline to order genetic testing of an individual plaintiff simply because the parents decline to be tested themselves. This is because genetic testing of a single plaintiff can still provide probative evidence of causation.[90]

Conversely, in *Burt,* the court twice repeated that they were faced with 'a close call' but ultimately concluded that the defendants had established good cause for the requested testing.[91] *Burt* is a birth-related medical negligence claim where the defendant sought genetic testing to explore potential genetic causes of the plaintiff's injuries. In this case, the defendant's expert was able to identify several genetic conditions that could have caused the plaintiff's harm, and was also able to point to the plaintiff's family history in order to justify genetic testing.[92] There was no need for the defendants to prove 'their case on the merits at this stage of the litigation'.[93]

The courts in *Thrash* and *Ortwein* reached similar conclusions to *Burt. Thrash* involved a case where the plaintiff claimed asbestos exposure was the cause of their mesothelioma, but the defendant sought genetic testing to rule out the *BAP1* gene as a cause of the plaintiff's harm.[94] Mesothelioma has long been argued to be a signature disease, only caused by asbestos exposure, but defendants are increasingly introducing gene mutations (such as *BAP1*) as possible causes of mesothelioma.[95] In *Thrash,* the plaintiff relied on expert testimony alleging that the *BAP1* gene 'does not cause cancer but…renders a person more susceptible to carcinogens'.[96] The court held this

> argument that a test showing the presence of BAP1 cannot prove lack of causation as a reason to deny the test is not persuasive. [Plaintiffs] argue that any increase in his susceptibility would be irrelevant and inadmissible, because the fact that a [Plaintiff] is more susceptible to injury does not relieve a tortfeasor from liability if the tortious conduct is still the proximate cause of [Plaintiff's] injury.[97]

The court observed that 'In effect, [Plaintiffs] are asking the Court to determine that their experts are more credible than [Defendants] expert, and to limit discovery based on that determination'.[98] The court determined that such a course of action was inappropriate and the test should be ordered because 'based on the report of [Defendant's] expert…the blood sample

[90] Several courts have ordered genetic testing of a plaintiff even where trio sequencing is unavailable, see, eg, *Prudence* (n 34) [50]; *Pederson* (n 34) [18].
[91] *Burt* (n 19) 6, 9.
[92] Ibid 6.
[93] Ibid 5.
[94] *Thrash* (n 19).
[95] See e.g, *Ortwein* (n 19)*; Thrash* (n 19)*; Holsten* (n 19)*; Cowger* (n 19).
[96] *Thrash* (n 19) 11.
[97] Ibid 10.
[98] Ibid 11, 'The court will not do so'.

would provide information that is highly relevant to the issue of causation'.[99] Similarly, *Ortwein* involved a case where the plaintiff alleged asbestos exposure caused their malignant mesothelioma and defendants argued the *BAP1* gene was a potential alternative cause.[100] In this case, the plaintiff submitted that the Court should conduct a preliminary hearing 'to determine whether [the defence's] expert opinion testimony is admissible in support of this discovery motion'.[101] However, the court refused.[102] The court's reasoning was that 'This presents fact specific issues of causation… The court will not resolve these issues on this motion', presumably because this was a matter for trial.[103] These cases demonstrate that US courts will order genetic testing so long as the defendant clearly specifies the relevant genetic condition or trait.

7.2.3. Australian Case Law

Some Australian courts have addressed the issue of reliability of genetic test results by determining that reliability is a matter for trial. In other words, the motion to compel genetic testing only requires courts to consider whether the test will 'shed light' on the issue of causation and issues of reliability can be determined by the parties' experts at trial. For example, in *Prudence,* the Court held that 'The parties are in a position to seek medical expert opinion as to the reliability of the test. In the event the [testing] sheds no light on [plaintiff's] condition, both parties may choose not to rely upon it' or 'to object to the tender of the report based on their experts' opinion'.[104] That case involved alleged medical mismanagement in the period leading to (and/or during) the final stages of the plaintiff's birth. The defendant argued the plaintiff's injuries, which included brain damage, were the result of genetic abnormality and requested additional genetic testing of the plaintiff and their mother (who was also a party to the proceedings).[105] The court ordered the requested testing and concluded that if the testing 'is not permitted, the defendant will be denied the opportunity to investigate a real central issue

[99] Ibid.
[100] *Ortwein* (n 3).
[101] Ibid 5. The plaintiff also suggested that increased susceptibility merely renders the Plaintiff an eggshell Plaintiff but does not relieve Defendant of liability so it is irrelevant, see ibid 10-11.
[102] Ibid 5.
[103] Ibid 18.
[104] *Prudence* (n 34) [78]-[79]. The court held that 'Once the report is served [following the genetic test], either party can object to it being tendered in evidence at trial', [77].
[105] The plaintiff had already had some genetic tests e.g. karyotyping.

in dispute, namely causation'.[106] This aligns with the US judgment in *Burt*, where the court held the reliability of the test was ultimately a matter for trial.[107]

Some Australian courts have explicitly considered the reliability of the proposed genetic testing. For example, in *PL*, the plaintiff alleged that their injuries, such as ASD and epilepsy, were caused by the defendant's negligent delay in diagnosis.[108] The defendants argued there was a possible genetic cause and sought genetic testing. Counsel for the plaintiff submitted that WES/WGS is 'unlikely to yield a result because it is designed to detect monogenic disorders…and therefore not helpful in detecting genetic factors that contribute to multifactorial disorders'.[109] In response, counsel for the defendant relied on an expert report suggesting that 'there are many causes of [ASD]…Causes include chromosomal abnormalities and single gene disorders. There is generally agreement that chromosomal microarray [and fragile X testing] should be done for every child with [ASD]'.[110] This expert report also noted that negative results do not 'exclude a genetic cause for [ASD] since the cause may be in one of the genes examined but cannot be detected for technical reasons or in a gene that was not examined as that gene has not yet been discovered as a cause of genetic disorder'.[111] The court in *PL* was persuaded by the defendant's experts, concluding that

> It's evident that…the aetiology of ASD is uncertain… medical science is prepared to say that it is possible that there is a connection between [P's] birth injury and his ASD. Equally medical science says it is possible that ASD has a genetic cause. The two may not be mutually exclusive…medical science may look for something approaching certainty before a scientific deduction is made. This is not the way the ordinary courts of justice operate. But it follows from this that there can be no objection to [D] undertaking the line of investigation proposed even though the science is not certain.[112]

The courts are therefore willing to order genetic testing 'even though the science is not certain'. This is because the legal standard of proof does not require certainty, it only requires that the facts supporting each element of the claim are 'more probable than not', or 'more *likely* than not'.[113]

Similarly, courts have not been inclined to accept the argument proposed by some plaintiffs that without other family members being tested, 'the result will be of a lower yield'.[114] For

[106] Ibid [77].
[107] Ibid [78]-[79].
[108] *PL* (n 34)
[109] Ibid [79], See also [62], [67]-[71], [74], [76].
[110] *Pederson* (n 34) [7].
[111] Ibid [8].
[112] Ibid [11]-[12].
[113] For more information on legal and scientific standards of proof, see Chapter 2.2.2.
[114] See eg, *Prudence* (n 34) [50]; *Pederson* (n 34) [18].

example, in the case of *Pederson*, the plaintiff alleged their Autistic Spectrum Disorder ('ASD') arose from the defendant's negligent medical treatment during the plaintiff's birth.[115] The defendant alleged there was a genetic cause to the plaintiff's ASD and sought a court order compelling the plaintiff to submit to genetic testing.[116] The court ordered the requested testing, noting that 'other members of the family have steadfastly decided against such participation [in genetic testing for the purposes of trio sequencing[117]]. I am not of the view that this devalues the procedure or renders it otiose'.[118] This sharply contrasts with the US case of *Fisher* where the Court held that the inability to test the plaintiff's relatives 'undercut[s] the purported value of WES, and thus weigh[s] against the Court's compelling plaintiff to submit to it'.[119] A potential explanation for this difference in approach could be that there is a greater emphasis on plaintiffs' interests in the US courts, as compared to the emphasis on administration of justice, including cost-efficiency, in NSW courts.[120]

In *Prudence,* counsel for the defendant explored the possibility of genetic testing producing ambivalent results.[121] Counsel submitted that 'if the result of the testing identifies a rare variant, the interpretation of that data may be difficult. However, the fact that an assessment of results may be difficult does not prevent a court from considering it and applying the court's usual process in considering medical data'.[122] Ultimately counsel for the defendant maintained that 'The mere existence of a difference in opinion is not sufficient to prevent the defendants from conducting an appropriate investigation'.[123] The Court ultimately agreed with the defendant's position.[124] The Court also emphasised that compelled genetic testing could actually produce evidence favouring the plaintiff's case:

> Once the whole genome testing has taken place, the result will fall into one of three categories:
>
> (a) 'it discloses no genetic abnormality or explanation for [P's] condition and therefore does not assist [D's] case'

[115] *Pederson* (n 34).
[116] Ibid [1]. The Court ultimately ordered Buccal swabs for the following testing: (a) Fragile X, (b) Array CGH, (c) WES, (d) WGS, see ibid [20].
[117] Trio sequencing involves genetic testing of the mother, father and child and it can be used to identify suspected genetic causes of disease, see, eg, Thaise Carneiro et al, 'Utility of trio-based exome sequencing in the elucidation of the genetic basis of isolated syndromic intellectual disability: illustrative cases' (2018) 11 *The Application of Clinical Genetics* 93; Marc Pauper et al, 'Long-read trio sequencing of individuals with unsolved intellectual disability' (2021) 29 *European Journal of Human Genetics* 637.
[118] *Pederson* (n 34) [18].
[119] *Fisher* (n 19) 18-19
[120] For more information, see Chapter 8.3.1 on recommendations for further research.
[121] *Prudence* (n 34) [66].
[122] Ibid.
[123] Ibid [67].
[124] See ibid [77]-[79]

(b) 'it gives ambivalent results or it does not proffer an opinion that supports a genetic abnormality, resulting in the report being neutral and perhaps unhelpful'

(c) 'it supports [D's] case that [P] has a genetic abnormality'[125]

Therefore, parties should be aware that the evidence could ultimately bolster the plaintiff's causation claim and undermine the defendant's expert 'who provided the ammunition to convince the court to compel the testing'.[126] For example, if the testing discloses no genetic explanation for the plaintiff's condition, then the plaintiff's case could actually be strengthened by ruling out genetics as a cause.

Overall, the reliability of the proposed genetic testing is a valid concern that has been raised by several plaintiffs' lawyers, but courts have typically concluded that reliability is a matter for trial. Courts will generally order the requested testing so long as it has the capacity to shed light on the issue of causation (under Australian law) or the plaintiff's physical or mental condition is in controversy and the testing is for a good cause (under US law). Courts *should* continue to compel testing so long as it meets this basic threshold and experts from both sides can then interpret the results and argue about these interpretations at trial. Reliability should typically not be an obstacle to any pre-trial motions to compel genetic testing.

Assuming the defendant has articulated the specific genes or genetic conditions they seek to explore, the testing will almost certainly be ordered. The report should be confined to the relevant genes/genetic condition at issue – this would lessen the impact of any stigma arising from unwanted or incidental findings. Then, once the results are available and the report is served, the parties can hire experts to interpret the raw data and reach their own conclusions as to the reliability of this information. In the event the testing sheds no light on the issue of causation or is likely to mislead or confuse the court, the parties may choose not to rely upon the report or they could object to the tender of the report based on their experts' opinion. If the report raises privacy/confidentiality concerns, the plaintiff could seek an order restricting the publication or disclosure of confidential evidence. In sum, genetic testing should be ordered so long as the test is directed towards causation of the plaintiff's injury and the defendant has

[125] Ibid [74]. Genetic test results, particularly in toxic torts, can be much more nuanced than simply revealing the presence/absence of a genetic abnormality or ambivalent results. In particular, in some circumstances, 'it is…possible that both the genetic condition and the [relevant] exposure [or negligence] could contribute to the plaintiff's symptoms', see Hoffman (n 2) 900. Poulter explains that in such situations, 'When it is not known whether the genetic variation facilitates toxic injury or is involved in an independent disease pathway, genetic testing will not assist causal analysis', see Susan Poulter, 'Genetic Testing in Toxic Injury Litigation: The Path to Scientific Certainty or Blind Alley?' (2001) 41(2) *Jurimetrics* 211, 213.
[126] Kording (n 58) 695.

identified a sufficient prospect that the findings of the proposed testing may reveal an underlying genetic trait or condition as an alternative cause.

7.3. Privacy

7.3.1. The Literature

Several scholars have expressed notable concern around the individual and familial privacy violations that could result from court-ordered genetic testing.[127] For example, Professor Mark Rothstein suggests that the defendant's desire to determine the validity of the plaintiff's claim should not automatically trump the plaintiff's privacy interests.[128] He highlights the 'public policy' reasons for this conclusion, such as the fact that genetic test results reveal 'information about the individual's relatives-past, present, and future'.[129] So, there is not only a general concern about how much can be learnt about the plaintiff from genetic testing, there is also the concern about what genetic testing of the plaintiff might reveal about their family.[130]

To some extent, these arguments reflect the notion of 'genetic exceptionalism', also known as 'genetic essentialism'. These terms encapsulate the notion that 'genetic information [is] so distinct in concept, practical implications, and moral import that it deserve[s] to be singled out from other types of health-related information'.[131] For example, Rothstein describes genetic information as 'touch[ing] the essence of humanity'[132] and highlights its 'enormous evolutionary, psychological, and social power'.[133] It is this perception that underlies Rothstein's views of genetic testing 'as an incursion on…privacy'.[134] Professor Anthony Niedwicki adopts a similar view when he purports that genetic information is inherently more

[127] See, eg, Rothstein (n 67); Niedwicki (n 64); Hoffman (n 2).
[128] See, eg, Rothstein (n 67) 895.
[129] Ibid 895-7.
[130] For an interesting discussion of when relatives might have a right to know and therefore a right to disclosure of confidential medical information, see, eg *ABC v St George's Healthcare NHS Trust* [2020] EWHC 455 where plaintiff's father had a genetic condition (Huntington's disease ('HD')) and his medical team (treating a related mental health condition that had led him to kill his wife) decided against disclosing that to the plaintiff who was pregnant and subsequently discovered that she also had the HD gene and there was a 50% chance she would have passed it on to her baby (she claimed she would have terminated the pregnancy had the genetic risk been disclosed to her). See also Michael Fay, 'Genetic risks, disclosure and foreseeable harm: An unanswered question after ABC v St George's Healthcare' (2016) 24 *Tort Law Review* 127.
[131] Thomas Murray, 'Is Genetic Exceptionalism Past Its Sell-By Date? On Genomic Diaries, Context, and Content' (2019) 19(1) *The American Journal of Bioethics* 13, 13.
[132] Rothstein (n 67) 896-7.
[133] Ibid 892.
[134] Ibid 894-5.

sensitive than other forms of medical information.[135] Professors Diane Hoffman and Karen Rothenberg also emphasise the apparently unique nature of genetic information when they assert that, 'Genetic tests reveal evidence of *immutable characteristics*'[emphasis added].[136]

Courts should be careful to avoid adopting the view that genetic information is inherently different from other forms of health-related information.[137] While acknowledging that 'genetic information has certain properties that warrant close attention', Professor Thomas Murray maintains that these properties do not launch genetic information 'into some unique universe of moral, legal, and policy concerns'.[138] He maintains that genetic data has 'its particular qualities that [deserve] to be understood and accommodated, but the similarities [are] even more important'.[139] In sum, 'genetic information [is] a sub-set of all health-related information' and should not be regarded 'as wholly distinctive in kind'.[140] Professors James Evans and Wylie Burke provide a helpful explanation of this point:

> The rest of the medical record is highly "identifying" in its own right, and many nongenetic diagnoses are immutable—for example, the diagnosis of multiple sclerosis or Alzheimer Disease. As these examples illustrate, the medical record contains much sensitive nongenetic information: in fact, we anticipate that most people would feel more comfortable sharing their CYP2C9 alleles with a third party than their social security number, previous hospitalizations, or history of testing for sexually transmitted diseases, all information likely to be found in the medical record. The purpose of the medical record is to provide specific and detailed medical information about a particular individual; by its nature it contains highly personal information… And while genomics applies a new technology to risk prediction, it does not necessarily provide information that is inherently different from the other predictors commonly used in health care, such as…family history.[141]

Despite his initial reservations, Rothstein ultimately adopts a similar view when he asserts that 'genetic testing to establish causation, narrowly defined and with a protective order,[142] should be permissible'.[143] So long as there is an adequate protective order prohibiting redisclosure of the genetic test results, evidence of the plaintiff's genetic profile should be discoverable when it is relevant to the issue of causation.[144]

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[135] Niedwicki (n 64) 338.
[136] Hoffman (n 2) 890-891.
[137] Murray (n 131) 14.
[138] Ibid.
[139] Ibid.
[140] Ibid.
[141] James Evans and Wylie Burke, 'Genetic Exceptionalism. Too much of a good thing?' (2008) 10(7) *Genetics in Medicine* 500, 500.
[142] Such as a protective order requiring the parties to keep the genetic information protected from disclosure outside the proceedings. For more on protective orders, see r 26(c) of *the Federal Rules of Civil Procedure* (US).
[143] Rothstein (n 67) 900.
[144] Ibid 899.

In contrast, Niedwicki argues that protective orders are insufficient to protect privacy. He maintains that

> a protective order is not likely to cover the situation in which an insurance company asks the applicant questions related to any known diseases or genetic defects. A court cannot issue a protective order allowing the person to lie or commit fraud while trying to obtain insurance. Even if a person refuses to answer a question about genetic conditions because of the protective order, the insurance company is likely to infer that a defect does exist and deny the application. The potential difficulty of obtaining insurance is a major reason people choose not to be genetically tested. Without any test results or any knowledge of a genetic disorder, the individual has no information to give to these entities.[145] [citations omitted]

This is certainly a valid concern, but it has been addressed (at least to some extent) through several relevant Insurance Standards and Codes which exclude many genetic test results from insurance underwriting.[146]

7.3.2. US Case Law

Despite acknowledging the plaintiff's privacy interests, many US courts have typically concluded that the benefits to the defendant outweigh any privacy concerns.[147] For example, in *Thrash,* the Court observed that 'While the act of drawing [the plaintiff's] blood is a relatively minor procedure, the test at issue here would reveal information about his long-term health and possibly, the health of [the plaintiff's] family members. The requested intrusion is therefore not trivial'.[148] Despite accepting that the plaintiff's 'expectation of privacy in his DNA is reasonable', the Court ultimately concluded that '[g]iven the potential significance of this test result', the 'Defendant's interest in obtaining this discovery outweighs [plaintiff's] privacy interests'.[149] In particular, the plaintiffs 'cannot be allowed to make these "very serious allegations without affording [Defendants] an opportunity to put their truth to the test"'.[150]

A similar conclusion was reached in the two cases of *Mandel* and *Burt.* In *Mandel,* a plaintiff alleged that asbestos exposure caused his mesothelioma.[151] In response to the defendant's request for genetic testing, counsel for the plaintiff argued that 'It's an extreme invasion of [the

[145] Niedwicki (n 64) 345.
[146] See eg, Australia's Moratorium on Genetic Tests in Life Insurance: Financial Services Council, *FSC Standard No 11: Moratorium on Genetic Tests in Life Insurance* (at 21 June 2019). Also California prevents life insurers from using predictive genetic testing as a condition for coverage: Underwriting on the Basis of Test of Genetic Characteristics, 761 Cal Ins Code §§ 10146–9 (1994); Sara Golru, 'Regulating the Use of Genetic Information in the Life Insurance Industry' (2020) 7 *UNSW Law Journal Forum* 1, 5, 8.
[147] See, eg, *Burt* (n 19) 7-8; *Thrash* (n 19) 10; *Mandel* (n 19) 12.
[148] *Thrash* (n 19) 10.
[149] Ibid 10-12.
[150] Ibid 10.
[151] *Mandel* (n 19).

plaintiff's] privacy rights, finding out that he has a genetic disposition or predisposition' but the court nevertheless ordered the requested testing.[152] In *Burt*, again the court ordered the requested testing, holding that 'The relevance of the plaintiff's genetic makeup outweighs the plaintiff's physical and privacy concerns relating to WES testing'.[153]

However, some US courts have placed great emphasis on the privacy interests of plaintiffs requested to undergo genetic testing. In denying the defendant's request for genetic testing, the Supreme Court of New York in *Rogers* referred to the 'vast scope of information accessible by genetic testing, and its potential misuse…the information about plaintiff that an unspecified genetic test would provide defendants is extraordinary'.[154] This genetic exceptionalism was also adopted by the US federal court in the case of *Fisher*.

The court in *Fisher* denied the defendant's requested testing, holding it was intrusive and overly broad.[155] The court appeared to suggest the testing amounted to little more than a genetic fishing expedition looking for any possible explanation rather than suggesting and testing for a particular genetic condition.[156] The court emphasised the 'sweeping invasion of…privacy' associated with WES.[157] The defendants submitted that the genetic test results can be interpreted 'in a very targeted fashion so that only conditions relevant to this lawsuit are disclosed. The family does not need to learn about other genetic conditions that [the plaintiff] or other family members may carry if they do not want this information'.[158] The court disagreed with the defendants and held that the

> potentially targeted disclosure of information does not satisfy plaintiff's, or the Court's, privacy concerns. Even if this genetic information is kept from X.S.F. and his family members for the time being, there is an invasion of privacy in the information having been gathered, and harm in the information simply existing. This information could well be disclosed against the family's wishes in the future, for instance, in conjunction with an insurance application, or as the result of a court proceeding or court order, or from a computer hack of electronic medical records... The Court is not persuaded that WES's potentially sweeping genetic revelations can successfully be limited through selective disclosure.[159]

Although these concerns are certainly valid, they could have been addressed through limiting the scope of the requested testing and implementing a protective order to restrict use and dissemination of the genetic test results. As the following paragraph reveals, there are a number

[152] Ibid 12.
[153] *Burt* (n 19) 7-8.
[154] *Rogers* (n 19) 295-7.
[155] *Fisher* (n 19).
[156] For a more detailed analysis of genetic fishing expeditions, see Chapter 7.5.
[157] Ibid 18.
[158] Ibid 23.
[159] Ibid 23-24.

of thorough steps that could be taken to limit privacy concerns in such cases. These steps are also outlined in Chapter 8 where a novel framework is proposed to guide the courts/litigants/legal professionals in understanding the benefits and drawbacks of genetic evidence. As Chapter 8 suggests, inconsistencies in the case law suggest there is a need for a framework to guide the court's decision-making, while ensuring some discretion is also maintained so that courts can still account for the nuances of a particular case.

In some cases, the courts have held that protective orders are sufficient to prevent any potential privacy violations. In *Ortwein,* the defendants submitted that the requested genetic testing of the deceased plaintiff's lung tissue would not violate their privacy because the plaintiff had 'placed the cause of her mesothelioma at issue by bringing this action' and the defendant 'sought only medical information that is directly relevant to the specific claim sued upon'.[160] The court ultimately ordered the testing on the basis that the genetic test results would be highly important and relevant to determining the validity of the plaintiff's claim.[161] However, the court also recognised the plaintiff's privacy concerns and issued 'a protective order to limit the "intrusiveness" of discovery and to avoid "unwarranted annoyance, embarrassment, or oppression"'.[162] The defendant was ordered to 'use the tissue sample and any and all information derived from the tissue samples solely for this case' and defence experts/attorneys 'cannot retain, use, or transfer [deceased plaintiff's] genetic information for potential use in further research…or subsequent litigation… [The defendants] must return or destroy the tissue sample and any and all information derived from the tissue sample at the conclusion of the case'.[163]

Similarly in *Burt,* the Court accepted that the plaintiff's 'privacy…concerns are valid. However…the stipulated protective order in this case is adequate to protect [plaintiff's] private genetic information from disclosure to third parties'.[164] Therefore, there are clear means of avoiding incursions on privacy, such as limiting the scope of the testing and/or the scope of expert reports and issuing protective orders restricting publication of the results.

[160] *Ortwein* (n 3) 9. The privacy interests in this case were complicated by the fact that the plaintiff had since deceased, see 13-15.
[161] Ibid 19.
[162] Ibid 19-20
[163] Ibid 19-20.
[164] *Burt* (n 19) 7.

7.3.3. Australian Case Law

The NSW Supreme Court has expressly considered privacy concerns when determining whether to order genetic testing.[165] For example, in *Pederson*, the defendant sought a court order compelling the plaintiff to submit to the 'taking of saliva samples for pathological testing for the purpose of genetic analysis'.[166] The Court ordered the requested testing but explained that the 'privacy of the plaintiff and the results of genetic testing [should] be maintained so far as it is within the power of the defendant to achieve that'.[167] The potential for misuse of genetic information was also recognised in *Prudence*.[168] The defendant requested additional genetic testing of the plaintiff and their mother (who was also a party to the proceedings).[169] The court ordered the requested testing and observed that the defendants 'agree that the report [concerning the genetic test results] is not to be used for scientific research unless the plaintiffs give their consent'.[170]

Some cases have gone one step further and raised the possibility of an order restricting publication of the test results. In *KF,* the plaintiff argued the defendant's negligent delay in diagnosis caused their brain damage.[171] The Court accepted the defendant's request for genetic testing of the plaintiff and noted:

> If any issue is raised by the [genetic] testing which causes concern about confidentiality of information, then it would be open to the parties to seek an order restricting publication. Of course, the content of any report served in the proceedings will be subject to the implied undertaking not to use information obtained by compulsory court process for a purpose other than use in the proceedings.[172]

Similarly in the case of *Plowman*, the court held

> the plaintiff submits that information of the kind which may be obtained, that is, information about the plaintiff's genetic structure, may, depending on its content, give rise to difficult and complex decisions about to whom the information ought be provided. That may be so, but whether it does or not, will depend on what the test results show. As well, if the plaintiff's tutor forms the opinion that the results actually throw up a difficult question, then the tutor is *able to make application to the Court for orders restricting the publication of the information* or, alternatively, should that be appropriate, permitting the publication of the material. This is *not a reason to refuse the order*, but may be a reason to reserve liberty to the plaintiff's tutor to apply for an appropriate order if so advised.[173] [emphasis added]

[165] See, eg, *Pederson* (n 34) [17]; *Plowman* (n 34) [84].
[166] *Pederson* (n 34) [1]. The Court ultimately ordered Buccal swabs for the following testing: (a) Fragile X, (b) Array CGH, (c) WES, (d) WGS, see ibid [20].
[167] Ibid [17].
[168] *Prudence* (n 34).
[169] The plaintiff had already had some genetic tests e.g. karyotyping.
[170] *Prudence* (n 34) [77].
[171] *KF* (n 34).
[172] Ibid [64].
[173] *Plowman* (n 34) [82].

This case involved allegedly negligent medical care provided to the plaintiff's mother at the time of plaintiff's birth, resulting in brain damage. The court ordered the requested genetic testing by the defendant, emphasising that the 'potential benefit to the defendant is significant' and the 'detriment to the plaintiff is not sufficient to tip the balance against ordering the [genetic] test'.[174]

Ultimately, the analysis of US and Australian case law reveals that courts are adopting a more 'genetic inclusivist' view, where genetics is treated in largely the same way as an order for any other medical examination.[175] However, it may be appropriate in some cases to make an order restricting publication or disclosure of the genetic test results to non-parties. It would also be appropriate to limit the scope of the testing, so that it only explores genetic variations that are relevant to the plaintiff's injury. As Hoffman and Rothenberg rightly argue, judges should consider privacy ramifications when evaluating requests to compel genetic tests.[176] Chapter 8 of this thesis calls for a framework to guide courts in determining how much weight should be given to privacy concerns in a given case.

7.4. Stigma & Trauma

7.4.1. Literature

In addition to privacy, one of the most prominent concerns associated with genetic information has historically revolved around the issue of stigma. These fears have also filtered through to the courtroom. In a 2007 survey of '104 circuit judges in Maryland', the judges showed 'reluctance to compel…genetic tests [due to] concerns about stigma'.[177] In particular, 'Judges were sensitive to situations where news of a genetic condition could be psychologically

[174] Ibid [82].
[175] It should also be briefly noted that the level of protection given to genetic privacy differs in US and Australian law. For more information on Australia's piecemeal state and federal privacy laws, see, eg, Margaret Otlowski and Dianne Nicol, 'The Regulatory Framework for Protection of Genetic Privacy in Australia' in Terry Sheung-Hung Kaan and Calvin Wai-Loon Ho (ed), *Genetic privacy: An evaluation of the ethical and legal landscape* (Imperial College Press, 2013); Lisa Eckstein et al, 'Australia: regulating genomic data sharing to promote public trust' (2018) 137(8) *Human Genetics* 583, 587; *Privacy Act 1988* (Cth) ss 6.2(d), 6FA(d), 16B(4), 95AA; National Health and Medical Research Council, *Use and Disclosure of Genetic Information to a Patient's Genetic Relatives under Section 95AA of the Privacy Act 1988 (Cth) – Guidelines for Health Practitioners in the Private Sector* (2014). For more information on genetic privacy laws in the US, see *Genetic Information Nondiscrimination Act* (GINA) Pub. L. 110–233, 122 Stat. 881 (May 21, 2008), 42 U.S.C. § 2000ff (2018); *Health Insurance Portability and Accountability Act* (HIPAA) 42 U.S.C. §§ 300gg-300gg-2 (2018), 45 C.F.R. pts. 160, 162, 164 (2018); the *Affordable Care Act* 42 U.S.C. §§ 18001–18122 (2018); Ellen Wright Clayton, et al, 'The law of genetic privacy: applications, implications, and limitations' (2019) 6(1) *Journal of Law and the Biosciences* 1.
[176] Hoffman (n 2) 905-906.
[177] Hoffman (n 2) 908.

devastating, as when there is no cure or treatment for it'.[178] However, assuming the condition was not 'lethal', 'the large majority of judges had no trouble compelling a test to prove or refute negligence as the *cause* of the plaintiff's injury, presumably because the plaintiff could terminate the case'.[179]

Legal scholars and practitioners have raised a number of psycho-social implications associated with court-ordered genetic testing.[180] This is because genetic testing carries the potential to reveal additional information that is only tangentially related or even entirely unrelated to the harm that is at issue in the litigation.[181] These scholars maintain that genetic conditions can stigmatise not only the individual diagnosed with the condition but also past, present and future blood relatives who may view the condition 'as a flaw in one's ancestors and a cloud hanging over future progeny for generations to come'.[182] This may lead to severe psychological trauma perhaps exacerbated by broader societal discrimination and feelings of being 'less worthy or unwanted by society'.[183] This additional information could breach the bioethical principle of nonmaleficence, by doing more harm than good, particularly where the plaintiff is 'being confronted with information that [they] preferred not to know'.[184]

Ordering plaintiffs to undergo genetic testing could also have a deterrent effect, resulting in plaintiffs withdrawing valid claims in the fear that they might discover an unwanted genetic condition that could affect not only themselves but also their blood relatives. This would also conflict with the bioethical principle relating to the 'right not to know' details of personal health status or genetic predispositions. Niedwicki suggests that when a court forces a plaintiff to undergo genetic testing 'for a disease that has no cure and no treatment…the court has provided the examinee with nothing less than death sentence'.[185]

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[178] Ibid.
[179] Hoffman (n 2136) 898-9.
[180] See, eg, Hirsch (53); Rothstein (n 67); Niedwicki (n 64).
[181] Mark Ellinger, 'DNA Diagnostic Technology: Probing the Problem of Causation in Toxic Torts' (1990) 3 *Harvard Journal of Law and Technology* 31, 33. See also Hirsch (n 53) 15 who maintains that the 'comprehensive nature' of genetic testing means that they 'carry a risk of incidental or secondary findings – genetic changes that are not the cause of the patient's presentation but are relevant to their health'.
[182] Rothstein (n 67) 894.
[183] Niedwicki (n 64) 344, 346.
[184] Rothstein (n 67) 897. See also Victoria Chico discussing the potential right not to know about genetic risk, Victoria Chico, 'Known Unknowns and Unknown Unknowns: The Potential and the Limits of Autonomy in Non-Disclosure of Genetic Risk' (2012) 3 *Journal of Professional Negligence* 162; Victoria Chico, *Genomic Negligence: An Interest in Autonomy as the Basis for Novel Negligence Claims Generated by Genetic Technology* (Taylor & Francis, 2011).
[185] Niedwicki (n 64) 295; see also 313: 'The results only give a person some insight into his or her future doom, while offering no hope for possible treatments or cures. For such diseases, the test results can simply be a death sentence, of which many individuals would prefer not to be made aware.'

These arguments are not far-fetched, as at least one court has faced the issue of compelling genetic testing where the plaintiff has a family history of an incurable and lethal disease.[186] In *Adacsi*, the plaintiff was injured in a house fire and sued the landlords of the house for negligence resulting in her debilitating injuries preventing employment.[187] The plaintiff had a significant family history of Huntington's Disease ('HD') which is an incurable genetic condition that radically reduces a person's lifespan. The defendant sought court-ordered genetic testing on the basis that medical professionals suggested some of the plaintiff's symptoms could relate to HD. Despite the plaintiff's objections, the court compelled the plaintiff to undergo genetic testing to determine whether her injuries related to HD, rather than the defendant's negligence.[188] Although this is a Canadian case, it is not unreasonable to foresee similar scenarios arising in other countries, including Australia and the US.

Some scholars are wary that courts and legal practitioners may not be placing sufficient emphasis on the ethical and social implications of genetic testing. These scholars suggest that the search for the truth should not be used to override all other interests.[189] The primary concern is that courts are prioritising the fair resolution of disputes and failing to consider the psychological and emotional trauma that could result from incidental findings in a court-ordered genetic test.[190]

However, genetic testing is not the only form of medical examination that carries the potential for incidental findings. In fact, most routine physical examinations could present plaintiffs with unwanted findings relating to life-threatening and/or incurable conditions. Gendron and Morgan explain

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[186] *Adacsi v Amin* [2013] ABCA 315 (Alberta Court of Appeal).

[187] Ibid. The genetic variation associated with Huntington's Disease is known to be highly penetrant so it has 'the ability to quantitatively demonstrate alternative causation by showing a genetic variation that is accepted by the scientific community to be practically synonymous with the afflicted disease' - In other words, such genetic variations

> confer a significantly increased susceptibility to the disease associated with that particular variation, whereas less penetrant variations may have little to no impact on one's health. In the case of highly penetrant variations, such as Huntington's disease, the variation has been shown to correlate almost one hundred percent with development of the disease, which makes the possibility of causation resulting from exposure highly unlikely. Therefore, in cases involving highly penetrant susceptibility genes, admission of such data will be extremely probative in a defense of alternative causation by the defendant and there is a very strong argument for their admission.

Champagne (n 65) 14-15.

[188] Ibid. See also Paul Appelbaum, 'The Double Helix Takes the Witness Stand: Behavioral and Neuropsychiatric Genetics in Court' (2014) 82 *Neuron* 946; Maya Sabatello and Paul Appelbaum, 'Behavioural Genetics in Criminal and Civil Courts' (2017) 25(6) *Harvard Review of Psychiatry* 289.

[189] Rothstein (n 67) 908; Niedwicki (n 64) 306.

[190] Hoffman (n 2) 894; Niedwicki (n 64) 306.

> A routine physical exam might turn up a heart murmur, or a mole possibly representing melanoma. A suspicious spot or pattern can be observed on a routine X-ray or MRI… The presence of these risks, well known to the medical community, is the reason why the exercise of clinical judgment by a learned physician is needed whenever bodies, blood, chromosomes, or DNA sequences are examined. The physician ordering [genetic testing] can respect the patient's wishes by declining to receive information that does not offer a definite or possible diagnosis. Someone can always request that a laboratory filter out and not report diagnostically irrelevant findings. The patient can also decline to receive information about "secondary findings"… In fact, it is actually easier to filter out unwanted information in the analysis of DNA sequence data than to avoid unwanted observations during physical examination or diagnostic imaging.[191]

Considering the similarities between genetic testing and other forms of medical examinations, it is important for courts to thoroughly consider, on the facts of each case, whether a defendant should be denied the right to this powerful method of scrutinising a plaintiff's causation case.[192] It is certainly not *every* case that will turn up issues of stigma and discrimination – many genetic test results will likely reveal no relevant mutations, and lethal genetic conditions are rare. However, the emotional trauma of knowing and the potential right not to know is just as important as issues of stigma and discrimination. It will therefore be up to the courts to determine, in each case, whether any detriment to the plaintiff outweighs the benefits of compelling testing to shed light on the issue of causation.

7.4.2. US Case Law

Despite the concerns arising in some of the literature, US courts have typically not considered issues of psychological trauma but instead focused their attention on the physical invasiveness of genetic testing. For example, the court in *Fisher* suggested that there was a 'sweeping invasion of personal integrity' associated with court-ordered genetic testing.[193] Counsel for the plaintiff in *Mandel,* a mesothelioma case, also maintained that there was significant trauma accompanying a blood sample for genetic testing.[194] They argued:

> Asking [the plaintiff] to allow the defendants to come in his home, his own personal sanctuary, and stick him with a needle in his last months on this planet is [an] extreme invasion…this is not something that [the plaintiff's family] take lightly. [The plaintiff] does not want to do this. This is not related to his treatment. This is not helping him survive longer. None of this.[195]

[191] Andrew Gendron and Thomas Morgan, 'Incomplete Penetrance: Whole-Exome Sequencing and Federal Courts' (2019) 1 *For The Defense* 1, 6.
[192] Ibid 2.
[193] *Fisher* (n 19) 18.
[194] *Mandel* (n 19) 12.
[195] Ibid 12.

Counsel for the plaintiff later elaborated that 'It's too much for him [the plaintiff]. It puts an extreme amount of stress on him. And he's in the final months of his life'.[196] The Court held that the plaintiff 'puts his physical condition in issue by filing the lawsuit. ... the examination [defendants] want is a blood draw which ... under today's technology is not unduly intrusive or painful. People get them as a matter of routine'.[197]

Several other courts have suggested genetic testing is 'minimally invasive'[198] and simply a 'routine procedure'.[199] *Harris* involved a birth-related medical negligence claim where the defendant's requested genetic testing on the basis that the plaintiff's injuries were potentially caused by Angelman's Syndrome.[200] Counsel for the plaintiff submitted that the 'test would subject the minor plaintiff to risk of physical injury, trauma, serious complications from contamination or infection, and risk of AIDS'.[201] The court disagreed with plaintiff's counsel and ultimately held that

> While defendant's expert testified that any potential risk to plaintiff as a result of the blood test is minimal, plaintiff has provided nothing more than the unsupported, conclusory statements of plaintiff's counsel regarding the potential dangers. We therefore conclude that since the litigant has placed her physical condition at issue, the trial court properly exercised its discretion when it ordered plaintiff to undergo a blood test that may determine the cause of her injuries.[202]

Similarly, *Cruz* was another birth-related medical negligence claim but in this case, the defendants alleged the plaintiff's injuries were the result of 'genetic alterations in blood clotting factors in either the plaintiff or his mother'.[203] The plaintiff's expert 'identified a number of risks associated with the drawing of blood, including infection, bleeding and bruising, arterial injury, thrombosis, needle breaking, and allergic reactions to any anaesthetic that might be needed'.[204] In ordering the requested testing, the court dismissed this testimony and held that there was 'no evidence that obtaining blood…would be other than a routine procedure'.[205]

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[196] Ibid 14.
[197] Ibid 8.
[198] *Cutting* (n 19) 3 – 'minimally invasive, one-time blood and urine draw'; *Simbolon* (n 19) 4 – 'Taking a blood sample is minimally invasive'; *Burt* (n 19) 7 - 'test is minimally invasive'; *Thrash* (n 19) - 'the act of drawing [Plaintiff's] blood is a relatively minor procedure'; *Phillips* (n 19) 8 – 'the blood test contemplated is relatively simple and requires plaintiff to do nothing more than provide a sample'.
[199] *Harris* (n 19) 109 - 'Blood tests are routine procedures in our everyday life'; *Cruz* (n 19) 652 – 'no evidence that obtaining blood…would be other than a routine procedure'.
[200] *Harris* (n 19).
[201] Ibid 107.
[202] Ibid 109.
[203] *Cruz* (n 19) 649.
[204] Ibid.
[205] Ibid 652.

7.4.3. Australian Case Law

Like the US cases, Australian cases have focused on the plaintiff's bodily integrity and physical invasiveness of the testing. In all the Australian cases, the courts ordered genetic testing despite the plaintiff's concerns that the process of obtaining a sample would be physically intrusive. For example, in *PL*, the defendants sought genetic testing in the form of a blood sample or buccal (saliva) sample.[206] The court held that the testing should be in the form of a buccal sample, acknowledging the fact that the plaintiff 'is hypersensitive to touch and finds the process of taking blood to be traumatic'.[207] Similarly, in *KF*, the plaintiff submitted the testing was 'highly intrusive' but the court disagreed and held there was only a limited 'degree of intrusion and distress'.[208] In *Plowman*, the plaintiff submitted that 'as an adult, [plaintiff] had a number of phobias and anxieties in relation to attending medical practitioners and having medical treatment'.[209] The court held these phobias were 'not sufficient to tell against the Court making the requisite order'.[210]

Some plaintiffs have asserted their right to bodily integrity as a reason to deny genetic testing. In *Wells*, counsel for the plaintiff submitted that plaintiff has a 'right of control and self-determination in respect of his…body, so that the taking of a mouth swab or a blood sample from the person impinges upon the bodily integrity of the person and should not be undertaken in the absence of legislative sanction'.[211] That case involved a plaintiff alleging that a motor vehicle accident precipitated labour and there was subsequent medical negligence at the time of the plaintiff's birth. The defendants maintained that the plaintiff's injuries, including brain damage, were the result of a genetic disorder. The court dismissed the plaintiff's submission that the sample could not be taken because it violates bodily integrity. The court acknowledged the 'potentially far-reaching operation of orders for genetic testing' but concluded that 'concerns of this type ought not stand in the way of making an order under Rule 23.4 UCPR in an appropriate case'.[212]

Some plaintiffs have raised the potential 'long-term' psychological damage that could accompany genetic testing. In *Pederson*, the plaintiff's mother claimed

[206] *PL* (n 34).
[207] Ibid [78].
[208] *KF* (n 34) [42], [60].
[209] *Plowman* (n 34) [50].
[210] Ibid [80].
[211] *Wells* (n 34) [38].
[212] *Wells* (n 34) [45]-[46].

> Given the uncertainty as to whether this testing will be able to demonstrate anything probative in [Plaintiff's] case and further, the distress and anxiety that he currently already suffers as a result of having had to participate in numerous medical examinations and assessments, I do not believe that it's in [Plaintiff's] best interest to undergo this genetic testing. If this testing were to proceed then I am extremely concerned about the long term implications for [Plaintiff] of what the procedure itself might inflict upon his psychological wellbeing.[213]

The court took 'the concerns of [Plaintiff's] mother seriously' but concluded that 'they are, with respect, insufficient to justify denying [Defendant] the opportunity to pursue this legitimate line of forensic enquiry'.[214] Ultimately, the Court held that 'Making every allowance for parental sensitivity and for the particular needs and limitations of [Plaintiff]…it does not seem to me to be unreasonable to require a buccal swab…and if necessary a second swab to be taken'.[215] Consistent with other courts, it was observed that the testing 'ought to be a quick, relatively painless procedure…I doubt very much whether such a procedure could possibly involve the risk of long term psychological damage'.[216] Therefore, courts have rightly been reluctant to accept a plaintiff's submissions that the process of obtaining a sample for genetic testing is in any way physically or psychologically traumatic.

7.5. Efficiency

7.5.1. US Case Law

Although this has not been a subject of much discussion in the literature, US and Australian courts have recognised that the efficiency of the court process could be undermined where parties are allowed to engage in broad 'fishing expeditions'. US courts have reached varying conclusions as to whether genetic testing constitutes a fishing expedition. For example, the court in *Rogers* denied the defendants' request for genetic testing on the basis that it constituted 'a mere fishing expedition that would cause undue delay' because the defendants 'offered no proof that there currently exists a scientifically reliable test to ascertain the genetic cause of plaintiff's behavioral issues and learning disabilities'.[217] Similarly in *Fisher,* the court held that even though the defendant's expert specifically denied that the testing constituted a fishing expedition, the defendant's failure to specify the genetic condition they sought to uncover

[213] *Pederson* (n 34) [10].
[214] Ibid [14].
[215] Ibid [15].
[216] Ibid [16].
[217] *Rogers* (n 19) 297-8.

through the genetic testing ultimately reinforced 'plaintiff's argument that defendants' Motions may well amount to little more than [a fishing] expedition'.[218] However, other cases reach the conclusion that the proposed genetic testing would *not* constitute a fishing expedition or would constitute a 'permissible' fishing expedition.[219]

In order to avoid fishing expeditions, US courts have also typically been reluctant to order genetic testing of non-parties. For example, the court in *Cruz* held exceptionally that:

> We do not hold that a parent is always to be treated as the child's agent for discovery purposes. But here mother and plaintiff were contemporaneously under the care of OBGYN, and plaintiff's malpractice claim includes charges that his injury resulted in part from the manner in which OBGYN treated mother during her pregnancy and plaintiff's delivery. Furthermore, in her capacity as plaintiff's mother, she has a definable economic interest in the outcome of the suit. If plaintiff is successful in obtaining a monetary award, mother's financial burdens resulting from her duty to care for plaintiff will be lessened.[220]

In addition, the Court in *Cutting* concluded that the plaintiff's mother should not be compelled to undergo genetic testing because she was not a party to proceedings (as required under r 35 FRCCP) and there is no inherent authority to compel her to submit.[221] Likewise, in the two cases of *Young* and *Meyers,* the Courts both held that the plaintiff's parents should not be compelled to undergo genetic testing because they were not parties.[222] In the more recent case of *Kallal,* the court noted that 'parental testing' was a 'novel issue' such that significant analysis was needed to determine whether parents were parties whose physical conditions were in controversy.[223] Unlike the plaintiff, who has put their health at issue by bringing the proceedings, non-parties should typically not be subjected to genetic testing unless they have consented to the proposed test/s.

7.5.2. Australian Case Law

In a number of Australian cases, the plaintiffs have submitted that the defendant's request for genetic testing was essentially a 'fishing expedition'.[224] As a result, the testing was argued to be inconsistent with the 'just, quick and cheap resolution of the real issues in dispute in the

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[218] *Fisher* (n 19) 22.
[219] See e.g. *Ortwein* (n 3) 16-18; *Cruz* (n 19) 653.
[220] *Cruz* (n 19) 652.
[221] *Cutting* (n 19) 4.
[222] *Young* (n 19) 123; *Meyers* (n 19) - Even though the mother was a party (as a guardian ad litem for the plaintiff), the father was a non-party. The judge therefore rejected compulsion of genetic testing because the defendant said it would not pursue testing if it could not obtain testing for *both* parents.
[223] *Kallal* (n 19) 11. The court remanded the case for further analysis – 'For this court to address the issue without any analysis or findings by the circuit court would not serve the interests of justice and the development of good law…it would be premature…the discovery order was granted without sufficient underpinning. A more thorough examination is necessary', 11-12.
[224] *KF* (n 34)*; Plowman* (n 34)*; Prudence* (n 34)*; Wells* (n 34) [86].

proceedings'.[225] However, in all of these cases, the courts held that the testing was not a fishing expedition so long as it had the capacity to 'shed light' on the issue of causation, which is a relatively low threshold test.[226] The courts also concluded that the testing was consistent with the just, quick, cheap resolution of the real issues because justice demands that the defendants are afforded the opportunity to explore the issue of causation even if there may be some delay to the trial.[227] A number of cases also considered that the potential quantum of the plaintiff's claim is relevant so that where the quantum is likely to be substantial, the defendant should be allowed to examine the plaintiff's genome in order to prepare to meet the plaintiff's claim.[228] Therefore, Australian courts are suitably inclined to hold that the requested testing is appropriate so long as it does not constitute a fishing expedition, any award of damages is likely to be substantial and the testing would not cause undue delay.

Although Australian courts are often willing to order genetic testing of the plaintiff/s, they have been very reluctant to compel non-parties to submit to genetic testing. For example, the court in *Wells* adopted similar reasoning to the US cases of *Cutting, Young* and *Meyers,* as the New South Wales Supreme Court kept 'in mind the potentially far-reaching operation of orders for genetic testing and the possible uses to which such testing can be put' and concluded that there was not 'a proper legal basis…for the Court to make an order for the plaintiff's tutor (his mother) to undertake medical examination'.[229] In *Prudence*, the plaintiff's mother was required to submit to genetic testing but solely on the basis that the mother was a 'separate plaintiff in the proceedings'.[230] As the plaintiff's mother was a party, r 23.4 of the UCPR allowed the court to order her to submit to genetic testing.[231]

[225] In *KF* (n 34), the plaintiff also went further and argued that 'this kind of test gives rise to issues of particular concern that go beyond this case to many, if not every, personal injury case'. The court concluded that the testing was appropriately confined to 'an examination which is relevant to the issues in the proceedings…the focus of the testing concerns [Plaintiff's] developmental and language disorder [so] determination of this interlocutory application, in the circumstances of this case, ought not be taken to have broader consequences, on some hypothetical basis, in other proceedings'.
[226] See, eg, *KF* (n 34)*; Plowman* (n 34).
[227] See, eg, *Prudence* (n 34) [51]-[52]; [76]-[73]; *Wells* (n 31) [107]-[109]. In *Sharif* (n 31), the court ordered the genetic testing even though a hearing date had been fixed. The court justified their position by observing that 'the causation issue is a serious one and…it would not be fair to [Defendants] to refuse to allow them to explore the issue even though some delay will be involved', [41].
[228] *Wells* (n 34) [104]; See also *PL* (n 34) [79]; *Wells* (n 34) [105].
[229] *Wells* (n 34) [111], [113].
[230] *Prudence* (n 34) cited in *Wells* (n 31) [74].
[231] *Prudence* (n 34) [80].

The law in NSW stipulates that the person required to undergo the medical examination must be 'a party'.[232] Despite this requirement, at least one Australian court has ordered non-parties to submit to genetic testing on the basis that such testing would be 'in accordance with the dictates of justice'.[233] In *Sharif*, a motor vehicle accident case, the plaintiff's mother and father (who were not parties to the proceedings) were also ordered to undergo genetic testing.[234] The judgment does not include any discussion of the fact that the parents were not parties to the proceedings. Instead, the court simply ordered the parents to submit to the testing according to the 'dictates of justice' per r 2.1 of the UCPR and s 61 of the CPA.[235] Presumably, the parents did not object to these orders being made.[236] Although trio sequencing (genetic testing of the mother, father and child) can provide probative evidence, courts should remain reticent to compel non-parties to submit to testing against their will.

7.6. Conclusion

This chapter maintained that defendants should have a right to examine the plaintiff's genome for the purpose of exploring medical causation. Part 7.1 provided an examination of the legal framework governing compelled genetic testing. The following part analysed the reliability of genetic testing. Part 7.3 began the analysis of the socio-economic ramifications of court-ordered genetic testing with a discussion of privacy. Subsequently, Part 7.4 went on to consider concerns of stigmatisation and emotional trauma. Finally, Part 7.5 explored the broader impact of court-ordered genetic testing on justice and the efficiency of the judicial system.

Ultimately, despite the concerns of some scholars, courts have typically weighed the competing interests in favour of compelling genetic testing.[237] As the following chapter will demonstrate, a Reference Guide is needed to prevent unfairness and ensure consistency in the interpretations and applications of genetic evidence across judgments and across jurisdictions. The section of the guide on court-ordered genetic testing would highlight concerns relating to a plaintiff's privacy and autonomy, and the potential for multi-generational stigma and trauma. It would explain how such concerns have often been outweighed by the potential benefits of the test

[232] Or 'a person for whose benefit a party is claiming relief under the *Compensation to Relatives Act 1897*', see *Uniform Civil Procedure Rules 2005* (NSW) ('*UCPR*') r 23.1(1)(b)(ii).
[233] See *Sharif* (n 34).
[234] Ibid [22].
[235] Ibid.
[236] Ibid; Vallance (n 54) 7.
[237] Although many of these cases are not necessarily toxic tort cases, the principles can easily be extrapolated to toxic tort scenarios.

results to litigants and the judicial system.[238] The guide would emphasise the importance of courts continuing to (1) limit the scope of testing; (2) issue protective orders; and, (3) prohibit testing of non-parties. This will ensure that the courts continue to avoid overly intrusive, unhelpful examinations. The guide would also explain that courts should consider ordering 'relevant genetic counselling be made available to the family at the defendant's expense' in order to minimise the effects of stigma and trauma.[239]

Court-ordered genetic testing will inevitably have a pivotal effect on toxic tort cases because plaintiffs' cases have collapsed based on compelled genetic test results revealing a genetic predisposition to their alleged harm.[240] As the science of genetics improves, it is highly likely that toxic tort plaintiffs will routinely be required to submit to genetic testing in order to identify potential alternative causes of their injury.[241] This will undoubtedly have a powerful impact on proof of causation in toxic torts.

[238] This is not to say that courts have not exercised their discretion to limit or prohibit genetic testing of some individuals, but this usually occurs in relation to non-parties to the proceedings.
[239] *Pederson* (n 34) [17]. In some cases defendants undertake to pay for counselling, see, eg, *PL* (n 34) [56], [122]; *Prudence* (n 34) [21].
[240] See, eg, *Bowen* (n 19); *Ortwein* (n 3).
[241] See, eg, Marchant (n 1) 23.

8. Chapter Eight: Conclusion and Recommendations

This thesis has examined the problem of causal uncertainty in toxic torts, as well as the different methods of proof, including epidemiological studies, toxicological studies, differential aetiology, and genetic markers. The study addressed the following research question, '*Does genetic information alleviate or exacerbate the causal uncertainty in toxic torts?*' This chapter begins with a summary of the key conclusions stemming from an analysis of the literature and case law relevant to this research question. Parts 8.2-8.3 outline the limitations of the study and provide recommendations for future research and practice.

8.1. No Single Method to Prove Causation

This thesis has ultimately shown how numerous complexities inevitably arise when science and the law intersect. The issue of causal indeterminacy has continually complicated proof of causation in toxic torts. Chapters 2 to 3 of this thesis has articulated the considerable obstacles that must be overcome in order to prove or disprove causation in Australian and US toxic tort litigation. These chapters provided significant historical and theoretical background information about the long-standing issue of causal uncertainty, and the limitations of more 'traditional' methods of proof of causation including epidemiology, toxicology, and differential aetiology. Chapter 4 introduced the potential scope for the emerging field of genetics to 'solve' this issue.

Chapters 5 to 7 analysed the literature and case law relating to genetic evidence, and reached the conclusion that this evidence will, and should, continue to be used as a method of proof in toxic torts (and indeed all personal injury cases) but litigants/lawyers/courts require scientific guidance (such as a Reference Guide) to minimise inconsistencies and help to prevent misuse of this information. In doing so, it has added to the growing chorus of voices calling for more innovative causal and evidentiary methods (i.e. the use of genetic evidence) to accommodate the special features of scientific evidence in toxic torts.

Comprehensive case law analysis is a crucial part of understanding the intricacies of the toxic tort causation doctrine, and the impact of genetic evidence as a method of proof. As Professor Gold explains,

> Judicial decisions have consequences…A court sets a precedent…The precedent is then applied (perhaps borrowed by another jurisdiction) in a second case that it doesn't fit quite as well and is then extended to a third case with unexpected, unjust, or unintelligible results. So it comes as no surprise that when courts misapprehend or misuse factual causation principles, practical concerns are as much at stake as is the theoretical coherence of doctrine.[1]

This has significant ramifications for 'factual causation [which] has proven to be the most durable, controversial, and intractable difficulty in toxic tort cases'.[2] Misapprehension and misuse of genetic evidence can lead to inconsistencies in the case law, as revealed in Chapters 5 to 7.

The comparative case law analysis undertaken in this thesis has ultimately demonstrated that issues of causal uncertainty affect both Australian and US toxic tort cases. However, US toxic tort litigants have exhibited a greater proclivity towards introducing genetic evidence to explore the issue of causation, with varying degrees of success. This demonstrates that genetic markers can provide valuable evidence of causation, or alternative causation, in addition to traditional forms of evidence such as epidemiological and/or toxicological studies. Yet, genetic evidence is not a single solution to the toxic tort causation problem. Genetic markers will only have utility where they are sufficiently valid, sensitive, and specific. Without further guidance on the utility of such markers, this evidence will only further confuse and mislead the judge or jury. This could exacerbate the problem of causal indeterminacy, leading to inconsistent case outcomes and posing further obstacles to meritorious claims. As articulated throughout the thesis, a Reference Guide could help to ensure that the probative value of genetic evidence is properly weighed against any potential harms. This guide would promote a better understanding of how to assess the validity and utility of different types of genetic evidence in order to ensure that courts/litigants avoid placing too much, or too little, emphasis on this evidence in a given case.

8.2. Limitations of the Study

The research undertaken in this thesis is limited by several factors, which have been acknowledged at several points throughout the thesis.

[1] Steve Gold, 'Drywall Mud and Muddy Doctrine: How Not to Decide a Multiple-Exposure Mesothelioma Case' (2015) 49 *Indiana Law Review* 117, 117.
[2] Ibid.

First, the research was restricted to an analysis of publicly-available recorded judicial opinions. This meant that any cases that have been privately negotiated, arbitrated, mediated, and/or settled were not able to be included in the analysis.

Second, it appears that genetic evidence has primarily been adduced in Australian tribunals, Australian local/specialist courts, or US trial courts with dispositions – such as settlements or jury verdicts – that do not generate judicial opinions. This suggests that such evidence is not being adduced in higher courts and/or that toxic tort cases involving this evidence are typically negotiated, arbitrated, mediated and/or settled. As a result, the data sample examined in this thesis is not representative of all toxic tort cases involving genetic evidence.

Third, several US cases analysed in this thesis involved jury verdicts. As juries typically do not provide reasons for their conclusion, it is particularly difficult to draw an inference from jury verdicts, unless there is a special verdict form in which the jury expressly makes a finding on the causation element specifically.

Despite the difficulty of drawing inferences from jury verdicts in the US and the varying rules of evidence that apply in Australian lower courts and tribunals, an isolated analysis of the use of genetic evidence to support or refute causation in such cases can still be fruitful. An analysis of these cases can still provide valuable insight into how litigants are using genetic evidence and (at least in the case of tribunal/lower court decisions) the willingness of legal decision-makers to adopt such evidence in determining causation.

8.3. Recommendations

The findings in this thesis have prompted a number of recommendations for research and practice.

8.3.1. Research

The Reference Guide proposed in the next section could help to ensure consistency and fairness across judgments, and across jurisdictions. Other steps, such as the use of assessors or ‘science panels’ (such as the panels used in the Bendectin or PFOA litigation), would certainly be beneficial in further guiding the court on the nature of genetic evidence in a

given case (particularly in mass torts).[3] However, such steps necessarily incur time delays and financial costs that may not be feasible in every case, particularly where the damages are not substantial. Further research is required to determine whether 'independent' scientific expert opinion (e.g., in the form of an assessor[4], court-appointed expert[5], referee[6], concurrent

[3] See, eg, Jonathan Beach, 'The Use of Assessors in Class Actions' (2015) 129 *Precedent* 15; Kyle Steenland, David Savitz and Tony Fletcher, 'Class Action Lawsuits: Can They Advance Epidemiologic Research?' (2014) 2 *Epidemiology* 167.

[4] Courts may appoint an 'assessor'. Assessors, also referred to as 'technical advisers' under American law, are 'expert guides of the court', who assist the judge during court proceedings to privately answer any questions that the judge might pose relating to the expert's area of expertise, see, eg, *Owners of SS Melanie v Owners of SS San Onofre* [1927] AC 162. However, assessors have only relatively rarely been appointed by Australian and American courts, see, eg, Tristram Hodgkinson and Mark James, *Expert Evidence: Law and Practice* (Sweet & Maxwell, 2015) 160; Anthony Dickey, 'The Province and Function of Assessors in English Courts' (1970) 33 *Modern Law Review* 494 where he explains that assessors are primarily appointed in the admiralty context in Anglo-Australian jurisprudence; Ian Freckelton, *Expert Evidence: Law, Practice, Procedure and Advocacy* (Thomson Reuters, 6th ed, 2019) 373. Nevertheless, there is growing support for adopting assessors particularly in class actions, see, eg, Beach (n 3).

[5] Arguably the most frequently suggested solution to the issue of expert bias is a court-appointed expert. Expert witnesses can be appointed by courts under both Australian and American law, see, eg, *Federal Court Rules 2011* (Cth) r 23.01; *Uniform Civil Procedure Rules 2005* (NSW) r 31.46; *Federal Rules of Evidence* (US) r 706. However, courts have only rarely availed themselves of this alternative to the traditionally adversarial form of expert evidence, see, eg, Tahirih Lee, 'Court-Appointed Experts and Judicial Reluctance: A Proposal to Amend Rule 706 of the Federal Rules of Evidence'(1988) 6(2) *Yale Law & Policy Review* 480; Jean Eggen, 'Toxic Torts and Causation: The Challenge of *Daubert* After the First Decade' (2003) 17 *National Resources & Environment* 213, 260. As succinctly explained by the Hon Garry Downes, the fallacy underlying the court-appointed expert lies in the unstated premise 'that in fields of expert knowledge there is only one answer', Garry Downes, 'Problems with Expert Evidence: Are Single or Court-Appointed Experts the Answer' (2006) 15 *Journal of Judicial Administration* 185, 186. In particular, even if appointing an expert would increase efficiency and assist the fact-finder, it prevents any testing of the expert's conclusions as 'there is nothing to test the expert evidence against', ibid 187. Moreover, in civil proceedings, parties are required to pay the costs of a court-appointed expert in addition to their own party-appointed expert, which can be difficult to justify to a client, David Sonenshein and Charles Fitzpatrick, 'The Problem of Partisan Experts and the Potential for Reform Through Concurrent Evidence' (2013) 32(1) *Review of Litigation* 1, 33. The great weight likely to be attached to the report of an independent court expert also means that 'The presence of a court-sponsored witness, who would most certainly create a strong, if not overwhelming, impression of "impartiality" and "objectivity", could potentially transform a trial by [judge or] jury into a trial by witness', *Kian v Mirro Aluminium Co* 88 FRD 351, 356 (Mich, 1980). As a result, court-appointed experts have almost fallen into disuse.

[6] Australian courts are increasingly referring an issue or issues to an independent expert, known as a 'referee', who will 'make inquiries, evaluate competing information, deliver findings of fact and report the analysis and the findings to the court', see, eg, See, eg, Freckelton (n 4) 377; *Federal Court Act 1976* (Cth) s 54A; This is a relatively new legislative power, see *Federal Justice System Amendment (Efficiency Measures) Act (No. 1) 2009* (Cth); Most state and territory courts can refer proceedings to referees for a report, see, eg: Court Procedures Rules 2006 (ACT) r 1531; Uniform Civil Procedure Rules 2005 (NSW) r 20.14; *Supreme Court Act 1979* (NT) s 26; *Supreme Court Act 1995* (Qld) s 255; Uniform Civil Procedure Rules 1999 (Qld) r 501; *Supreme Court Act 1935* (SA) s 67; Supreme Court Rules 2000 (Tas) r 574; Supreme Court (General Civil Procedure) Rules 2005 (Vic) r 50.01; *Supreme Court Act 1935* (WA) s 50. As Lee J observed in 2018, it 'may be the time has come for the Court to establish a regular practice of appointing a referee to inquire and provide a report to the Court', *Lifeplan Australia Friendly Society Ltd v S & P Global Inc* [2018] FCA 379 [41]. The Hon Robert McClelland MP observed in his second reading speech that 'the procedural flexibility with which a referee can deal with a question, along with their technical expertise, will allow a referee to more quickly get to the core of technical issues and reduce the cost and length of trials of litigants', Commonwealth, *Parliamentary Debates*, House of Representatives, 3 December 2008, 12296 (Robert McClelland, Attorney-General). Unless otherwise ordered by the court, the referee's opinion must be provided in a written report, which the court may then choose to adopt in whole or in part, vary or reject in its entirety, see, eg, *Federal Court Rules 2011*(Cth) rr 28.66-28.67; *Uniform Civil Procedure Rules 2005* (NSW) rr 20.23-20.24. Therefore, the decisions of referees

evidence[7], or 'science panel[8]) would assist in clarifying the role and nature of genetic evidence in a given case. In any event, the Reference Guide proposed in this thesis represents a more universally applicable baseline that can be used to ensure the appropriate and consistent use of genetic evidence, without the parties incurring any unnecessary financial or time costs.

The Australian jurisprudence also seems to suggest a greater emphasis on the factor of cost-efficiency of justice in the context of court-ordered genetic testing (the courts are less likely to authorise testing when the damages are small in scale). However, the US appears to place more attention on privacy and stigma rights of the plaintiff and their relatives. This may suggest a 'plaintiff interests' focus in the US and more of an 'administration of justice' logic

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are not automatically binding on the parties. In *Park Rail Developments Pty Ltd v RJ Pearce Associates Pty Ltd*, Smart J outlined some criteria for consideration when determining whether to refer a question to a referee, see (1987) 8 NSWLR 123, 130. California has enacted similar provisions for the appointment of referees, see, eg, *California Code of Civil Procedure* §§ 638-9; see also Judicial Council of California, *Use and Cost of References in General Civil Cases: A Report to the California Legislature* (Report, August 2004). Therefore, Australian and American courts appear to be quite receptive to the use of referees.

[7] For example, Justice Garling observes that concurrent evidence overcomes the issue of junk science because if the opinions of a pseudo-expert 'are admitted and form a part of the discourse, the other experts can be relied upon to expose their lack of scientific rigour and authenticity', see eg, Peter Garling, 'Concurrent Expert Evidence: The New South Wales Experience' (University of Oxford, Faculty of Law, 1 December 2015) 23; Peter Garling, 'Concurrent Evidence: Perspective of an Australian Judge' (Procedural Justice Discussion Group, Faculty of Law, University of Oxford, 16 October 2013) 18. In addition, one of the primary advantages of the hot tub method is that judges are able to directly question experts in an effort to reveal any extreme opinions and expert bias, Gary Edmond, 'Conventions in Science and Law: Merton and the Hot Tub: Scientific Conventions and Expert Evidence in Australian Civil Procedure' (2009) 72 *Law and Contemporary Problems* 159, 164. The success of the hot tub method is reflected in the fact that it is increasingly being adopted by Australian and international courts, especially in cases where there are complex scientific issues, such as toxic torts, see, eg, Australian Vioxx class action (Peterson & Ors v Merck, Sharpe & Dohme (Austl.) Pty Ltd & Anor (VID 451 of 2006); Alexandra Kennedy-Breit, 'Admissibility of Expert Evidence to Prove Causation in Toxic Torts' (2017) 53(1) *Tort Trial & Insurance Practice Law Journal* 139, 153; For example, the Supreme Court of New South Wales now mandates the presumptive use of concurrent expert evidence in all proceedings in which a claim is made for damages for personal injury or disability 'unless there is a single expert appointed or the court grants leave for expert evidence to be given in an alternate manner', Supreme Court of New South Wales, *Practice Note SC CL 5: Supreme Court Common Law Division – General Case Management List*, 29 January 2007, cls 36-40; The 'hot tub' method has also attracted academic interest in the United States, although it has not yet been adopted in the US, see, eg, Kennedy-Breit (n 7); Megan Yarnall, 'Dueling Scientific Experts: Is Australia's Hot Tub Method a Viable Solution for the American Judiciary' (2009) 88(1) *Oregon Law Review* 311; Lisa Wood, 'Experts in the Hot Tub' (2007) 21 *Anti-Trust* 95; David Sonenshein and Charles Fitzpatrick, 'The Problem of Partisan Experts and the Potential for Reform Through Concurrent Evidence' (2013) 32(1) *Review of Litigation* 1. Despite this growing support in favour of the method, Freckelton provides the following caution: 'the utility of the procedure will remain dependent upon the skills and articulateness of experts, the adoption of focused and fair procedures by trial judges, and the constructive involvement of well-briefed counsel', Freckelton (n 4) 438.

[8] See, eg, the use of the 'science panel' in the PFAS litigation, Steenland, Savitz and Fletcher (n 3). The use of these panels are primarily helpful in class actions where little scientific data already exists to shed light on the issue of causation.

in Australia. An investigation into these two different approaches could be a possible basis for further research.

Some scholars have also argued a different approach to causation, such as a proportional liability/probabilistic causal contribution model, would help to remedy the issue of causal indeterminacy in toxic torts.[9] However, as Gold acknowledges, even if courts adopt a different model of causation, they would still need to understand genetics because it will continue to be used as a method of proof.[10] The proposed Reference Guide outlined in this thesis would arguably be a suitable means of helping to ensure a proper understanding of this evidence. The issue of court-appointed experts, assessors, science panels, and/or a different approach to causation is beyond the scope of this thesis, but the findings outlined in this thesis could inform further research on these topics.

8.3.2. Practice

Ultimately, the thesis notion of a Reference Guide emerges as a significant step to prevent the misunderstanding and misuse of genetic evidence. It is designed for toxic tort stakeholders, but it could also easily be extrapolated to non-toxic tort scenarios where genetic evidence is likely to be used. Although there have been relatively few recorded opinions analysing genetic evidence, this method of proof is becoming increasingly important in a range of legal areas. This thesis has shown how this evidence has been used in toxic torts, and personal injury cases

[9] Steve Gold, 'When Certainty Dissolves into Probability – A Legal Vision of Toxic Causation for the Post-Genomic Era' (2013) 70(1) *Washington & Lee Law Review* 237; Jennifer Champagne, 'Genetic Testing and Testimony in Toxic Tort Litigation' (2011) 13(1) *North Carolina Journal of Law & Technology* 1; Noah Smith-Drelich, 'Performative Causation' (2020) 93(3) *Southern California Law Review* 379; Alexandra Lahav, 'Chancy Causation in Tort Law' (2022) *Journal of Tort Law*. See also Joseph Sanders et al, 'Differential Etiology: Inferring Specific Causation in the Law from Group Data in Science' (2021) 63 *Arizona Law Review* 851 where the authors propose an application of the Bradford-Hill Criteria, supplemented by considerations of internal and external validity, to assist courts in answering specific-causation questions and overcoming the 'G2i' problem (i.e. the problem of reasoning from group data to individual cases). See also David Rosenberg, 'The Causal Connection in Mass Exposure Cases: A "PublicLaw" Vision of the Tort System' (1984) 97 *Harvard Law Review* 849, 925 where Rosenberg argues that the specific causation requirement should be replaced by class action-based proportional recovery.

[10] Gold, 'When Certainty Dissolves into Probability (n 9) 397.

more broadly (such as medical negligence claims). However, such evidence could also be used in other contexts, such as employment law[11], criminal law[12], family law[13], and life insurance.[14]

In addition, the research undertaken in this thesis indicates there is scope for more appropriate education and training for legal professionals. Such training could include, though not be limited to, CPD seminars on genetic evidence in civil and/or criminal litigation, or undergraduate/postgraduate courses in genetics and the law. This could help to ensure professionals are consistently provided with relevant, up-to-date knowledge on the rapidly advancing field of genetics, and its implications for different legal practice areas.

A New Reference Guide

As a result of the steady rise in the number of cases, it is hardly surprising that several scholars have emphasised the importance of legal practitioners, courts, and litigants familiarising themselves with genetic data.[15] The thesis asserts that an important step towards realising this

[11] See, eg, Nunzia Cannovo, Mariano Paternoster and Claudio Buccelli, 'Predictive genetic tests for employment purposes: Why not?' (2010) 29 *Medicine and Law* 419; Anne Mainsbridge, 'Employers and Genetic Information: A New Frontier For Discrimination' (2002) 2 *Macquarie Law Journal* 61; Jean Macchiaroli Eggen, 'Toxic Reproductive and Genetic Hazards in the Workplace: Challenging the Myths of the Tort and Workers' Compensation Systems' (1992) 60(5) *Fordham Law Review* 843; Joan Flaherty, 'Toxicogenomics and Workers' Compensation: A Reworking of the Bargain' (2009) 12(2) *Journal of Health Care Law & Policy* 267; Kathryn J Sedo, 'Workers' Compensation, Social Security Disability, SSI and Genetic Testing' (2007) *Journal of Law, Medicine & Ethics* 74; Michael Baram, 'Genetic Testing for Susceptibility to Disease from Exposure to Toxic Chemicals: Implications for Public and Worker Health Policies' (2001) 41(2) *Jurimetrics* 165.

[12] See, eg, Rhanae Rego, 'A Critical Analysis of Post-Conviction Review in New South Wales' (2021) 2(3) *The Wrongful Conviction Law Review* 305; Scott Elder and Anderson Kemp, 'Genomics in the Courtroom: The Current Landscape of DNA Technology in Criminal and Civil Litigation' (2021) 88(1) *Defense Counsel Journal* 1; Maya Sabatello and Paul S Appelbaum, 'Behavioral Genetics in Criminal and Civil Courts' (2017) 25(6) *Harvard Review of Psychiatry* 289; Felix Ralph, 'Convictions through Kith and Kin: Legal, Policy and Ethical Issues in DNA Familial Matching and Genetic Metadata' (2018) 29(3) *Current Issues in Criminal Justice* 243; Stephen J Morse, 'Genetics and Criminal Responsibility' (2011) 15(9) *Trends in Cognitive Sciences* 378; Deborah Denno, 'Courts' Increasing Consideration of Behavioral Genetics Evidence in Criminal Cases: Results of a Longitudinal Study' (2011) 2011 *Michigan State Law Review* 967.

[13] See, eg, Maya Sabatello and M.D. Appelbaum, 'Psychiatric Genetics in Child Custody Proceedings: Ethical, Legal, and Social Issues' (2016) 4(3) *Current Genetic Medicine Reports* 98; Edward S Dove et al, 'Familial genetic risks: how can we better navigate patient confidentiality and appropriate risk disclosure to relatives?' (2019) 45(8) *Journal of Medical Ethics* 504.

[14] See, eg, Sara Golru, 'Regulating the Use of Genetic Information in the Life Insurance Industry' (2020) 7 *UNSW Law Journal Forum* 1.

[15] Randi Weiss et al, 'The Use of Genetic Testing in the Courtroom' (1999) 34(3) *Wake Forest Law Review* 889, 913; Gary Marchant, 'Genetic Data in Toxic Tort Litigation' (2016) 45(2) *The Brief* 22, 22-23; David Hirsch and David Amor, 'Exome and Genome Sequencing in Litigation' (2020) (156) *Precedent* 15, 18; Sarah Vallance and Margaret Brain, 'The Appropriateness of Genetic Testing in Cerebral Palsy Cases' (2016) (133) *Precedent* 4, 5; Diane E Hoffman and Karen H Rothenberg, 'Judging Genes: Implications of the Second Generation of Genetic Tests in the Courtroom' (2007) 66 *Maryland Law Review* 858, 905-6; Edward Ramos et al, 'Genomic Test Results and the Courtroom: The Roles of Experts and Expert Testimony' (2016) 44 *The Journal of Law, Medicine & Ethics* 205, 205-210.

goal would be by introducing a reference guide for all jurisdictions (also referred to as guidelines or a framework) to assist litigants/lawyers/courts in determining the weaknesses and strengths of genetic evidence as a method of proof. [16] Professors Diane Hoffman and Karen Rothenberg highlight the significance of educating judges on the scientific reliability of genetic information as 'judges are the final arbiters of whether genetic test results will play a role in any given case: judges decide whether a test should be compelled as well as whether a test result should be admitted into evidence'.[17] The establishment of a Reference Guide is therefore important to ensure equality and fairness, especially in light of the fact that even within the same jurisdiction, there is substantial judicial disagreement regarding when and how to admit and compel genetic tests.[18] This Guide could take the form of a bench-book style model so that Courts could use and access such specific expert guidelines as a resource in a particular case.[19]

Chapters 4 to 6 of this thesis could form the basis of any reference guide because of the comprehensive analysis of the case law, and scientific and legal issues, canvassed in those chapters. In particular, the reference guide could have the following structure. First, the guidelines could begin with a few sections explaining the science, including the meaning of genetics, genomics, genetic mutations, epigenetics, gene expression, toxicogenomics, genome-wide association studies, the different types of genetic tests, and genetic markers. Chapter 4 of this thesis provides an indication of the potential contents and format of the introductory sections of the guidelines.

Second, the guidelines could then move on to examine genetic markers of exposure/effect as a method of proving or disproving causation. It would highlight the importance of ensuring sufficient specificity and sensitivity of the genetic markers, as well as the need for the genetic

[16] The guidelines could also explore other topics, beyond causation, such as sub-cellular asymptomatic harm, or a duty to warn genetically susceptible individuals (including the idiosyncratic response defence), or the use of genetic evidence in assessing damages. A discussion of these topics is beyond the scope of the thesis. For more information, see, eg, Andrew Askland and Gary Marchant, 'Genetic Data and Toxic Torts: Intimations of Statistical Reductionism' in Richard Sharp, Gary Marchant and Jamie Grodsky (eds), *Genomics and Environmental Regulation* (The John Hopkins University Press, 2008) 89; Steve Gold, 'The More We Know, the Less Intelligent We Are – How Genomic Information Should, and Should Not, Change Toxic Tort Causation Doctrine' (2010) 34(2) *Harvard Environmental Law Review* 369, 413; Gary Marchant, 'Genetic Data in Toxic Tort Litigation' (2016) 45(2) *The Brief* 22, 23-6. Litigation regarding pathogen-related illnesses could also use genetic evidence as a means to locate the cause of outbreaks.
[17] Hoffman and Rothenberg (n 15) 864.
[18] See, eg, Diane Hoffmann and Karen Rothenberg, 'When Should Judges Admit or Compel Genetic Tests?' (2005) 310 (5746) *Science* 241, 242; Ramos et al (n 15) 207.
[19] For an example of a reference guide, see, eg, Federal Judicial Center, *Reference Manual on Scientific Evidence* (National Academy of Sciences, 3rd ed, 2011). Planning is currently underway for the fourth edition of this Manual.

samples to be collected in a timely manner to ensure reliability. Chapter 5 of this thesis illustrates the key case law that could be discussed in this section of the guidelines.

Third, the guidelines could provide an analysis of genetic markers of susceptibility. It would emphasise the key difference between predisposition (where the genes increase risk regardless of exposure) and susceptibility (where the genes only increase risk when the individual is exposed to a toxic substance). The role of gene-gene and gene-environment interactions would form a crucial part of this section of the guidelines, as well as an explanation of the varying types of interaction (such as additive, synergistic, or antagonistic). The role of gene penetrance would also need to be outlined in this section. In addition, it is important to discuss the need for the mutation/s to be detected in the correct type of tissue (e.g. non-cancerous tissue). It would also need to highlight the significance of positive family history, as well as positive genetic test results. This section should stress that the genetic test results should be valid, and not overstated. It would explain that genetic markers are typically not determinative of individual causation because their sensitivity, specificity and predictive value are population-based, not individual attributes.[20] Chapter 6 of this thesis demonstrates the scientific information and case law that could be included in this section of the guidelines.

Finally, the guidelines could conclude with a discussion of court-ordered genetic testing. This section would flag the dangers posed to a plaintiff's privacy and autonomy, and the potential for multi-generational stigma and trauma. It would underline the need for specific and scientifically justified genetic testing, where defendants must provide a clear indication of the condition or genetic trait they expect to discover. This section would raise the possibility of limiting the scope of the requested testing, so that it only explores genetic variations that are relevant to the plaintiff's injury, and implementing a protective order to restrict publication or disclosure of the genetic test results to non-parties. It would outline the need to prohibit testing of non-parties, who, unlike the plaintiff, have not put their health at issue by bringing the proceedings. It would also explain the significance of making genetic counselling available to affected parties, so as to minimise the effects of stigma and trauma.

The guidelines could loosely follow the format of the latter half of this thesis. For example, the guidelines could have the following structure:

[20] Gold, 'The More We Know' (n 16) 400; Steve Gold, 'The Holy Grail? The Potential of Genomics to Shape Toxic Tort Litigation' (2016) 58(4) *DRI For the Defense: Toxic Torts and Environmental Law* 59, 65.

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8.4. Final Thoughts

This thesis has maintained that there is no single scientific method that can conclusively prove toxic tort causation. Despite the optimism of some scholars and practitioners, genetic evidence is by no means a solution to the problem of causal indeterminacy. Without a proper understanding of this evidence, it could exacerbate the problem of causal uncertainty. However, if used properly, this evidence could shed light on causation, especially when viewed alongside all the other available evidence. Genetic information should 'be treated as *one piece of evidence among many*'.[21] Litigants, lawyers and courts should be aware of the limitations of this evidence and avoid overselling it as a solution to the causal indeterminacy problem. It is important that all the available evidence is considered in a given case, such as toxicological studies, epidemiological studies, individual medical records (e.g., cholesterol level, diabetic, smoker etc.), lifestyle factors (diet, exercise, stress), in addition to any individual genetic/epigenetic/proteomic/toxicokinetic data and family medical history. The research undertaken in this thesis ultimately demonstrates the value of creating a Reference Guide to clarify the role and nature of genetic evidence in toxic torts, and indeed in all civil litigation.

[21] Susan Haack, *Evidence Matters: Science, Proof and Truth in the Law* (Cambridge University Press, 2014) 71-2.

9. Bibliography

9.1. Articles/Books/Reports

Adami et al, H-O ‘Toxicology and Epidemiology: Improving the Science with a Framework for Combining Toxicological and Epidemiological Evidence to Establish Causal Inference’ (2011) 122 *Toxicological Sciences* 223

Adelman, David, 'The False Promise of the Genomics Revolution for Environmental Law' (2005) 29 *Harvard Environmental Law Review* 117

Adeney, Elizabeth, 'The Challenge of Medical Uncertainty: Factual Causation in Anglo-Australian Toxic Tort Litigation' (1993) 19(1) *Monash University Law Review* 23

Alexander-Dann, Benjamin, et al, ‘Developments in Toxicogenomics: Understanding and Predicting Compound-induced Toxicity from Gene Expression Data’ (2018) 14(4) *Molecular Omics* 213

Allan, Sonia, 'Access to Information About Donors by Donor-Conceived Individuals: A Human Rights Analysis' (2013) 20(3) *Journal of Law and Medicine* 655

Al Yemni, Eman, et al, ‘Integrated Analysis of Whole Exome Sequencing and Copy Number Evaluation in Parkinson’s Disease’ (2019) 9(3344) *Scientific Reports* 1

Anderson, William, Lynn Levitan and Kieran Tuckley, 'The “Any Exposure” Theory Round II: Court Review of Minimal Exposure Expert Testimony in Asbestos and Toxic Tort Litigation Since 2008' (2012) 22 *Kansas Journal of Law & Public Policy* 1

Appelbaum, Paul S, 'Behavioural Genetics and the Punishment of Crime' (2005) 56(1) *Psychiatric Services* 25

Appelbaum, Paul S, 'The Double Helix Takes the Witness Stand: Behavioral and Neuropsychiatric Genetics in Court' (2014) 82 *Neuron* 946

Appelbaum, Paul S, Nicholas Scurich and Raymond Raad, 'Effects of Behavioral Genetic Evidence on Perceptions of Criminal Responsibility and Appropriate Punishment' (2015) 21(2) *Psychology, Public Policy and Law* 134

Arnold, Bruce Baer and Wendy Bonython, 'Sharing the Book of Life: Privacy, The New Genomics and Health Sector Managers ' (2015) 12(4) *Privacy Law Bulletin* 103

Askland, Andrew, and Gary Marchant, ‘Genetic Data and Toxic Torts: Intimations of Statistical Reductionism’ in Richard Sharp, Gary Marchant and Jamie Grodsky (eds), *Genomics and Environmental Regulation* (The John Hopkins University Press, 2008)

Aspinwall, Lisa G., Teneille R. Brown and James Tabery, 'The Double-Edged Sword: Does Biomechanism Increase or Decrease Judges' Sentencing of Psychopaths?' (2012) 337(6096) *Science* 846

Australian Institute of Health and Welfare, 'Mesothelioma in Australia' (Report, November 2018)

Australian Law Reform Commission, *Essentially Yours: The Protection of Human Genetic Information in Australia* (Report No 96, May 2003)

Australian Law Reform Commission, 'Evidence' (Interim Report No 26, 1985)

Australian Law Reform Commission, 'Evidence' (Report No 38, 1987)

Australian Law Reform Commission, *For Your Information: Australian Privacy Law and Practice* (Report No 108, 2008)

Australian Law Reform Commission, *Genes and Ingenuity: Gene Patenting and Human Health* (Report No 99, 2004)

Australian Law Reform Commission, *Managing Justice: A Review of the Federal Justice System* (Report No 89, 2000)

Bachyrita, Peter, 'The Causal Mechanism Theory of Legal Causation' (2021) 34(1) *Ratio Juris* 57

Bailey, Lisa and Robyn Prueitt, ‘Case Law Highlights SouthEast: Genomics in Toxic Tort Litigation - Are We There Yet?’ (2016) 17 *Environmental Litigation and Toxic Torts Committee Newsletter* 26

Bandza, Alexander, 'Epidemiological-Study Reanalyses and Daubert: A Modest Proposal to Level the Playing Field in Toxic Tort Litigation' (2012) 39 *Ecology Law Quarterly* 247

Baram, Michael, 'Genetic Testing for Susceptibility to Disease from Exposure to Toxic Chemicals: Implications for Public and Worker Health Policies' (2001) 41(2) *Jurimetrics* 165

Barlow-Stewart, Kristine et al, 'Verification of Cnsumers' Experiences and Perceptions of Genetic Discrimination and its Impact on Utilization of Genetic Testing' (2009) 11(3) *Genetics in Medicine* 193

Barnes, David, 'Too Many Probabilities: Statistical Evidence of Tort Causation' (2001) 64 *Law and Contemporary Problems* 191

Bartha, Áron and Balázs Gyorffy, 'Comprehensive Outline of Whole Exome Sequencing Data Analysis Tools Available in Clinical Oncology' (2019) 11 *Cancers* 1725

Beach, Jonathan, 'Causation: The Interface Between the Scientific and Legal Methods' (2022) 49 *University of Western Australia Law Review* 113

Beach, Jonathan, 'The Use of Assessors in Class Actions' (2015) 129 *Precedent* 15

Beazley, Margaret, 'Speech: An Insight into Appellate Justice in New South Wales' (2017) *Australian Bar Review* 55

Beck, James, 'The Coming Ubiquity: Product Liability Implications of Pharmacogenomic Advances' (2015) 57(9) *DRI For The Defense: Drug and Medical Device* 33

Beecher-Monas, Erica, 'Circumventing Daubert in the Gene Pool' (2007) 43 *Tulsa Law Review* 241

Beecher-Monas, Erica, 'Lost in Translation: Statistical Inference in Court' (2014) 46(4) *Arizona State Law Journal* 1057

Bender, Leslie, 'An Overview of Feminist Torts Scholarship' (1993) 78(4) *Cornell Law Review* 575

Ben-Hamo, Rotem, et al, 'Predicting and Affecting Response to Cancer Therapy Based on Pathway-level Biomarkers' (2020) 11(3296) *Nature Communications* 1

Berger, Margaret and Aaron Twerski, 'Uncertainty and Informed Choice: Unmasking *Daubert*' (2005) 104 *Michigan Law Review* 257

Berger, Margaret, 'Science for Judges VII: Regulating Pharmaceuticals and Scientific Issues Regarding Asbestos' (2007) 15(3) *Journal of Law and Policy* 983

Berkman, Benjamin, 'Refuting the Right Not to Know' (2017) 19 *Journal of Health Care Law & Policy* 1

Bernstein, Anita, 'Formed by Thalidomide: Mass Torts as a False Cure for Toxic Exposure' (1997) 97 *Columbia Law Review* 2153

Bernstein, David and Eric Lasker, 'Defending Daubert: It's Time to Amend Federal Rule of Evidence 702' (2015) 57 *William and Mary Law Review* 1

Bernstein, David, ‘Getting to Causation in Toxic Tort Cases’ (2008) 74(1) *Brooklyn Law Review* 51

Berryessa, Colleen, 'Judges' views on Evidence of Genetic Contributions to Mental Disorders in Court' (2016) 27(4) *The Journal of Forensic Psychiatry & Psychology* 586

Berryessa, Colleen, 'Judicial Stereotyping Associated with Genetic Essentialist Biases toward Mental Disorders and Potential Negative Effects on Sentencing' (2019) 53(1) *Law & Society Review* 202

Betta, Michela, *The Moral, Social and Commercial Imperatives of Genetic Testing and Screening: The Australian Case* (2006) vol 30

Billauer, Barbara Pfeffer, 'Daubert Debunked: A History of Legal Retrogression and the Need to Reassess “Scientific Admissibility”' (2015) 21 *Suffolk Journal of Trial and Appellate Advocacy* 1

Bitas, Basil, ‘A Common Law View of Causation, Science and Statistical Evidence in the Courtroom’ (2011) 23(1) *Singapore Academy of Law Journal* 307

Black, Michael, 'Genetics in the Courtroom' (2003) 26(3) *UNSW Law Journal* 755

Bock, Gregory and Jamie Goode, *Genetics of Criminal and Antisocial Behaviour* (John Wiley & Sons, 1996)

Bonython, Wendy and Bruce Arnold, 'Disclosure 'downunder': Misadventures in Australian Genetic Privacy Law' (2014) 40(3) *Journal of Medical Ethics* 168

Bonython, Wendy and Bruce Arnold, 'Privacy, Personhood, and Property in the Age of Genomics' (2015) 4(3) *Laws* 377

Bonython, Wendy and Bruce Baer Arnold, 'Beyond the Corporeal: Extending Propertisation of Body Parts to Derivative Information' (2016) 23(3) *Journal of Law and Medicine* 709

Boston, Gerald, 'A Mass Exposure Model of Toxic Causation: The Content of Scientific Proof and the Regulatory Experience' (1993) 18 *Columbia Journal of Environmental Law* 181

Bradshaw, Rachel, 'The use and misuse of DNA profiles in Australia ' (2013) 37 *Australian Bar Review* 17

Bras, Jose and Andrew Singleton, ‘Exome Sequencing in Parkinson’s Disease’ (2011) 80(2) *Clinical Genetics* 104

Brennan, Troyen, 'Helping Courts with Toxic Torts: Some Proposals Regarding Alternative Methods for Presenting and Assessing Scientific Evidence in Common Law Courts' (1989) 51 *University of Pittsburgh Law Review* 1

Brent, Robert, 'The Complexities of Solving the Problem of Human Malformations' (1986) 13 *Clinics Perinatology* 491

Brice, Susan and Whitney Christian, 'The Use of Genetic Evidence to Defend Against Toxic Tort Claims—Part I' (2017) 29(9) *Intellectual Property & Technology Law Journal* 3

Brice, Susan and Whitney Christian, 'The Use of Genetic Evidence to Defend Against Toxic Tort Claims—Part II' (2017) 29(10) *Intellectual Property & Technology Law Journal* 9

Brice, Susan and Whitney Christian, 'The Use of Genetic Evidence to Defend Against Toxic Tort Claims - Part III' (2017) 29(11) *Intellectual Property & Technology Law Journal* 3

Brilmayer, Lea and Lewis Kornhauser, 'Review: Quantitative Methods and Legal Decisions' (1978) 46 *The University of Chicago Law Review* 116

Broadbent, Alex, 'Epidemiological Evidence in Proof of Specific Causation' (2011) 17 *Legal Theory* 237

Brown, Rachel, 'Balancing Privacy and Proof: Discovery of Nonparty Medical Records' (2018) 21(2) *Journal of Health Care Law & Policy* 189

Bunn, Franklin, 'The Triumph of Good over Evil: Protection by the Sickle Gene Against Malaria' (2013) 121(1) *Blood* 20

Callahan, Christina, 'Molecular Epidemiology: Future Proof of Toxic Tort Causation' (2001) 8(1) *Environmental Lawyer* 147

Campbell, Michael and David Machin, *Medical Statistics: A Commonsense Approach* (Wiley, 1990)

Cannovo, Nunzia, Mariano Paternoster and Claudio Buccelli, 'Predictive Genetic Tests for Employment Purposes: Why Not?' (2010) 29 *Medicine and Law* 419

Carneiro, Thaise, et al, 'Utility of Trio-based Exome Sequencing in the Elucidation of the Genetic Basis of Isolated Syndromic Intellectual Disability: Illustrative Cases' (2018) 11 *The Application of Clinical Genetics* 93

Carpenter, Mark and George Ware, *Defending Pesticides in Litigation* (Thomson West, 2005)

Carruth, Russellyn and Bernard Goldstein, 'Relative Risk Greater Than Two in Proof of Causation in Toxic Tort Litigation' (2001) 41(2) *Jurimetrics* 195

Cashman, Peter, 'Class Actions and Toxic Torts' (2005)(69) *Precedent* 4

Cedar, Megan, 'A Dose of Reality: The Struggle with Causation in Toxic Tort Litigation' (2014) 51(4) *Houston Law Review* 1147

Cepelewicz, Barry and Eric Watt Wiechmann, 'Genetic Injury in Toxic Tort Cases: What Science Can and Cannot Prove' (1995) 62(2) *Defence Counsel Journal* 201

Cetrulo, Lawrence, *Toxic Torts Litigation Guide* (Thomson-West, 1st ed, 2002)

Champagne, Jennifer, 'Genetic Testing and Testimony in Toxic Tort Litigation: "Admissibility and Evaluation"' (2011) 13(1) *North Carolina Journal of Law & Technology* 1

Chan, Bertram, *Biostatics for Epidemiology and Public Health using R* (Springer, 2016)

Chen, Sining and Giovanni Parmigiani, 'Meta-analysis of BRCA1 and BRCA2 Penetrance' (2007) 25(11) *Journal of Clinical Oncology* 1329

Chen, Xiao-He, Shuwen Huang and David Kerr, 'Biomarkers in Clinical Medicine' (2011) 163 *IARC Scientific Publications* 303

Cheng, Edward, 'The Consensus Rule: A New Approach to Scientific Evidence' (2022) 75 *Vanderbilt Law Review* 407

Chico, Victoria, *Genomic Negligence: An Interest in Autonomy as the Basis for Novel Negligence Claims Generated by Genetic Technology* (Taylor & Francis, 2011)

Chico, Victoria, 'Known Unknowns and Unknown Unknowns: The Potential and the Limits of Autonomy in Non-Disclosure of Genetic Risk' (2012) 3 *Journal of Professional Negligence* 162

Childs, John, 'Toxicogenomics: New Chapter in Causation and Exposure in Toxic Tort Litigation' (2002) *Defence Counsel Journal* 441

Chin, Jacqueline and Alistair Campbell, 'What – if anything – is special about genetic privacy?' in Terry Sheung-Hung Kaan and Calvin Wai-Loon Ho (ed), *Genetic Privacy: An Evaluation of the Ethical and Legal Landscape* (Imperial College Press, 2013)

Christie, Edward, 'Toxic Mould Litigation: A New Sunrise Industry for Lawyers?' (2005) 16 *Insurance Law Journal* 281

Christodoulou, Katja, 'Next Generation Exome Sequencing of Paediatric Inflammatory Bowel Disease Patients Identifies Rare and Novel Variants in Candidate Genes' (2013) 62 *Gut* 977

Clark, Stuart and Christina Harris, 'The Past, Present and Future of Product Liability and Other Mass Tort Class Actions in Australia' (2009) 32(3) *UNSW Law Journal* 1022

Clayton, Ellen et al, 'A Systematic Literature Review of Individuals' Perspectives on Privacy and Genetic Information in the United States' (2018) 13(10) *PLOS One* e0204417

Clayton, Ellen et al, 'The Law of Genetic Privacy: Applications, Implications, and Limitations' (2019) 6(1) *Journal of Law and the Biosciences* 1

Clermont, Kevin, 'Death of Paradox: The Killer Logic Beneath the Standards of Proof' 88(3) *Notre Dame Law Review* 1061

Cohen, Laurence, *The Probable and the Provable* (Oxford University Press, 1977)

Collins, Francis et al, 'Human Molecular Genetics and Genomics – Important Advances and Exciting Possibilities' (2021) 384 *New England Journal of Medicine* 1

Collins, Lynda, 'Material Contribution to Risk in the Canadian Law of Toxic Torts' (2016) 91(2) *Chicago-Kent Law Review* 567

Commonwealth, Royal Commission into the Use and Effects of Chemical Agents on Australian Personnel in Vietnam, *Final Report* (1985)

Cranor, Carl, *Regulating Toxic Substances: A Philosophy of Science and the Law* (Oxford University Press, 1993)

Cranor, Carl, *Tragic Failures: How and Why We are Harmed by Toxic Chemicals* (Oxford University Press, 2017)

Criado Perez, Caroline, 'Invisible Women: Data Bias in a World Designed for Men' (Random House UK, 2020)

Crick, Francis and James Watson, 'Molecular Structure of Nucleic Acids; a Structure for Deoxyribose Nucleic Acid' (1953) 171 *Nature* 737

Crowley, Eileen et al, ‘Prevalence and Clinical Features of Inflammatory Bowel Diseases Associated With Monogenic Variants, Identified byWhole-Exome Sequencing in 1000 Children at a Single Center’ (2020) 158(8) *Gastroenterology* 2208

Daeid, Nic et al, *The Use of Statistics in Legal Proceedings: A Primer for Courts* (The Royal Society of Edinburgh, 2020)

Danne, Alexander, 'McTear v Imperial Tobacco: Understanding the Role and Limitations of Expert Epidemiological Evidence in Scientific Litigation' (2006) 13 *Journal of Law and Medicine* 471

Davies, Geoffrey, 'Court Appointed Experts' (2005) 5(1) *Queensland University of Technology Law and Justice Journal* 89

Dawkins, Richard, *The Selfish Gene* (Oxford University Press, 2016)

Denno, Deborah, 'Courts' Increasing Consideration of Behavioral Genetics Evidence in Criminal Cases: Results of a Longitudinal Study' (2011) *Michigan State Law Review* 967

D'Entremont, James, 'Fear Factor: The Future of Cancerphobia and Fear of Future Disease Claims in the Toxicogenomic Age' (2006) 52(3) *Loyola Law Review* 807

Dickey, Anthony, 'The Province and Function of Assessors in English Courts' (1970) 33 *Modern Law Review* 494

Donaldson, Peter et al, *Genetics of Complex Disease* (Taylor & Francis, 2016)

Dore, Michael, 'A Proposed Standard for Evaluating the Use of Epidemiological Evidence in Toxic Tort and Other Personal Injury Cases' (1985) 28(3) *Howard Law Journal* 677

Doudna, Jennifer and Samuel Sternberg, *A Crack in Creation: Gene Editing and the Unthinkable Power to Control Evolution* (Houghton Mifflin Harcourt, 2017)

Dove, Edward S et al, 'Familial Genetic Risks: How Can we Better Navigate Patient Confidentiality and Appropriate Risk Disclosure to Relatives?' (2019) 45(8) *Journal of Medical Ethics* 504

Downes, Garry, 'Problems with Expert Evidence: Are Single or Court-Appointed Experts the Answer' (2006) 15 *Journal of Judicial Administration* 185

Dreyfuss, Rochelle and Dorothy Nelkin, 'The Jurisprudence of Genetics' (1992) 45(2) *Vanderbilt Law Review* 313

Eaton, Joseph, Kara Kapke, and Apryl Underwood, ‘Medical Genetics in Chemical Exposure Cases: Genetic Testing of a Plaintiff – The Pros and Cons’ (2012) 54(1) *DRI: For the Defense* 58

Eaton, David, 'Scientific Judgment and Toxic Torts – A Primer in Toxicology for Judges and Lawyers' (2003) 12(1) *Journal of Law and Policy* 5

Eckstein, Lisa et al, 'Australia: Regulating Genomic Data Sharing to Promote Public Trust' (2018) 137(8) *Human Genetics* 583

Edmond, Gary, 'Conventions in Science and Law: Merton and the Hot Tub: Scientific Conventions and Expert Evidence in Australian Civil Procedure' (2009) 72 *Law and Contemporary Problems* 159

Edmond, Gary and David Mercer, 'Litigation Life: Law-Science Knowledge Construction in (Bendectin) Mass Toxic Tort Litigation' (2000) 30(2) *Social Studies of Science* 265

Edmond, Gary and David Mercer, ‘The Secret Life of (Mass) Torts; the “Bendectin Litigation” and the Construction of Law-Science Knowledges’(1997) 20(3) *UNSW Law Journal* 666

Eggen, Jean, 'Toxic Torts and Causation: The Challenge of Daubert After the First Decade' (2003) 17 *National Resources and Environment* 213

Eggen, Jean, 'Toxic Reproductive and Genetic Hazards in the Workplace: Challenging the Myths of the Tort and Workers' Compensation Systems' (1992) 60(5) *Fordham Law Review* 843

Eggen, Jean, *Toxic Torts in a Nutshell* (Thomson Reuters, 4th ed, 2010)

Eggleston, Richard, *Evidence, Proof and Probability* (Orion Publishing, 2nd ed, 1983)

Elder, Scott, and Anderson Kemp, ‘Genomics in the Courtroom: The Current Landscape of DNA Technology in Criminal and Civil Litigation’ (2021) 88(1) *Defense Counsel Journal* 1

Ellinger, Mark, 'DNA Diagnostic Technology: Probing the Problem of Causation in Toxic Torts' (1990) 3 *Harvard Journal of Law & Technology* 31

Erlich, Yaniv and Arvind Narayanan, 'Routes for Breaching and Protecting Genetic Privacy' (2014) 15(6) *Nature Reviews Genetics* 409

Evans, James, and Wylie Burke, ‘Genetic Exceptionalism. Too Much of a Good Thing?’ (2008) 10(7) *Genetics in Medicine* 500

Everett, Margaret, 'Can you Keep a (Genetic) Secret? The Genetic Privacy Movement' (2004) 13(4) *Journal of Genetic Counseling* 273

Faigman, David, et al, 'How Good is Good Enough? Expert Evidence Under Daubert and Kumho' (2000) 50 *Case Western Reserve Law Review* 645

Faigman, David et al, *Modern Scientific Evidence: The Law and Science of Expert Testimony* (Thomson West, 2009)

Farahany, Nita, 'Neuroscience and Behavioral Genetics in US Criminal Law: an Empirical Analysis' (2015) 2(3) *Journal of Law and Biosciences* 485

Farber, Daniel, 'Toxic Causation' (1987) 71 *Minnesota Law Review* 1219

Farlow, Janice, et al, 'Whole-Exome Sequencing in Familial Parkinson Disease' (2016) 73(1) *JAMA Neurology* 68

Faunce, Thomas, 'Abandoning the Common Law: Medical Negligence, Genetic Tests and Wrongful Life in the Australian High Court' (2007) 14 *Journal of Law and Medicine* 469

Faunce, Thomas, Ruth Townsend and Alexandra McEwan, 'The Vioxx Pharmaceutical Scandal: Peterson v Merke Sharpe & Dohme (Aust) Pty Ltd (2010) 184 FCR 1' (2010) 18(1) *Journal of Law and Medicine* 38

Fay, Michael, 'Genetic risks, Disclosure and Foreseeable Harm: An Unanswered Question after ABC v St George's Healthcare' (2016) 24 *Tort Law Review* 127

Finkelstein, Michael and William Fairley, 'A Bayesian Approach to Identification Evidence' (1969) 83(3) *Harvard Law Review* 489

Fischer, David, 'Insufficient Causes' (2005) 94 *Kentucky Law Review* 277

Flaherty, Joan, 'Toxicogenomics and Workers' Compensation: A Reworking of the Bargain' (2009) 12(2) *Journal of Health Care Law & Policy* 267

Ford, Judy, 'A Potent Mix: Cautionary Tales of Chemical Mixtures' (2005) 69 Precedent 27

Frank, Patricia and M Alice Ottoboni, *The Dose Makes the Poison: A Plain-Language Guide to Toxicology* (John Wiley & Sons, 3rd ed, 2011)

Freckelton, Ian, 'Epidemiology Evidence and Causation' (2004) 63 *Plaintiff: Journal of the Australian Plaintiff Lawyers Association* 18

Freckelton, Ian, *Expert Evidence: Law, Practice, Procedure and Advocacy* (Thomson Reuters, 6th ed, 2019)

Freckelton, Ian et al, *Expert Evidence and Criminal Jury Trials* (Oxford University Press, 2016)

Gad, Shayne, *Statistics and Experimental Design for Toxicologists and Pharmacologists* (CRC Press, 4th ed, 2005)

Gahl, William, et al, 'Genetic Approaches to Rare and Undiagnosed Diseases' in Robert Kliegman and Joseph St Geme (eds), *Nelson Textbook of Pediatrics* (Elsevier, 2020)

Garling, Peter, 'Concurrent Evidence: Perspective of an Australian Judge' (Procedural Justice Discussion Group, Faculty of Law, University of Oxford, 16 October 2013)

Garling, Peter, 'Concurrent Expert Evidence: The New South Wales Experience' (University of Oxford, Faculty of Law, 1 December 2015)

Garner, Bryan and Henry Campbell Black, *Black's Law Dictionary* (Thomson Reuters, 10th ed, 2014)

Garner, Samuel and Jiyeon Kim, 'The Privacy Risks of Direct-to-Consumer Genetic Testing: A Case Study of 23andMe and Ancestry' (2019) 96 *Washington University Law Review* 1219

Garrison, Jordan K, 'Courts Face the Exciting and the Inevitable: DNA in Civil Trials' (2004) 23(2) *The Review of Litigation* 435

Gastwirth, Joseph, 'The Role of Statistical Evidence in Civil Cases' (2020) 7 *Annual Review of Statistics and Its Application* 39

Geistfeld, Mark, 'The Doctrinal Unity of Alternative Liability and Market-Share Liability' (2006) 155 *University of Pennsylvania Law Review* 447

Gendron, Andrew and Thomas Morgan, 'Incomplete Penetrance: Whole-Exome Sequencing and Federal Courts' (2019) 1 *For The Defense* 1

Gialluisi, Alessandro, et al, 'Whole Exome Sequencing Study of Parkinson Disease and Related Endophenotypes in the Italian Population' (2020) 10(1362) *Frontiers in Neurology* 1

Giulano, Douglas, 'Mixed Dust Claims - The Next Asbestos, or Much Ado About Nothing?' (2006) 1 *FIU Law Review* 107

Givoni, Sharon and Rahul Shah, 'DNA testing kits and privacy: A Teaspoon of Spit Helps the Medicine Go Down' (2020) 16(9) *Privacy Law Bulletin* 167

Glasenapp, Logan, 'Judicially Sanctioned Environmental Injustice: Making the Case for Medical Monitoring' (2019) 49(1) *New Mexico Law Review* 59

Golan, Tan, 'Epidemiology, Tort, and the Relations between Science and Law in the Twentieth-Century American Courtroom' in Mario Biagioli and Jessica Riskin (eds), *Nature Engaged: Science in Practice from the Renaissance to the Present* (Palgrave MacMillan, 2012)

Gold, Steve, 'A Fitting Vision of Science for the Courtroom' (2013) 3(1) *Wake Forest Journal of Law & Policy* 1

Gold, Steve, 'Causation in Toxic Torts: Burdens of Proof, Standards of Persuasion, and Statistical Evidence' (1986) 96 *The Yale Law Journal* 376

Gold, Steve, 'Drywall Mud and Muddy Doctrine: How Not to Decide a Multiple-Exposure Mesothelioma Case' (2015) 49 *Indiana Law Review* 117

Gold, Steve, 'The Holy Grail? The Potential of Genomics to Shape Toxic Tort Litigation' (2016) 58(4) *DRI For the Defense: Toxic Torts and Environmental Law* 59

Gold, Steve, 'The More We Know, the Less Intelligent We Are - How Genomic Information Should, and Should Not, Change Toxic Tort Causation Doctrine' (2010) 34(2) *Harvard Environmental Law Review* 369

Gold, Steve, 'The Reshapement of the False Negative Asymmetry in Toxic Tort Causation' (2011) 37(3) *William Mitchell Law Review* 1507

Gold, Steve, 'When Certainty Dissolves into Probability - A Legal Vision of Toxic Causation for the Post-Genomic Era' (2013) 70(1) *Washington & Lee Law Review* 237

Gold, Steve, Michael Green and Joseph Sanders, 'Epidemiological Evidence in Toxic Torts' in Michael Freeman and Maurice Zeegers (eds), *Forensic Epidemiology* (Academic Press, 2016)

Gold, Steve, Michael Green and Joseph Sanders, *Scientific Evidence of Factual Causation: An Educational Module* (The National Academics of Science, Engineering and Medicine, October 2016)

Gold, Victor, 'Limiting Discretion to Exclude Prejudicial Evidence' (1984) 18 *University of California Davis Law Review* 59

Goldberg, Richard, *Causation and Risk in the Law of Torts: Scientific Evidence and Medicinal Product Liability* (Hart Publishing, 1999)

Goldberg, Richard, 'Epidemiological Uncertainty, Causation, and Drug Product Liability' (2014) 59(4) *McGill Law Journal* 777

Goldberg, Richard (ed), *Perspectives on Causation* (Hart Publishing, 2011)

Goldberg, Richard, 'Using Scientific Evidence to Resolve Causation Problems in Product Liability' in Richard Goldberg, *Perspectives on Causation* (Hart Publishing, 2011)

Golberg, Richard, 'Vaccine Damage Schemes in the US and UK Reappraised: Making Them Fit for Purpose in the Light of Covid-19' (2022) *Legal Studies* 1

Goldring, John, 'An Introduction to Statistical "Evidence"' (2003) 23 *Australian Bar Review* 239

Goldstein, Bernard, 'Toxic Torts: The Devil is in the Dose' (2008) 16(2) *Journal of Law and Policy* 551

Golru, Sara, 'Regulating the Use of Genetic Information in the Life Insurance Industry' (2020) 7 *UNSW Law Journal Forum* 1

Goodie, Jo, 'Toxic Tort and the Articulation of Environmental Risk' (2008) 12 *Law Text Culture* 69

Gostin, Lawrence and J Hodge, Jr, 'Genetic Privacy and the Law: An End to Genetic Exceptionalism' (1999) 40 *Jurimetrics* 21

Goven, Joanna, 'Assessing Genetic Testing: Who are the "lay experts"?' (2008) 85(1) *Health Policy* 1

Graham, Duncan, 'Causation Problems in Medical Negligence Cases' (2020) 157 *Precedent* 20

Graham, Kenneth, 'State Adaptation of the Federal Rules: The Pros and Cons' (1990) 43(2) *Oklahoma Law Review* 293

Gray, John, and Richard Faulk, 'Negligence in the Air? Should Alternative Liability Theories Apply in Lead Paint Litigation?' (2008) 25 *Pace Environmental Law Review* 147

Gray, Kimberly, ‘NIEH’s Environmental Genome Project’ (2004) 15(4) *Epidemiology* 139

Green, Garrett, et al, ‘Specificity of Genetic Biomarker Studies in Cancer Research: A Systematic Review’ (2016) 11(7) *PLoS ONE* 1

Green, Michael, 'All You Ever Wanted to Know About Adequate Proof of Causation in Tort Law' (2018) 9(3) *Journal of European Tort Law* 308

Green, Michael, *Bendectin and Birth Defects: The Challenges of Mass Toxic Substances Litigation* (University of Pennsylvania Press, 1996)

Green, Michael, ‘Expert Witnesses and Sufficiency of Evidence in Toxic Substances Litigation: The Legacy of *Agent Orange* and Bendectin Litigation’ (1992) 86 *Northwestern University Law Review* 643

Green, Michael, 'Second Thoughts About Apportionment in Asbestos Litigation' (2008) 37(3) *Southwestern University Law Review* 531

Green, Michael, ‘Science is to Law as the Burden of Proof is to Significance Testing’ (1997) 37(2) *Jurimetrics* 205

Green, Michael, 'The Future of Proportional Liability: The Lessons of Toxic Substances Causation' in Stuart Madden (ed), *Exploring Tort Law* (Cambridge University Press, 2005)

Green, Michael, 'The Intersection of Factual Causation and Damages' (2006) 55(2) *DePaul Law Review* 671

Grey, Betsy and Gary Marchant, 'Biomarkers, Concussions, and the Duty of Care' (2015) 5 *Michigan State Law Review* 1911

Grey, Betsy, 'Causal Proof in the Pandemic' (2020) 10 *Wake Forest Law Review Online* 124

Grodsky, Jamie, 'Genetics and Environmental Law: Redefining Public Health' (2005) 93 *California Law Review* 171

Grodsky, Jamie, 'Genomics and Toxic Torts: Dismantling the Risk-Injury Divide' (2007) 59(6) *Stanford Law Review* 1671

Gunningham, Neil, 'Asbestos-Related Diseases and Workers’ Compensation' (2011) 34 *Sydney Law Review* 269

Haack, Susan, *Evidence Matters: Science, Proof and Truth in the Law* (Cambridge University Press, 2014)

Hall, Laura, Alastair Iles and Rachel Morello-Frosch, 'Litigating Toxic Risks Ahead of Regulation: Biomonitoring Science in the Courtroom' (2012) 31(1) *Stanford Environmental Law Journal* 3

Hallinan, Dara, Michael Friedewald and Paul De Hert, 'Genetic Data and the Data Protection Regulation: Anonymity, Multiple Subjects, Sensitivity and a Prohibitionary Logic Regarding Genetic Data?' (2013) 29(4) *Computer Law & Security Review* 317

Hamer, David, '"Chance would be a fine thing": Proof of Causation and Quantum in an unpredictable world' (1999) 23 *Melbourne University Law Review* 557

Hamer, David, 'Mind the Evidential Gap: Causation and Proof in Amaca Pty Ltd v Ellis' (2009) 31(3) *Sydney Law Review* 465

Hamer, David, ''Factual causation' and 'scope of liability': What's the difference?' (2014) 77(2) *The Modern Law Review* 155

Hamer, David, 'The Civil Standard of Proof Uncertainty: Probability, Belief and Justice' (1994) 16(4) *Sydney Law Review* 506

Hart, Herbert Lionel Adolphus and Tony Honoré, *Causation in the Law* (Clarendon Press, 2nd ed, 1985)

Hartley, Kirk and David Schwartz, 'A Lawyer's Guide to Genomics in Toxic Tort Cases: Part 1' *Law360* (online at 17 July 2018) <https://www.law360.com/articles/1063736/a-lawyer-s-guide-to-genomics-in-toxic-tort-cases-part-1>

Hazel Genn, Manchester Concurrent Evidence Pilot (Interim Report, January 2012)

Henderson, Thomas, 'Legal Aspects of Disease Clusters: Toxic Tort Litigation: Medical and Scientific Principles in Causation' (1990) 132 *American Journal of Epidemiology* 69

Herbst, Arthur, Howard Ulfelder and David Poskanzer, 'Adenocarcinoma of the Vagina: Association of Maternal Stilbestrol Therapy with Tumor Appearance' (1971) 284 *New England Journal of Medicine* 878

Hill, Austin Bradford, 'The Environment and Disease: Association or Causation?' (1965) 58(5) *Proceedings of the Royal Society of Medicine* 295

Hirsch, David and David Amor, 'Exome and Genome Sequencing in Litigation' (2020)(156) *Precedent* 15

Hirsch, David, 'Important Cases in Medical Negligence' [2019] 153 *Precedent* 4

Hite, Allison, 'Who's to Blame - How Genetic Information Will Lead to More Accurate Decisions in Toxic Tort Litigation' (2012) 63(4) *South Carolina Law Review* 1031

Hodgkinson, Tristram and Mark James, *Expert Evidence: Law and Practice* (Sweet & Maxwell, 2015)

Hoffmann, Diane and Karen Rothenberg, 'Judging Genes: Implications of the Second Generation of Genetic Tests in the Courtroom' (2007) 66 *Maryland Law Review* 858

Hopp, Anthony, Jeremy Goldkind and David Cummings, 'Differential Diagnosis and Daubert: Preventing the Misuse of Differential Etiology to Prove Causation in Toxic Tort Cases' (2017) 84(1) *Defence Counsel Journal* 1

Horvath, George, 'Federal District Court Decisions on the Admissibility of Expert Witness Testimony: An Empirical Study and a Revision of the Conventional Narrative in the Toxic Tort Context' (2020) 88 *University of Cincinnati Law Review* 515

Hughston, Vance and Tina Jowett, 'In the Native Title "Hot Tub": Expert Conferences and Concurrent Expert Evidence in Native Title' (2014) 6(1) *Land, Rights, Laws: Issues of Native Title* 1

Iglesias, Alejandro, 'The Usefulness of Whole-exome Sequencing in Routine Clinical Practice' (2014) 16(12) *Genetics in Medicine* 922

International Human Genome Sequencing Consortium, 'Finishing the Euchromatic Sequence of the Human Genome' (2004) 431 *Nature* 931

James, Robert, 'Role of Toxicology in Toxic Tort Litigation: Establishing Causation' (1994) 61(1) *Defence Counsel Journal* 28

Jarvis, Howard, Paige Sensenbrenner and Laura Whitmore, 'Genetics and Genomics: Making the Invisible Visible' (2015) *For the Defense* 64

Jayne, Thomas, 'The Use and Abuse of the Differentia Diagnosis to Prove Causation in Toxic Torts' (2010) 60(3) *FDCC Quarterly* 204

Jobin, Paul, 'The Valuation of Contaminated Life: RCA in Taiwan and the Compensation of Toxic Exposure' (2021) *East Asian Science, Technology and Society: An International Journal* 1

Johnson, Elizabeth, 'Beryllium: The Changing Face of Toxic Tort Litigation in Pennsylvania' (2005) 13(2) *Pennsylvania State Environmental Law Review* 239

Johnson, Hope, et al, 'Justice For Pollution Victims in China and Australia' (2015) 18(1) *The Australasian Journal of Natural Resources Law and Policy* 77

Jordan, W.M and J.K. Anand, 'Pulmonary embolism' (1961) 278(7212) *Lancet* 1146

Keane, Adrian and Paul McKeown, *The Modern Law of Evidence* (Oxford University Press, 10th ed, 2014)

Kennedy-Breit, Alexandra, 'Admissibility of Expert Evidence to Prove Causation in Toxic Torts' (2017) 53(1) *Tort Trial & Insurance Practice Law Journal* 139

Keough, William, 'Human Genetic Information, Genetic Registers and the Subpoena Duces Tecum: Balancing Privacy, Confidentiality and the Administration of Justice' (2004) 16(2) *Bond Law Review* 141

Khan, Fazal, 'Preserving Human Potential as Freedom: A Framework for Regulating Epigenetic Harms' (2010) 20 *Health Matrix* 259

Kirby, Michael, 'Playing God? Owning God? - Patenting and the Human Genome' (2003) 26(3) *UNSW Law Journal* 770

Kirk, Edwin, 'The Genes That Make Us: Human Stories from a Revolution in Medicine' (Scribe Publications, 2020)

Klein, Andrew, 'Causation and Uncertainty: Making Connections in a Time of Change' (2008) 49 *Jurimetrics* 5

Klug, William, et al, *Concepts of Genetics* (Pearson Education, 11th ed, 2015)

Kording, Niccol and Janine DuMontelle, 'An Overview of Admissibility of Genetic Test Results in Federal Civil Actions: An Uncertain Destiny' (1998) 19(4) *Whittier Law Review* 681

Krajewska, Atina, 'The right to personality in (post)-genomic medicine: a new way of thinking for the new frontier' (2011) 1 *European Human Rights Law Review* 54

Ku, Chee-Seng, David Cooper and George Patrinos, 'The Rise and Rise of Exome Sequencing' (2016) 19 *Public Health Genomics* 315

Kuchenbaecker, Karoline, 'Risks of Breast, Ovarian, and Contralateral Breast Cancer for *BRCA1* and *BRCA2* Mutation Carriers' (2017) 317(23) *Journal of the American Medical Association* 2402

Kuhlen, Michaela, ‘Family-based germline sequencing in children with cancer’ (2019) 38(9) *Oncogene* 1367, 1367

Kumar, Miiko, 'Admissibility of Expert Evidence: Proving the Basis for an Expert’s Opinion' (2011) 33 *Sydney Law Review* 427

Ky, Patrick, 'Qualifications, Weight of Opinion, Peer Review and Methodology: A Framework for Understanding the Evaluation of Science in Merits Review' (2012) 24(2) *Journal of Environmental Law* 207

Lacaze, Paul, Jane Tiller and Ingrid Winship, ' Population DNA screening for medically actionable disease risk in adults' (2022) 216(6) *Medical Journal of Australia* 278

Lahav, Alexandra, 'Chancy Causation in Tort Law' (2022) 15(1) *Journal of Tort Law* (Forthcoming)

Lai, Jessica C, 'D’Arcy v Myriad Genetics: a demand for the “made” or “non-information” and clear subject matter' (2016) 47(5) *International Review of Intellectual Property and Competition Law* 537

Laleng, Per and Charles Feeny, 'Law and Epidemiological Evidence: Double, Toil and Trouble' (2022) 49 *University of Western Australia Law Review* 159

Laubach, Kerriann, 'Epigenetics and Toxic Torts: How Epidemiological Evidence Informs Causation' (2016) 73(2) *Washington & Lee Law Review* 1019

Laurie, Graeme, *Genetic Privacy: A Challenge to Medico-Legal Norms* (Cambridge University Press, 2002)

Lee, Jungnyum, 'The presence and future of the use of DNA-information and the protection of genetic informational privacy: a comparative perspective (United Kingdom, Germany, South Korea) (2016) 44(1) *International Journal of Law, Crime and Justice* 212

Lee, Tahirih, 'Court-Appointed Experts and Judicial Reluctance: A Proposal to Amend Rule 706 of the Federal Rules of Evidence' (1988) 6(2) *Yale Law & Policy Review* 480

Liepina, Ruta, Giovanni Sartor and Adam Wyner, 'Arguing about causes in law: a semi-formal framework for causal arguments' (2020) 28 *Artificial Intelligence and Law* 69

Li, Kequi, ‘Increased leukemia-associated gene expression in benzene-exposed workers’(2014) 4(5369) *Scientific Reports* 1

Lin, Albert, 'Beyond Tort: Compensating Victims of Environmental Toxic Injury' (2005) 78 *Southern California Law Review* 1439

Lipp, Barry, 'Mass Tort Class Actions under the Federal Court of Australia Act: Justice for All or Justice Denied' (2002) 28(2) *Monash University Law Review* 361

Lipton, Andrew, 'Proving Toxic Harm: Getting Past Slice and Dice Tactics' (2014) 45 *McGeorge Law Review* 707

Liu, Zhichao, et al, 'Toxicogenomics: A 2020 Vision' (2019) 40(2) *Trends in Pharmacological Sciences* 92, 101-2

Long, Peter, 'Toxic Torts: A Beginner's Guide' (2005)(69) *Precedent* 18

Lucassen, Anneke and Roy Gilbar, 'Alerting relatives about heritable risks: the limits of confidentiality' (2018) 361 *Biomedical Journal* k1409

Mackie, J.L, 'Causes and Conditions' (1965) 2(4) *American Philosophical Quarterly* 261

Madden, Bill and Tina Cockburn, 'Privacy : the balance in litigation : KF By Her Tutor RF v Royal Alexandra Hospital for Children known as the Children's Hospital Westmead' (2011) 19(1) *Australian Health Law Bulletin* 7

Madden, Stuart, *Toxic Torts Deskbook* (Taylor & Francis, 1992)

Mainsbridge, Anne, 'Employers and Genetic Information: A New Frontier For Discrimination' (2002) 2 *Macquarie Law Journal* 61

Marchant, Gary, 'Emerging Technologies and the Courts' (2019) 55(4) *Court Review* 146

Marchant, Gary, 'Genetic Data in Toxic Tort Litigation' (2006) 14 *Journal of Law and Policy* 7

Marchant, Gary, 'Genetic Data in Toxic Tort Litigation' (2016) 45(2) *The Brief* 22

Marchant, Gary, 'Genetic Susceptibility and Biomarkers in Toxic Injury Litigation' (2000) 41(1) *Jurimetrics* 67

Marchant, Gary, 'Genetics and Toxic Torts' (2001) 31 *Seton Hall Law Review* 949

Marchant, Gary and Jason Robert, 'Genetic Testing for Autism Predisposition: Ethical, Legal and Social Challenges' (2008) 9(2) *Houston Journal of Health Law & Policy* 203

Marchant, Gary, 'Genomics and Toxic Substances: Part I - Toxicogenomics' (2003) 33 *Environmental Law Reporter* 10071

Marchant, Gary, 'Toxicogenomics and Toxic Torts' (2002) 20(8) *Trends in Biotechnology* 329

Mason, Keith, 'Fault, Causation and Responsibility: Is tort law just an instrument of corrective justice?' (2000) 19 *Australian Bar Review* 201

McClellan, Peter, 'New Method with Experts – Concurrent Evidence' (2010) 3 *Journal of Court Innovation* 259

McCulloch, J, 'Whistling in the Dark: The Royal Commission into Agent Orange', in K. Maddock and B. Wright (eds), *War: Australia and Vietnam* (Harper & Row, 1987)

McGarity, Thomas, 'Proposal for Linking Culpability and Causation to Ensure Corporate Accountability for Toxic Risks' (2001) 26(1) *William & Mary Environmental Law and Policy Review* 1

McHale, Cliona, 'Chromosome Translocations in Workers Exposed to Benzene' (2008) (39) *JCNI Monographs* 74

McIvor, Claire, 'Debunking some Judicial Myths about Epidemiology and its Relevance to UK Tort Law' (2013) 21 *Medical Law Review* 553

McMillan, Catriona, ' ABC v St George's Healthcare Trust and Ors: A new duty of care?' (2020) 24 *The Edinburgh Law Review* 394

McWhirter, Rebekah, Carolyn Johnston and Jo Burke, 'Disclosure of Genetic Results to At-risk Relatives without Consent: Issues for Health Care Professionals in Australia' (2019) 27(1) *Journal of Law and Medicine* 108

McWhirter, Rebekah and Margaret Otlowski, 'Regulation of Non-consensual Genetic Testing in Australia: Use of Samples from Deceased Persons' (2016) 24 *Journal of Law and Medicine* 150

Meggiolaro, Natalia et al, 'Disclosure to genetic relatives without consent - Australian genetic professionals' awareness of the health privacy law' (2020) 21(1) *BMC Medical Ethics* 13

Melville, Ellen, 'Gating the Gatekeeper: *Tamraz v. Lincoln Electric Co.* and the Expansion of Daubert' (2012) 53(6) *Boston College Law Review* 195

Mendelson, Danuta, *The New Law of Torts* (Oxford University Press, 2007)

Meneely, Philip, et al, *Genetics: Genes, Genomes, and Evolution* (Oxford University Press, 2017)

Menell, Peter, 'The Limitations of Legal Institutions for Addressing Environmental Risks' (1991) 5 *Journal of Economic Perspectives* 93

Merrill, Ray, *Fundamentals of Epidemiology and Biostatistics: Combining the Basics* (Jones & Bartlett, 2013)

Metcalfe, Sylvia et al, 'Australians' views on personal genomic testing: focus group findings from the Genioz study' (2018) 26(8) *European Journal of Human Genetics* 1101

Michaelidou, Kleita, 'Whole exome sequencing establishes diagnosis of Charcot-Marie-Tooth 4J, 1C, and X1 subtypes'(2020) 8(4) *Molecular Genetics & Genomic Medicine* 1

Michell, Paul and Renu Mandhane, 'The Uncertain Duty of the Expert Witness'' (2005) 42 *Alberta Law Review* 635

Middleton, Anna et al, 'Members of the public in the USA, UK, Canada and Australia expressing genetic exceptionalism say they are more willing to donate genomic data' (2020) 28(4) *European Journal of Human Genetics* 424

Mill, John Stuart, *System of Logic* (John W. Parker, 1843)

Miller, Amalia and Catherine Tucker, 'Privacy Protection, Personalized Medicine, and Genetic Testing' (2018) 64(10) *Management Science* 4648

Miller, Chris, 'NESS for Beginners' in Richard Golberg (ed), *Perspectives on Causation* (Hart Publishing, 2011)

Miller, Ian and Marcio Sotero de Menezes, '*SCN1A Seizure Disorders*' in Adam Ardinger et al (eds), *Gene Reviews* (US National Library of Medicine, 2007-2022)

Milne, Roger and Antonis Antoniou, 'Modifiers of Breast and Ovarian Cancer Risks for *BRCA1* and *BRCA2* mutation carriers' (2016) 23(10) *Endocrine-Related Cancer* T69

Montenegro, Gladys, et al, 'Exome sequencing allows for rapid gene identification in a Charcot-Marie-Tooth family' (2011) 69(3) *Annals of Neurology* 464

Morse, Stephen J, 'Genetics and Criminal Responsibility' (2011) 15(9) *Trends in Cognitive Sciences* 378

Mukherjee, Siddhartha, *The Gene: An Intimate History* (The Bodley Head, 2016)

Murray, Thomas, 'Gene exceptionalism and 'future diaries': is genetic information different from other medical information? ' in Mark Rothstein (ed), *Genetic Secrets: Protecting Privacy and Confidentiality in the Genetic Era* (Yale University Press, 1997)

Murray, Thomas, 'Is Genetic Exceptionalism Past Its Sell-By Date? On Genomic Diaries, Context, and Content' (2019) 19(1) *The American Journal of Bioethics* 13

Neals Ellis, L, Jr, 'Introduction' in D Alan Rudlin (ed), *Toxic Tort Litigation* (American Bar Association, 2007) 10

Neutra, Raymond, Carl Cranor and David Gee, 'The Use and Misuse of Bradford Hill in US Tort Law' (2018) 58(2) *Jurimetrics* 127

Newson, Ainsley et al, 'Genetics and insurance in Australia: Concerns around a self-regulated industry' (2017) 20 *Public Health Genomics* 247

Nicol, Dianne et al, 'Time to get serious about privacy policies: the special case of genetic privacy' (2014) 42 *Federal Law Review* 149

Niedwiecki, Anthony, 'Science Fact or Science Fiction? The Implications of Court-Ordered Genetic Testing Under Rule 35' (2000) 34 *University of San Francisco Law Review* 295

Nielsen, Jane and Dianne Nicol, 'The Legal Vacuum Surrounding Access to Gene-based Research Materials and Data' (2016) 24(1) *Journal of Law and Medicine* 72

Nielsen, Morten Ebbe Juul, Nana Cecilie Halmsted Kongsholm and Jens Schovsbo, 'Property and human genetic information' (2019) 10(1) *Journal of Community Genetics* 95

Nolan, Donal, 'Causation and the Goals of Tort Law' in Andrew Robertson and Tang Hang Wu (eds), *The Goals of Private Law* (Hart, 2009)

Noonan, Megan, 'The Doctor Can't See You Yet: Overcoming the "Injury" Barrier to Medical Monitoring Recovery for PFAS Exposure' (2020) 45 *Vermont Law Review* 287

Novelli, Giuseppe et al, 'Genetic tests and genomic biomarkers: regulation, qualification and validation' (2008) 5(2) *Clinical Cases in Mineral and Bone Metabolism* 149

Novey, Lawrence, 'Collective Judicial Management of Mass Toxic Tort Controversies: Lessons and Issues from the Agent Orange Litigation' (1998) 27(10) *Social Science and Medicine* 1071

Oosthuizen, J and M Cross, ‘Establishing Cause, What Does that Mean from an Epidemiological and Legal Perspective?’ (2018) 35 *Environmental and Planning Law Journal* 426

Otlowski, Margaret, 'Establishing the offence of non-consensual genetic testing in Australia: A call for action' (2013) 21 *Journal of Law and Medicine* 335

Otlowski, Margaret, 'Disclosing genetic information to at-risk relatives: new Australian privacy principles, but uniformity still elusive' (2015) 202(6) *Medical Journal of Australia* 335

Otlowski, Margaret and Dianne Nicol, 'The Regulatory Framework for Protection of Genetic Privacy in Australia' in Terry Sheung-Hung Kaan and Calvin Wai-Loon Ho (ed), *Genetic privacy: An evaluation of the ethical and legal landscape* (Imperial College Press, 2013)

Otlowski, Margaret, S. Taylor and Y. Bombard, 'Genetic discrimination: International perspectives' (2012) 13 *Annual Review of Genomics and Human Genetics* 433

Otlowski, Margaret et al, 'The use of legal remedies in Australia for pursuing allegations of genetic discrimination: Findings of an empirical study' (2007) 9 *International Journal of Discrimination and the Law* 3

Pardo, Michael, 'A Comment on Statistical Evidence and Standards of Proof' (2018) 25 *Supreme Court Economic Review* 59

Pardo, Michael, 'The Paradoxes of Legal Proof: A Critical Guide' (2019) 99(1) *Boston University Law Review* 233

Pauper, Marc, et al, ‘Long-read trio sequencing of individuals with unsolved intellectual disability’ (2021) 29 *European Journal of Human Genetics* 637

Pendergast, Peggy and Harold Hirsh, 'The Dalkon Shield in Perspective' (1986) 5 *Medicine and Law* 35

Pepe, Margaret, et al, ‘Phases of Biomarker Development for Early Detection of Cancer’ (2001) 93(14) *Journal of the National Cancer Institute* 1054

Peters, Sara, 'Shifting the Burden of Proof on Causation: The One Who Creates Uncertainty Should Bear its Burden' (2020) 13(2) *Journal of Tort Law* 237

Phillips, Tarryn, 'Proof, Probability and the Plaintiff: Epistemological Challenges in the Medico-Legal Field' in Marie-Andree Jacob and Anna Kirkland (eds), *Research Handbook on Socio-Legal Studies of Medicine and Health* (Edward Elgar, 2020)

Pierce, Benjamin, *Genetics: A Conceptual Approach* (Macmillan Learning, 7th ed, 2020)

Pierce, Jon, 'Toxicogenomics: Toward the Future of Toxic Tort Causation' (2003) 5(1) *North Carolina Journal of Law & Technology* 33

Pioro, Mark et al, 'Understanding the use of "genetic predispositon" in Canadian legal decisions' (2013) 7(1) *McGill Journal of Law and Health* 1

Plunkett, James, 'Causation in the High Court of Australia: A matter of common sense?' (2019) 10(153) *Precedent* 11

Pormeister, Kart, 'Genetic data and the research exemption - is the GDPR going too far?' (2017) 7(2) *International Data Privacy Law* 137

Porta, Miquel, *Dictionary of Epidemiology* (Oxford University Press, 2008)

Porta, Miquel and John Last, *Oxford Dictionary of Public Health* (Oxford University Press, 2nd ed, 2018)

Poulter, Susan, 'Genetic Testing in Toxic Injury Litigation: The Path to Scientific Certainty or Blind Alley?' (2001) 41(2) *Jurimetrics* 211

Poulter, Susan, 'Genetic testing in toxic injury litigation: The path to scientific certainty or blind ally?' (2001) 41(2) *American Bar Association* 211

Price, Rohan, 'The need for a regulatory response to diagnosis fraud in mesothelioma cases' (2011) 19 *Journal of Law and Medicine* 196

Prosser, William, 'Proximate Cause in California' (1950) 38 *California Law Review* 369

Putz, Nicholas, 'Developing Exposure-Based Preconception Tort Liability: A Scientific Challenge to Traditional Tort Concepts' (2016) 66(2) *Catholic University Law Review* 475

Quinn, Paul and Liam Quinn, 'Big genetic data and its big data protection challenges' (2018) 34(5) *Computer Law & Security Review* 1000

Ralph, Felix, 'Convictions through Kith and Kin: Legal, Policy and Ethical Issues in DNA Familial Matching and Genetic Metadata' (2018) 29(3) *Current Issues in Criminal Justice* 243

Ramos, Edward et al, 'Genomic Test Results and the Courtroom: The Roles of Experts and Expert Testimony' (2016) 44 *The Journal of Law, Medicine & Ethics* 205

Rares, Steven, 'Using the "Hot Tub" – How Concurrent Expert Evidence Aids Understanding Issues' (2013) 95 *Intellectual Property Forum Journal of the Intellectual Property Society of Australia and New Zealand* 28

Reda, Manon et al, 'Implementation and use of whole exome sequencing for metastatic solid cancer' (2020) 51(10264) *EBio Medicine* 1

Rego, Rhanae, 'A Critical Analysis of Post-Conviction Review in New South Wales' (2021) 2(3) *The Wrongful Conviction Law Review* 305

Rheingold, Paul and N Jacobson, 'The Toxic Tort Cause of Action: Law and Procedure' in Norman Landau and Michael Canavan Paul Rheingold (ed), *Toxic Torts: Tort Actions for Cancer and Lung Disease due to Environmental Pollution* (The Association of Trial Lawyers of America, 1977)

Ricci, Paolo and Natalie Gray, 'Toxic Torts and Causation: Towards an Equitable Solution in Australian Law – Part I: Legal Reasoning with Uncertainty' (1998) 21(3) *UNSW Law Journal* 787

Ricci, Paolo and Natalie Gray, 'Toxic torts and Causation: Towards an Equitable Solution in Australian Law - Part II' (1999) 22(1) *UNSW Law Journal* 155

Rice, Stephen, 'Argument's Design: The Post Hoc Ergo Propter Hoc Fallacy in Legal Argument and Analysis' (2020) 89 *The University of Missouri-Kansas City Law Review* 279

Richards, Ira and Marie Bourgeois, 'The Toxicologist as Expert Witness' in *General and Applied Toxicology* (John Wiley & Sons, 2009)

Robertson, David W., 'Causation in the Restatement (Third) of Torts: Three Arguable Mistakes' (2009) 44 *Wake Forest Law Review* 1007

Roisman, Anthony, Martha Judy and Daniel Stein, 'Preserving Justice – Defending Toxic Tort Litigation' (2004) 15(1) *Fordham Environmental Law Review* 191

Romano, Alessandro, 'God's Dice: The Law in a Probabilistic World' (2016) 41(1) *University of Dayton Law Review* 57

Rosenberg, David, 'The Causal Connection in Mass Exposure Cases: A "Public Law" Vision of the Tort System' (1984) 97 *Harvard Law Review* 851

Rothman, Kenneth, Sander Greenland and Timothy Lash, *Modern Epidemiology* (Wolters Kluwer, 3rd ed, 2008)

Rothstein, Mark, 'Preventing the Discovery of Plaintiff Genetic Profiles by Defendants Seeking to Limit Damages in Personal Injury Litigation' (1996) 71(4) *Indiana Law Journal* 877

Rothstein, Mark, et al, 'The Ghost in Our Genes: Legal and Ethical Implications of Epigenetics' (2009) 19 *Health Matrix* 1

Rubenstein Reiss, Dorit and Rachel Heap, 'Using and Misusing Legal Decisions: Why Anti-Vaccine Claims about NVICP are Wrong' (2019) 20 *Minnesota Journal of Law, Science & Technology* 191

Sabatello, Maya, 'Psychiatric Genetic Essentialism and Stigma in Child Custody Proceedings: Public Views' (2021) 8(2) *Journal of Law and the Biosciences* 1

Sabatello, Maya and M.D. Appelbaum, 'Psychiatric Genetics in Child Custody Proceedings: Ethical, Legal, and Social Issues' (2016) 4(3) *Current Genetic Medicine Reports* 98

Sabatello, Maya and Paul Appelbaum, 'Behavioral Genetics in Criminal and Civil Courts' (2017) 25(6) *Harvard Review of Psychiatry* 289

Sanders, Joseph, 'Applying Daubert Inconsistently? Proof of Individual Causation in Toxic Tort and Forensic Cases' (2010) 75 *Brooklyn Law Review* 1367

Sanders, Joseph, 'Causation in Asbestos Cancer Cases (and Beyond?)' in Richard Goldberg (ed), *Perspectives on Causation* (Hart Publishing, 2011)

Sanders, Joseph, et al, 'Differential Etiology: Inferring Specific Causation in the Law from Group Data in Science' (2021) 63 *Arizona Law Review* 851

Sanders, Joseph, and Julie Machal-Fulks, 'The Admissibility of Differential Diagnosis Testimony to Prove Causation in Toxic Tort Cases: The Interplay of Adjective & Substantive Law' (2001) 64(4) *Law and Contemporary Problems* 107

Sanders, Joseph, 'The "Every Exposure" Cases and the Beginning of the Asbestos Endgame' (2014) 88 *Tulane Law Review* 1153

Sankar, Pamela and Lisa Parker, 'The Precision Medicine Initiative's All of Us Research Program: An agenda for research on its ethical, legal, and social issues' (2017) 19(7) *Genetics in Medicine* 743

Schlein, Daniel, 'New frontiers for genetic privacy law: the Genetic Information Nondiscrimination Act of 2008' (2008) 19 *George Mason University Civil Rights Law Journal* 311

Schmitz-Spanke, Simone, 'Toxicogenomics – What added Value Do These Approaches Provide for Carcinogen Risk Assessment?' (2019) 173 *Environmental Research* 157

Schwartz, David and Christopher Seaman, 'Standards of Proof in Civil Litigation: An Experiment from Patent Law' (2013) 26(2) *Harvard Journal of Law and Technology* 429

Schwarze, Katharina, 'Are whole-exome and whole-genome sequencing approaches cost-effective? A systematic review of the literature' (2018) 20(10) *Genetics in Medicine* 1122

Scudder, Nathan et al, 'Policy and regulatory implications of the new frontier of forensic genomics: direct-to-consumer genetic data and genealogy records' (2019) 31(2) *Current Issues in Criminal Justice* 194

Sedo, Kathryn J, 'Workers' Compensation, Social Security Disability, SSI and Genetic Testing' (2007) *Journal of Law, Medicine & Ethics* 74

Serrano-Pozo, Alberto, Sudeshna Das and Bradley Hyman, 'APOE and Alzheimer's disease: advances in genetics, pathophysiology, and therapeutic approaches' (2021) 20(1) *The Lancet Neurology* 68

Sexton, Terrence, 'Toxicogenomics: Toward the Future of Toxic Tort Causation' (2003) 5(1) *North Carolina Journal of Law & Technology* 33

Shabani, Mahsa and P. Borry, 'Rules for processing genetic data for research purposes in view of the new EU General Data Protection Regulation' (2018) 26(2) *European Journal of Human Genetics* 149

Shabani, Mahsa and Luca Marelli, 'Re-identifiability of genomic data and the GDPR: Assessing the re-identifiability of genomic data in light of the EU General Data Protection Regulation' (2019) 20(6) *EMBO Reports* e48316

Shi, Xinghua and Xintao Wu, 'An overview of human genetic privacy' (2017) 1387(1) *Annals of the New York Academy of Sciences* 61

Smith, Jeremiah, 'Legal Cause in Actions of Tort' (1911) 25 *Harvard Law Review* 103

Smith-Drelich, Noah, 'Performative Causation' (2020) 93(3) *Southern California Law Review* 379

Sonenshein, David and Charles Fitzpatrick, 'The Problem of Partisan Experts and the Potential for Reform Through Concurrent Evidence' (2013) 32(1) *Review of Litigation* 1

Sontakke, Yogesh Ashok, *Principles of Clinical Genetics* (Jaypee Brothers Medical Publishers, 2018)

Srivastava, Siddharth et al, 'Meta-analysis and multidisciplinary consensus statement: exome sequencing is a first-tier clinical diagnostic test for individuals with neurodevelopmental disorders' (2019) 21(11) *Genetics in Medicine* 2413

Stapleton, Jane, 'Compensating Victims of Disease' (1985) 5(2) *Oxford Journal of Legal Studies* 248

Stapleton, Jane, 'Factual Causation' (2010) 38 *Federal Law Review* 467

Stapleton, Jane, 'The Two Explosive Proof-of-Causation Doctrines Central to Asbestos Claims' (2009) 74 *Brooklyn Law Review* 1011

Stauch, Marc, 'Loss of Chance in Medical Negligence' (1997) 17 *Oxford Journal of Legal Studies* 205

Steel, Sandy, *Proof of Causation in Tort Law* (Cambridge University Press, 2015)

Steenland, Kyle, David Savitz and Tony Fletcher, 'Class Action Lawsuits: Can They Advance Epidemiologic Research?' (2014) 2 *Epidemiology* 167

Stewart, Antony, *Basic Statistics and Epidemiology: A Practical Guide* (Radcliffe Publishing, 3rd ed, 2010)

Stickley, Amanda, 'Long term exposure to asbestos satisfies test for causation' (2012) 32 *QLD Lawyer* 22

Stojanovic, Jelena Rumi, et al, 'Diagnostic and Clinical Utility of Clinical Exome Sequencing in Children With Moderate and Severe Global Developmental Delay / Intellectual Disability' (2020) 35(2) *Journal of Child Neurology* 116

Strong, Thomas, 'Alternative Therapies of Morning Sickness'(2001) 33 *Clinical Obstetrics & Gynecology* 653

Sulyok, Katalin, 'Managing Uncertain Causation in Toxic Exposure Cases: Lessons for the European Court of Human Rights from U.S. Toxic Tort Litigation' (2017) 18(4) *Vermont Journal of Environmental Law* 519

Summers, Andrew, 'Common-Sense Causation in the Law' (2018) 38(4) *Oxford Journal of Legal Studies* 793

Suter, Sonia, 'GINA at 10 years: the battle over 'genetic information' continues in court' (2019) 5(3) *Journal of Law and the Biosciences* 495

Taylor, Mark, *Genetic Privacy and the Law: A Critical Perspective on Privacy Protection* (Cambridge University Press, 2012)

The American Law Institute, *Restatement of the Law (Second), Torts* (The American Law Institute, 1965)

The American Law Institute, *Restatement of the Law (Third), Torts: Liability for Physical and Emotional Harm* (The American Law Institute, 2010)

The ENCODE Project Consortium, 'An integrated encyclopaedia of DNA elements in the human genome' (2012) 489 *Nature* 57

Tiller, Jane et al, 'Genetic discrimination by Australian insurance companies: a survey of consumer experiences' (2020) 28(1) *European Journal of Human Genetics* 108

Turley, Jonathan, 'Anonymity, Obscurity and Technology: Reconsidering Privacy in the Age of Biometrics' (2020) 100 *Boston University Law Review* 2179

Turton, Gemma, *Evidential Uncertainty in Causation in Negligence* (Hart Publishing, 2016)

Vallance, Sarah and Margaret Brain, 'The appropriateness of genetic testing in cerebral palsy cases' (2016)(133) *Precedent* 4

Van Dyke, John, 'The Dalkon Shield: A "Primer" in IUD Liability' (1978) 6(1) *Western State University Law Review* 1

Varela, Ignacio, 'Exome sequencing identifies frequent mutation of the SWI/SNF complex gene PBRM1 in renal carcinoma' (2011) 469(7331) *Nature* 539

Venter, Craig et al, 'The Sequence of the Human Genome' (2001) 291 *Science* 1304

Wagoner, Joseph et al, 'Radiation as the Cause of Lung Cancer Among Uranium Miners' (1965) 273 *New England Journal of Medicine* 181

Wambuguh, Oscar, *Examining the Causal Relationship Between Genes, Epigenetics, and Human Health* (IGI Global, 2019)

Watson, Penelope, 'Novel Damages Claims in Toxic Torts: Medical Monitoring and Fear of Future Disease' (2005)(69) *Precedent* 12

Weaver, Ian et al, 'Epigenetic Programming by Maternal Behaviour' (2004) 7 *Nature Neuroscience* 847

Webb, Penny and Christopher Bain, *Essential Epidemiology: An Introduction for Students and Health Professionals* (Cambridge University Press, 2nd ed, 2010)

Weed, Douglas, 'Causation: An Epidemiologic Perspective (in Five Parts)' (2003) 12(1) *Journal of Law and Policy* 43

Weiner, Christopher, 'Transgenerational Tort Liability for Epigenetic Disease' (2011) 13 *DePaul Journal of Health Care Law* 319

Weiss, Randi et al, 'The Use of Genetic Testing in the Courtroom' (1999) 34(3) *Wake Forest Law Review* 889

Wild, Christopher, 'Biomarkers of Exposure and Effect' in Timothy Rebbeck, Christine Ambrosone and Peter Shields (eds), *Molecular Epidemiology: Applications in Cancer and Other Human Diseases* (Informa Healthcare, 2008)

Williams, C R, 'Burdens and standards in civil litigation' (2003) 25(2) *Sydney Law Review* 165

Wong, Terry, 'Characterizing the Harms of Compromised Genetic Information for Article III Standing in Data Breach Litigation' (2020) 53 *Columbia Journal of Law and Social Problems* 461

Wood, Lisa, 'Experts in the Hot Tub' (2007) 21 *Anti-Trust* 95

Worthey, Elizabeth, 'Making a definitive diagnosis: Successful clinical application of whole exome sequencing in a child with intractable inflammatory bowel disease' (2011) 13(3) *Genetics in Medicine* 255

Wright, Richard, 'Acts and Omissions as Positive and Negative Causes' in Jason W Neyers, Erika Chamberlain and Stephen GA Pitel (eds), *Emerging Issues in Tort Law* (Hart Publishing, 2007)

Wright, Richard, 'Causation in Tort Law' (1985) 73 *California Law Review* 1735

Wright, Richard, 'Proving Causation: Probability versus Belief' in Richard Goldberg (ed), *Perspectives on Causation* (Hart Publishing, 2011)

Wright, Richard, 'The NESS Account of Natural Causation: A Response to Criticisms' in Richard Goldberg (ed), *Perspectives on Causation* (Hart Publishing, 2011)

Yarnall, Megan, 'Dueling Scientific Experts: Is Australia's Hot Tub Method a Viable Solution for the American Judiciary' (2009) 88(1) *Oregon Law Review* 311

Zhang, Luoping, et al, 'Chromosome-wide aneuploidy study (CWAS) in workers exposed to an established leukemogen, benzene' (2011) 32(4) *Carcinogenesis* 605

Zhang, Luoping, et al, 'The Nature of Chromosomal Aberrations Detected in Humans Exposed to Benzene'(2002) 32(1) *Critical Reviews in Toxicology* 1

Ziegler, Andreas et al, 'Personalized medicine using DNA biomarkers: a review' (2012) 131 *Human Genetics* 1627

Zuckerman, Adrian, et al, *Zuckerman on Australian Civil Procedure* (LexisNexis Butterworths, 2018)

9.2. Cases

ABC v St George's Healthcare NHS Trust & Ors [2020] EWHC 455

Abrams v City of Chicago 811 NE 2d 670 (Ill, 2004)

Accord Chapman v Procter & Gamble Distributing, LLC, 766 F 3d 1296 (11th Cir, 2014)

Adacsi v Amin [2013] ABCA 315 (Alberta Court of Appeal)

Addington v Texas, 441 US 418 (1979)

Adeels Palace Pty Ltd v Moubarak (2009) 239 CLR 420

Agee v Purdue Pharmaceuticals 2004 WL 5352989 (WD Okla, Nov 22, 2004), aff'd, 242 F Appx 512 (10th Cir, 2007)

Agius v Amaca and Anor [2007] NSWDDT 13

Alder (as litigation guardian for Alder) v Khoo [2013] QSC 312

Allen v Pa Eng'g Corp, 102 F 3d 194 (5th Cir, 1996)

Allen v United States 588 F Supp 247 (D Utah, 1984)

Allison v McGhan Medical Corp 184 F 3d 1300 (11th Cir, 1999)

Amaba Pty Ltd v Booth; Amaca Pty Ltd v Booth [2010] NSWCA 344

Amaca v Booth (2011) 246 CLR 36

Amaca Pty Limited (Under NSW Administered Winding Up) v Booth & Anor; Amaba Pty Limited (Under NSW Administered Winding Up) v Booth & Anor [2011] HCATrans 276 (4 October 2011)

Amaca Pty Limited (Under NSW Administered Winding Up) v Booth & Anor; Amaba Pty Limited (Under NSW Administered Winding Up) v Booth & Anor [2011] HCATrans 277 (5 October 2011)

Amaca Pty Ltd v CSR Ltd & Anor [2015] VSC 582

Amaca Pty Ltd v Ellis & Ors [2009] HCATrans 296 (4 November 2009)

Amaca Pty Ltd v Ellis [2010] HCA 5; (2010) 240 CLR 111; (2010) 263 ALR 576

Amaca Pty Ltd v Hannell (2007) 34 WAR 109

Amaca Pty Ltd v Moss [2007] WASCA 162

Amaca Pty Ltd v Tullipan [2014] NSWCA 269

Anderson v Cryovac, Inc, No. 82-1672-S (D Mass, 1985)

Anderson v Minneapolis, St.Paul & Sault Ste. Marie. Ry. Co. (1920) 179 NW 45

Anthony v Small Tube Mfg Corp 580 F Supp 2d 409 (ED Penn, 2008)

Association for Molecular Pathology v Myriad Genetics Inc (2013) 569 US 576

Australian Vioxx class action (Peterson & Ors v Merck, Sharpe & Dohme (Austl.) Pty Ltd & Anor (VID 451 of 2006)

Barker v Corus (UK) plc (2006) 2 AC 572

Bartel v John Crane, Inc, 316 F Supp 2d 603 (ND Ohio, 2004), *aff'd sub nom. Lindstrom v A-C Prod. Liab. Trust*, 424 F 3d 488 (6th Cir, 2005)

Bennett v Fieser, 1994 WL 542089 (D Kan, 25 February 1994)

Bennett v Minister for Community Welfare (1992) 176 CLR 408

Berry v CCL Secure Pty Ltd [2020] HCA 27

Best v Lowe's Home Centers, Inc., 563 F 3d 171 (6th Cir, 2009)

Bettisworth v BNSF Railway Co 2020 WL 3498139 (D Neb, June 29, 2020)

Betts v Whittingslowe (1945) 71 CLR 637

BHP Billiton Ltd v Dunning [2015] NSWCA 55

BHP Billiton Ltd v Hamilton & Anor [2013] SASCFC 75

Blackmon v American Home Products Corp, 346 F Supp 2d 907 (SD Tex, 2004)

Blackwell v Wyeth 408 Md 575 (Md, 2009)

BNSF Ry Co v Phillips 434 SW 3d 675 (Tex App Fort Worth, May 22, 2014)

Boal v Electric Storage Battery 98 F 2d 815 (3rd Cir, 1938)

Bonner v ISP Techs Incorporated 259 F 3d 924 (8th Cir, 2001)

Bonnington Castings Ltd v Wardlaw (1956) AC 613

Booth v Fourmeninapub Pty Ltd [2020] NSWCA 57

Bostic v Georgia-Pacific Corp 439 S W 3d 332 (Tex, 2014)

Bowen v. E.I. DuPont de Nemours &. Co., No 97C 06-194, 2005 WL 1952859 (Del Super Ct, 5 August 2005)

Briggs v RTL Mining & Earthworks [2019] VMC004

Briginshaw v Briginshaw (1938) 60 CLR 336

Brock v Merrell Dow Pharmaceuticals 874 F 2d 307 (5th Cir, 1989)

Brooks v Stone Architecture, PA, 934 So 2d 350, 352-54 (Miss Ct App, 2006)

Burleson v Texas Department of Criminal Justice 393 F 3d 577 (5th Cir, 2004)

Burt v Winona Health Services, 2018 WL 11222161 (D Minn, 26 February 2018)

Burt v Winona Health, 2018 WL 3647230 (D Minn, 1 August 2018)

Byers v Secretary of HHS 2010 WL 5663019 (Fed Cl, Nov 30, 2010)

Cano v Everest Mineral Corp 362 F Supp 2d 814 (WD Tex, 2005)

Caraker v Sandoz Pharms., 188 F Supp 2d 1026 (SD Ill, 2001)

Carter v American Oil Co 139 F 3d 1158 (7th Cir, 1998)

Castillo v EI DuPont de Nemours & Co 854 So 2d 1264 (Fla, 2003)

Cynthia Bernadette Murray (Legal Personal Representative of James Noel Murray (Decd) and Marcelle Agnes Murray) and Repatriation Commission [1997] AATA 117

D'Arcy v Myriad Genetics Inc [2014] FCAFC 115

D'Arcy v Myriad Genetics (2015) 258 CLR 334; 89 ALJR 924

D'Argenio v VWA [2016] VCC 1955

Daubert v Merrell Dow Pharmaceuticals, Inc (1993) 509 US 579

Daniel v Holroyd City Council [2016] NSWDC 239

Dasreef v Hawchar (2011) 243 CLR 588

Daubert v Merrell Dow Pharmaceuticals Inc (1993) 509 US 579; 113 S Ct 2786

De Groot v The Nominal Defendant [2005] NSWCA 61

DeLuca v Merrell Dow Pharms., Inc., 911 F 2d 941 (3rd Cir, 1990)

DeLuca v Merrell Dow Pharmaceuticals 791 F Supp 1042 (DNJ, 1992), *affd*, 6 F 3d 778 (3rd Cir, 1993)

Deribeaux v Sec'y of HHS 717 F 3d 1363 (Fed Cir, 2013)

Devon County Council v EB & Ors (Minors) [2013] EWHC 968

Dodd-Anderson v Stevens, 1993 WL 273373 (D Kan, 4 May 1993)

Doe v Ortho-Clinical Diagnostics 440 F Supp 2d 465 (MDNC, 2006)

Donaldson v Cent Ill Pub Serv Co 767 NE 2d 314 (Ill, 2002)

Dougherty and Repatriation Commission (Veterans' entitlements) [2019] AATA 706

Dow Chemicals (Australia) Ltd v Director, Chemicals Notification and Assessment [1999] AATA 1023

Dunn v Sandoz Pharmaceuticals Corp 275 F Supp 2d 672 (MDNC, 2003)

Dura (Australia) Constructions Pty Ltd v Hue Boutique Living Pty Ltd (No 3) [2012] VSC 99

Durden v Secretary of Dept of HHS 2007 WL 4962000

Dustin W. Holsten, and Katlin A Holsten v Amalgamated Sugar Co. LLC, et al., No 18-L-1664 (Ill Cir, Madison Co, 2018)

Dwyer ex rel Dwyer v Secretary of HHS 2010 WL 892250

Eastbury v Genea Limited (formerly known as Sydney IVF Limited) [2015] NSWSC 1834

Easter v Aventis Pasteur 358 F Supp 2d 574 (ED Tex, 2005)

East Metropolitan Health Service v Ellis (by his next friend Ellis) [2020] WASCA 147

Easum v Miller, 92 P 3d 794 (Wyo, 2004)

Edwards v Blomeley [2002] NSWSC 460

Edwards v Safety-Kleen Corp 61 F Supp 2d 1354 (SD Fla, 1999)

Elbourne v Gibbs [2006] NSWCA 127

Ellis v South Australia [2006] WASC 270

EMI Australia Ltd v BES [1970] 2 NSWR 238 (appeal dismissed (1970) 44 ALJR 360)

Enright v Eli Lilly & Co 570 NE 2d 198 (NY, 1991)

Environmental Defense Fund v. Environmental Protection Agency 598 F 2d 62 (DC Cir, 1978)

Ergon Energy Corporation Ltd v Rice-McDonald & Ors [2009] QSC 213

Evans v Queanbeyan City Council [2011] NSWCA 230

Evers, Keith Leonard v Racecar Preparation and Management Pty Ltd [2013] VCC 517

Fabrizi v Rexall Sundown Inc. 2004 WL 1202984 (WD Pa, June 4, 2004)

Fairchild v Glenhaven Funeral Services Ltd [2002] UKHL 22

Fairchild v Glenhaven Funeral Services (2003) 1 AC 32

Faoro v Secretary of HHS 2016 WL 675491 (Fed Cl, Jan, 29, 2016)

Farley-Smith v Repatriation Commission [2005] AATA 968

Farley-Smith v Repatriation Commission [2010] AATA 637

Farley-Smith v Repatriation Commission [2012] FCA 80

Farraj and another v King's Healthcare NHS Trust and another (2010) 1 WLR 2139

Fernandez v Tubemakers of Australia Ltd [1975] 2 NSWLR 190

Fisher for XSF v Winding Waters Clinic, PC 2017 WL 574383 (D Or, 13 February 2017) *aff'd* 2017 WL 4780616 (D Or, 22 October 2017)

Fitzgerald v Penn (1954) 91 CLR 268

Forbes v Selleys Pty Ltd [2002] NSWSC 547

Forbes v Selleys Pty Ltd [2004] NSWCA 149

Ford Motor Co v Boomer 736 S.E.2d 724 (Va., 2013)

Foxley v TAC [2021] VCC 1222

French v QBE Insurance (Australia) Ltd (2011) 58 MVR 214

Frye v United States 293 F 1013 (DC Cir, 1923)

Gail Lucille Ingham et al v Johnson & Johnson et al (Trial Transcript, Cir Ct of the City of St Louis, vol 18A, 26 June 2018)

General Electric Co v Joiner (1997) 522 US 136; 118 S Ct 512

Georgia-Pac. Corp. v Stephens, 239 SW 3d 304 (Tex App, 2007)

Gill v Ethicon Sarl (No 5) [2019] FCA 1905

Glastetter v Novartis Pharms. Corp. 252 F 3d 986 (8th Cir, 2001)

Gloria Webb v Repatriation Commission [1997] FCA 1130

Godfrey v Secretary of HHS, 2014 WL 3058353 (Not reported in Fed Cl)

Gough and Comcare (Compensation) [2020] AATA 4669

Grassis v Johns-Manville Corp 591 A 2d 671 (NJ Super, 1991)

Gregg v Scott [2005] UKHL 2

Gregg v V-J Auto Parts, Co, 943 A 2d 216 (Pa, 2007)

Grover v Eli Lilly & Co 591 NE 2d 696 (Ohio, 1992)

Haber v Walker [1963] VR 339

Hall v Baxter Healthcare Corporation 947 F Supp 1387 (D Or, 1996)

Hall v Conoco Inc., 886 F 3d 1308 (10th Cir, 2018)

Hallquist, ex rel Hallquist v EI Dupont De Nemours No. A-6223-12T2, 2014 NJ Super Unpub LEXIS 2458 (Super Ct App Div, Oct 10, 2014)

Hamilton v BHP Billiton Limited [2012] SADC 25

Hamilton v State of New South Wales [2013] NSWSC 1437

Harris v KEM Corp No 85 Civ 2127(WK), 1989 WL 200446 (SDNY, 1989)

Harris v Kem Corp, No 85 Civ 2127(WK), 1990 US Dist LEXIS 11150 (SDNY, 1990)

Harris v Mercy Hospital 596 N E 2d 160, 163 (Ill App, 1992)

Harris v Secretary of HHS, 2014 WL 3159377 (Not reported in Fed Cl)

Harriton (by her tutor) v Stephens [2004] NSWCA 93

Harriton v Stephens (2006) 226 CLR 52

Hartog v Comcare [2017] AATA 1164

Hawker and Ors v Miller [2011] SASCFC 76

Haynes v Hamilton County 883 SW 2d 606 (Tenn., 1994)

Hazeal v Local Government Association Workers Compensation Schemes (Corporation of the City of Whyalla) [2006] SAWCT 36

Heller v Shaw Industries, Inc 167 F 3d 146 (3rd Cir, 1999)

Hendrian v Safety-Kleen Systems, Inc., No 08-14371 (ED, Mich, 2014)

Hendrix v Evenflo Co, 255 FRD 568 (ND Fla, 2009) aff'd, 609 F 3d 1183 (11th Cir, 2010)

Henricksen v ConocoPhillips Co, 605 F Supp 2d 1142 (ED Wash, 2009)

Herman & Maclean v Huddleston, 459 US 375 (1983)

Herskovits v Group Health Coop 99 Wash 2d 609, 664 P2d 474 (1983)

Hirst v Nominal Defendant [2005] Qd R 133

Hodge v WorkCover [2008] SAWCT 21

Honeysett v The Queen (2014) 253 CLR 122

Hopkins v Secretary of HHS 84 Fed Cl 530 (2008)

Hotson v East Berkshire Health Authority [1987] AC 750

Hunt v Repatriation Commission [2016] AATA 554

Hunt v Repatriation Commission [2017] AATA 697

Hunt v Repatriation Commission [2019] FCA 1191

Hupp v United States 563 F Supp 25 (SD Ohio, 1982)

Improvement Co v Munson 81 US 442, 448 (1872)

In re Accutane Products Liability 511 F Supp 2d 1288 (MD Fla, 2007), *aff'd,* Rand v. Hoffman La Roche Inc., 291 Fed App'x 249 (11th Cir, 2008)

In re 'Agent Orange' Products Liability Litigation 534 F Supp 1046 (EDN, 1982), cert. denied, 465 US 1067 (1984)

In re "Agent Orange" Products Liability Litigation 611 F Supp 1223 (EDNY, 1985)

In re 'Agent Orange' Products Liability Litigation 818 F 2d 145 (2nd Cir, 1987), cert. denied, 484 US 1004 (1988)

In Re Bendectin Litigation 857 F 2d 290 (6th Cir, 1988)

In re Breast Implant Litigation 11 F Supp 2d 1217 (D Colo, 1998)

In re Dalkon Shield Cases, 599 F Supp 1351, 1356-57 (D Md, 1984)

In re Dalkon Shield Punitive Damages Litigation, 613 F Supp 1112 (ED Va, 1985)

In Re Dow Corning Corporation 541 BR 643 (ED Mich, 2015)

In re Ephedra Products Liability Litigation 393 F Supp 2d 181 (SDNY, 2005)

In re Hanford Nuclear Reservation Litigation 292 F 3d 1124 (9th Cir, 2002)

In re Heparin Products Liability Litigation 803 F Supp 2d 712 (ND Ohio, 2011)

In Re Joint Eastern and Southern District Asbestos Litigation, 827 F Supp 1014 (SDNY, 1993)

In re Lipitor (Atorvastatin Calcium) Marketing, Sales Practices & Products Liability Litigation (No II) MDL 2502, 892 F 3d 624 (4th Cir, 2018)

In re Paoli R.R. Yard PCB Litig., 35 F 3d 717 (3rd Cir, 1994)

In re Prempro Products Liability Legislation, 586 F 3d 547 (8th Cir, 2009)

In re Rezulin Prods. Liab. Litig., MDL No 1348, 00 Civ. 2843(LAK), 2004 WL 2884327, 3 (SDNY Dec 10, 2004)

In re Rezulin Products Liability Litigation 369 F Supp 2d 398 (SDNY, 2005)

In re Silicone Gel Breast Implants Products Liability Litigation 318 F Supp 2d 879 (CD Cal, 2004)

In re TMI Litigation 193 F 3d 613 (3rd Cir, 1999)

In re Toxic Substances Cases, No. AD 03-319, 2006 WL 2404008 (Pa Ct Com P Aug 17, 2006)

In re WR Grace & Co., 355 BR 462 (Bankr D Del, 2006)

In re Zostavax (Zoster Vaccine Live) Products Liability Litigation, MDL No 2848, Civ 18-md-2848, 2022 WL 952179 (ED Penn, Mar. 30, 2022)

International Union, United Automobile, Aerospace and Agricultural Implement Workers of America, UAW v Pendergrass, 878 F 2d 389 (DC Cir, 1989)

Jessica Blackford-Cleeton and Brandon Cleeton v AK Steel Corp., No 15-L-17 (Richland County Circuit Court, IL)

John Bolton Humphreys v Repatriation Commission [2005] AATA 610

Johnson v Arkema, Inc 685 F 3d 452 (5th Cir, 2012)

Johnson & Johnson Talcum Powder Cases, 249 Cal Rptr 3d 642 (Cal App, 2019)

John William Booth v Amaca Pty Limited and Amaba Pty Limited [2010] NSWDDT 8

John William Suthern v Unilever Australia Ltd [2007] ACTSC 81

Jones v Dunkel (1959) 101 CLR 298

Joseph Thrash, et al v The Boeing Co 2018 WL 2573097 (ND Cal, 2 March 2018)

Julia Farr Services Inc v Hayes [2003] NSWCA 37

June v Union Carbide Corp 577 F 3d 1234 (10th Cir, 2009)

Kallal v Lyons No 4-20-0319 (Il App, 4th Dist, 4 May 2021)

Kane v Motorola, Inc, 779 NE 2d 302 (Ill App, 2002)

Kaous v Lutheran Medical Center 30 NYS 3d 663 (NY App Div, 2016)

Kavanagh v Akhtar (1998) 45 NSWLR 588

Kennedy v Collagen Corp 161 F 3d 1226 (9th Cir, 1998)

KF By Her Tutor RF v Royal Alexandra Hospital for Children known as the Children's Hospital Westmead and Anor [2010] NSWSC 891

Kian v Mirro Aluminium Co 88 FRD 351 (Mich, 1980)

Kilpatrick v Breg, Inc., 613 F 3d 1329 (11th Cir, 2010)

King v Western Sydney Local Health Network [2013] NSWCA 162

Kirk v Schaeffler Group USA 2014 WL 2807681 (WD Mo, June 20, 2014)

Kirk v Schaeffler Group US 887 F 3d 376 (8th Cir, 2018)

Knight v Kirby Inland Marine Inc 482 F 3d 347 (5th Cir, 2007)

Kolakowski v Secretary of HHS 2010 WL 5672753 (Fed Cl, Nov 23, 2010)

Koljibabic v BHP Billiton Nickel West Pty Ltd [2008] WADC 165

Kriloff v Providence Health & Services, 2016 WL 11121002 (D Or, 12 January 2016)

Kumho Tire Co Ltd v Carmichael (1999) 526 US 137; 119 S Ct 1167

Kurnell Passenger and Transport Service Pty Limited v Randwick City Council (2009) 230 FLR 336

Landrigan v Celotex Corp 605 A 2d 1079 (NJ Supp Ct, 1992)

Larsen v Grace Worldwide (Aust) Pty Limited (No 2) [2015] NSWSC 1224

Lavender v Bayer Corp (W Va Cir, No 93-C-226-K, May 29, 1998)

Leach v EI DuPont de Nemours & Co, 01-C-608 (W Va, 2005)

Leslie Hubbard v Military Rehabilitation and Compensation Commission [2009] AATA 363

Lifeplan Australia Friendly Society Ltd v S & P Global Inc [2018] FCA 379

Lilley v Comcare [2003] AATA 738

Liyanage v Western Australia (2017) 51 WAR 359

Lofgren v Motorola Inc., No. CV 93-05521, 1998 WL 299925 (Ariz Super Ct, June 1, 1998)

Lola Merle Evans v Queanbeyan City Council and Anor [2010] NSWDDT 7

Lo Presti v Ford Motor Company of Australia Ltd [No 2] [2008] WASC 12

Lowes v Amaca Pty Ltd [2011] WASC 287

Mahony v J Kruschich (Demolitions) Pty Ltd (1985) 156 CLR 522

Mallard v The Queen (2003) 28 WAR 1

Mandel v American Int'l Indus, No BC644175 (LA County, 28 June 2017)

Manko v United States, 636 F Supp. 1419, 1434 (WD Mo, 1986) *aff'd in part*, 830 F 2d 831 (8th Cir, 1987)

March v E & MH Stramare Pty Ltd (1991) 171 CLR 506

Marmo v IBP Inc 360 F Supp 2d 1019 (D Neb, 2005)

Marsh v Valyou, 977 So 2d 543 (Fla, 2007)

Matsuyama v Birnbaum (2008) 452 Mass 1

Mayhue v Sparkman 653 NE 2d 1384 (Ind, 1995)

McCullock v HB Fuller Co, 61 F 3d 1038 (2nd Cir, 1995)

McDonald v State Rail Authority (NSW) & Others [1998] NSWDDT 4

McGhee v National Coal Board (1972) 3 All ER 1008

McGhee v National Coal Board [1973] 1 WLR 1

McLoughlin and Military Rehabilitation and Compensation Commission, Re [2006] AATA 825

McMunn v Babcock & Wilcox Power Generation Group, Inc (2017) 869 F 3d 246

Meadows v Khan (2019) 4 WLR 26

Medalen v Tiger Drylac USA, Inc, 269 F Supp 2d 1118 (D Minn, 2003)

Medlin v The State Government Insurance Commission (1995) 182 CLR 1

Meister v Med. Eng'g Corp., 267 F 3d 1123 (DC Cir, 2001)

Merck & Co v Garza 347 SW 3d 256 (Tex, 2011)

Merck Sharp & Dohme (Australia) Pty Ltd v Peterson [2011] FCAFC 128

Merrell Dow Pharmaceuticals, Inc v Havner 953 S W2d 706

Metabolife International, Inc. v Wornick 264 F 3d 832 (9th Cir, 2001)

Meyers v Intel Corp, No D66911 (Del Super Ct, 11 June 2015)

Michelle Anne Vasiliu v Comcare [2009] AATA 719

Mills v Bristol-Myers Squibb Co 2011 WL 4708850 (D Ariz, Oct 7, 2011)

Milward v Acuity Specialty Products Group 664 F Supp 2d 137 (D Mass, 2009), *rev'd* 639 F 3d 11 (1st Dist, 2011)

Milward v Acuity Specialty Products Group, 969 F Supp 2d 101 (D Mass, 2013), *aff'd sub nom, Milward v Rust-Oleum Corp.*, 820 F 3d 469 (1st Cir, 2016)

Moore v Ashland Chem. Inc., 151 F 3d 269 (5th Cir, 1998)

Mount Isa Mines Ltd v Pusey (1971) 125 CLR 383

Munro v Regents of University of California 263 Cal Rptr 878 (Cal App, 1989)

Murphy v Secretary of HHS 2016 US Claims LEXIS 677

Nader v Urban Transit Authority of New South Wales (1985) 2 NSWLR 501

Naomi Guzman v ExxonMobil Corp, ExxonMobil Oil Corp, Humble Inc, and Intracoastal Tubular Services Inc, No. 693–606 (La Dist Ct, 24th Dist, 2013) Jury Verdicts LEXIS 9774

National Bank of Commerce v Associated Milk Producers, Inc., 22 F Supp 2d 942 (ED Ark, 1998), aff'd, 191 F 3d 858 (8th Cir, 1999)

National Bank of Commerce v Dow Chemical Company 965 F Supp 1490 (ED Ark, 1996), *aff'd,* 133 F 3d 1132 (8th Cir, 1998)

National Research Development Corporation v Commissioner of Patents (1959) 102 CLR 252

Nicholson v Atlas Steel Foundry and Engineering Co Ltd (1957) 1 WLR 613

Nominal Defendant v Clancy [2007] NSWCA 349

Norris v Baxter Healthcare 397 F 3d 878 (10th Cir, 2005)

Norton Australia Pty Ltd v Streets Ice Cream Pty Ltd (1968) 120 CLR 635

NSW Insurance Ministerial Corporation (formerly Gio of NSW) v Gomes Matter No Ca 40052/96 [1998] NSWSC 584

Ortwein v CertainTeed Corp., et al., Alameda County Superior Court No. RG13701633 (Cal Super Ct, 12 December, 2014)

Overseas Tankship (UK) Ltd v Morts Dock & Engineering Co Ltd (The Wagon Mound (No 1)) [1961] AC 388

Owners of SS Melanie v Owners of SS San Onofre [1927] AC 162

Parker v BHP Billiton Limited [2011] SADC 104

Parker v Mobil Oil Corp., 16 AD 3d 648, (NY App Div, 2005)

Parker v Mobil Oil Corporation 857 NE 2d 1114 (NY, 2006)

Parker v Mobil Oil Corp 793 NYS 2d 434 (NY App Div, 2005), *aff'd* NE 2d 1114 9NY, 2006), *reargument denied,* 861 NE 2d 104 (NY, 2007)

Park Rail Developments Pty Ltd v RJ Pearce Associates Pty Ltd (1987) 8 NSWLR 123

Paulette Rosina Mitchell v Repatriation Commission [1991] AAT 446

Pederson v Northern NSW Local Health District [2020] NSWSC 741

Perri v Adriatic Concrete Pty Ltd [2015] NSWWCCPD 70

Perry v Novartis Pharms. Corp., 564 F Supp 2d 452 (ED Pa, 2008)

Peterson v Merck Sharpe & Dohme (Australia) Pty Ltd (2010) 266 ALR 1; [2010] FCA 180

Phillips v Christianacare Health System, No 06-05-013 (Del Super Ct, 27 June 2008)

PL by her tutor TL v Dunstan [2020] NSWSC 297

Plowman v Sisters of St John of God Inc [2014] NSWSC 333

Pohl v NGK Metals Corp 2006 Phila Ct Com Pl LEXIS 472

Pohl v NGK Metals Corp 936 A.2d 43 (Pa Super, 2007)

Polaino v Bayer Corp 122 F Supp 2d 63 (D Mass, 2000)

Precision Valve Australia Pty Ltd v Nanda [2012] NSWWCCPD 48

Prudence McDonald v Dr Ng;; Matthew McDonald by his tutor Prudence McDonald v Dr Ng [2018] NSWSC 1050

Pryde and Telstra Corporation Limited (Compensation) [2016] AATA 811

Purkess v Crittenden (1965) 114 CLR 164

Ranes v Adams Labs., Inc., 778 NW 2d 677 (Iowa, 2010)

Rankin v Idoko Pty Ltd & Another (2000) 19 NSWCCR 607

Raynor v Merrell Pharms. Inc. 104 F 3d 1371 (DC Cir, 1997)

Reardon v Bonutti Orthopaedic Services Ltd 316 Ill App 3d 699; 737 NE2d 309; 249 Ill Dec 919 (2000)

Reid v Delta Electricity [2009] NSWWCCPD 49

Repatriation Commission v Farley-Smith [2007] FCA 1058

Repatriation Commission v Gloria Webb [1998] FCA 1411

Re JS (a minor) [1980] 1 All ER 1061

Richard Ortwein, et al v Certainteed Corporation, et al, No RG 13701633, 2016 Jury Verdicts LEXIS 67523

Richardson v Richardson Merrell, Inc. 857 F 2d 823 (DC Cir, 1988)

Rider v Sandoz Pharms Corp 295 F 3d 1194 (11th Cir, 2002)

Rimbert v Eli Lilly & Co 2009 WL 2208570 (DNM, July 21, 2009), aff'd, 647 F 3d 1247 (10th Cir, 2011)

Rite Aid Corp v LevyGray, 876 A 2d 115 (Md App, 2005), aff'd, 894 A 2d 563 (Md, 2006)

RK, on behalf of AK v Secretary of HHS 2015 WL 10936124

Robert Ingham et al v Johnson & Johnson et al 608 SW3d 663, 711(Mo Ct App, No ED107476, 23 June 2020)

Robertson v Counselman 686 P 2d 149 (Kan, 1984)

Robyn Kathleen Cornish and Repatriation Commission [1997] AATA 336

Rogers-Duell v Chen 974 NYS 2d 769 (NY Sup Ct, 2013)

Rosenberg v Percival (2001) 205 CLR 434

Rowe v McCartney (1976) 2 NSWLR 72

Rowlands v State of New South Wales (2009) 74 NSWLR 715

Ruff v Ensign-Bickford Industries, Inc. 168 F Supp 2d 1271 (D Utah, 2001)

Rufo v Hosking (2004) 61 NSWLR 678

Rutherford v Owens-Illinois 941 P2d 1203 (Cal, 1997)

R v Karger No SCCRM-98-224 [2001] SASC 64

Schenk v Novartis Pharmaceuticals Corp 2014 WL 3656904 (D Ariz, July 23, 2014)

Schlagenhauf v Holder 379 US 104 (1964)

Schuler v Central Sydney Area Health Service [2009] NSWSC 523

Seaman v Seacor Marine L.L.C., 326 Fed Appx 721 (5th Cir, 2009)

See v Commissioner of Police [2017] NSWDC 6

Seltsam Pty Ltd v McGuinness (2000) 49 NSWLR 262; [2000] NSWCA 29

Sequenom, Inc v Ariosa Diagnostics, Inc [2019] FCA 1011

Sharif Zraika by his tutor Halima Zraika v Walsh [2014] NSWSC 1774

Shaw v Amaca Pty Ltd and Anor [2008] NSWDDT 3

Shaw v BHP Billiton Ltd [2015] SADC 3

Sheridan v NGK Metals Corp 609 F 3d 239 (3rd Cir, 2010)

Shyface v Secretary of HHS 165 F 3d 1344 (Fed Cir, 1999)

Sienkiewicz v Greif (UK) Ltd [2011] UKSC 10

Simanski v Secretary of HHS 115 Fed Cl 407 (2014) *aff'd*, 601 Fed Appx 982 (Fed Cir, Feb 26, 2015)

Simbolon v North Memorial Health Care, No 27-CV-09-19205 (D Minn, 18 August 2010)

Sinclair v Resi Corporation and Anor [2003] NSWDDT 1

Sindell v Abbott Laboratories (1980) 26 Cal 3d 593

Sindell v Abbott Laboratories (1980) 607 P 2d 924 (Cal, 1980)

Smith v Commonwealth of Australia (No 2) [2020] FCA 837

Smith v Leech Brain & Co. Ltd (1962) 2 QB 405

Snyder v Secretary of Department of HHS, 2009 WL 332044 (Fed Cl, Feb 12, 2009)

Snyder v Secretary of HHS 553 Fed Appx 994, 996 (Fed Cl, Jan 28, 2014

Soldo v Sandoz Pharmaceuticals Corp 244 F Supp 2d 434 (WD Pa, 2003)

South Australia v Ellis (2008) 37 WAR 1

Stanley v City of Philadelphia 69 Pa D & C 4th 63 (Ct CP, 2004)

Sterling v Velsicol Chemical Corporation 647 F Supp 303 (WD Tenn, 1986)

Stone & Rolls Ltd (in liq) v Moore Stephens (a firm) (2009) 3 WLR 455

Strong v Woolworths (2012) 246 CLR 182

Stubbs v City of Rochester, 134 NE 137 (NY, 1919)

Sucher v Secretary of HHS 2010 WL 1370627 (Fed Cl, Mar 15, 2010)

Summers v Certainteed Corp., 886 A 2d 240 (Pa Super, 2005)

Summers v Tice (1948) 33 Cal 2d 80

Sutera v Perrier Group of America Inc 986 F Supp 655 (D Mass, 1997)

Tabet v Gett (2010) 240 CLR 537

Tamraz v Lincoln Electric Company 620 F 3d 665 (6th Cir, 2010)

Telstra Corporation Ltd v Pine Rivers Shire Council [2001] QPELR 350

Tetro v Town of Stratford 458 A 2d 5 (Conn, 1983)

Tindall v American Furniture Co 306 4 SE 2d 894 (NC, 1939)

Tobacco Institute of Australia Ltd v Australian Federation of Consumer Organisations Inc (1992) 111 ALR 61

Tompkin v American Tobacco WL 36113663 (ND, Ohio 2001)

Tompkin v Philip Morris USA, Inc 362 F 3d 882 (6th Cir, 2004)

Trainer v Secretary of HHS 2013 WL 4505803 (Fed Cl, July 24, 2013)

Travel Compensation Fund v Robert Tambree t/as R Tambree and Associates [2005] HCA 69

Tudor Capital Australia Pty Limited v Christensen [2017] NSWCA 260

Tuite v The Queen (2015) 49 VR 196

United States v Fatico, 458 F Supp 388 (EDNY, 1968)

United States v Schipani, 289 F Supp 43 (EDNY, 1968), *aff'd,* 414 F 2d 1262 (2nd Cir, 1969)

Van Soest v BHP Billiton Limited [2013] SADC 81

Village of Buffalo Grove v Board of Trustees of the Buffalo Grove Firefighters' Pension Fund 141 NE 3d 1200 (Ill Appell Ct, Jan 17, 2020)

Vyner v Waldenberg Brothers Ltd [1946] KB 50

Wade-Greaux v Whitehall Laboratories 874 F Supp 1441, 1456-57 (VI, 1994), *aff'd* 46 F 3d 1120 (3rd Cir, 1994)

Wallace v Kam (2013) 250 CLR 375

Walsh v BASF Corp 191 A 3d 838 (Pa Super Ct, 2018)

Walsh v BASF Corp 234 A 3d 446 (Pa, 2020)

Waters v Secretary of HHS 2014 WL 300936 (Fed Cl, Jan 7, 2014)

Webb and Repatriation Commission [2001] AATA 633

Wells by his tutor McGuffog v Hunter New England Local Health District [2018] NSWSC 1877

Wells v Shell Oil Co (DCE Texas, Jury verdict March 2, 1998)

Wendell v GlaxoSmithKline LLC, 858 F 3d 1227 (9th Cir, 2017)

Westberry v Gislaved Gummi AB, 178 F 3d 257 (4th Cir, 1999)

White Constructions Pty Ltd v PBS Holdings Pty Ltd [2019] NSWSC 1166

Wilcox v Homestake Mining Co 619 F 3d 1165 (10th Cir, 2010)

Wintz v Northrop Corp 110 F 3d 508 (7th Cir, 1997)

Wojcik v General Carrying Pty Ltd [2021] VSC 233

Wood v R (2012) 84 NSWLR 581

Woolworths Ltd v Strong [2010] NSWCA 282

Wright v Willamette Industries, Inc., 91 F 3d 1105 (8th Cir, 1996)

X County Council v A Mother, A Father, Y, Z (Acting through their Children's Guardian) [2013] EWHC 953

X v Sydney Children's Hospitals Specialty Network & Anor (No 4) [2011] NSWSC 1310

Young v Burton 567 F Supp 2d 121 (DDC, 2008)

Young v United States, 2015 WL 5823025, 311 FRD 117 (D NJ, 2015)

Zandi v Wyeth a/k/a Wyeth, Inc., No 27-CV-06-6744, 2007 WL 3224242 (Minn Dist Ct, Oct 15, 2007)

Zeller v Secretary of HHS 2008 WL 3845155 (Fed Cl, July 30, 2008)

Zuchowicz v United States 140 F 3d 381 (2nd Cir, 1998)

9.3. Legislation

Affordable Care Act 42 USC §§ 18001–18122 (2018)

California Code of Civil Procedure

California Evidence Code (St Paul, West Publishing Co, 2010)

Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§300aa-1-300aa-34

Civil Law (Wrongs) Act 2002 (ACT)

Civil Liability Act 1936 (SA)

Civil Liability Act 2002 (Tas)

Civil Liability Act 2002 (NSW)

Civil Liability Act 2003 (Qld)

Civil Procedure Act 2005 (NSW)

Civil Procedure Rules 1998 (UK)

Court Procedures Rules 2006 (ACT)

Disability Discrimination Act 1992 (Cth)

Disability Discrimination and Other Human Rights Legislation Amendment Act 2009 (Cth)

Dust Diseases Tribunal Act 1989 (NSW)

Evidence (National Uniform Legislation) Act 2011 (NT)

Evidence Act 1995 (Cth)

Evidence Act 2001 (Tas)

Evidence Act 2004 (NI)

Evidence Act 2008 (Vic)

Evidence Act 2011 (ACT)

Federal Court Act 1976 (Cth)

Federal Court Rules 2011 (Cth)

Federal Justice System Amendment (Efficiency Measures) Act (No. 1) 2009 (Cth)

Federal Rules of Civil Procedure (US)

Federal Rules of Evidence 1975 (US)

General Data Protection Regulation 2016

Genetic Information Nondiscrimination Act of 2008 Pub L No 110-233, 122 Stat. 881 (May 21, 2008), 42 USC § 2000ff (2018)

Health Insurance Portability and Accountability Act (HIPAA) 42 USC §§ 300gg-300gg-2 (2018), 45 CFR pts. 160, 162, 164 (2018)

Human Tissue Act 1983 (NSW)

Illinois Supreme Court Rules

Patents Act 1990 (Cth)

Privacy Act 1988 (Cth)

Supreme Court (General Civil Procedure) Rules 2005 (Vic)

Supreme Court (General Civil Procedure) Rules 2005 (Vic)

Supreme Court Act 1935 (SA)

Supreme Court Act 1935 (WA)

Supreme Court Act 1979 (NT)

Supreme Court Act 1995 (Qld)

Supreme Court Rules 1987 (NT)

Supreme Court (General Civil Procedure) Rules 2005 (Vic)

Underwriting on the Basis of Test of Genetic Characteristics, 761 Cal Ins Code §§ 10146–9 (1994)

Uniform Civil Procedure Rules 1999 (Qld)

Uniform Civil Procedure Rules 2005 (NSW)

Uniform Civil Rules 2020 (SA)

Workers Compensation Act 1987 (NSW)

Wrongs Act 1958 (Vic)

9.4. Other

ArrayXpress, 'The Application of Genomic Technologies to Benzene Litigation' (White Paper, ArrayXpress, 4 December 2014)

ArrayXpress, 'Next Generation Sequencing in Toxic Tort Litigation' (White Paper, ArrayXpress, 4 December 2014)

Committee on Applications of Toxicogenomic Technologies to Predictive Toxicology and Risk Assessment, *Applications of Toxicogenomic Technologies to Predictive Toxicology and Risk Assessment* (National Academies Press, 2007)

Committee on Assessing Interactions among Social, Behavioral, and Genetic Factors in Health, *Genes, Behavior, and the Social Environment: Moving Beyond the Nature/Nurture Debate* (National Academies Press, 2006)

Committee on the Relationship Between Oral Contraceptives and Breast Cancer, Institute of Medicine: Division of Health Promotion and Disease Prevent, *Oral Contraceptives & Breast Cancer* (National Academies Press, 1991)

Commonwealth, *Parliamentary Debates*, House of Representatives, 3 December 2008, vol 12296 (Robert McClelland, Attorney-General)

Cooney, Elizabeth, 'On the Frontier of Genetic Technologies', *Harvard Medical School* (online, 19 November 2015) <https://hms.harvard.edu/news/frontier-genetic-technologies>

Edelman, James, 'Understanding Causation and Attribution of Responsibility' (Speech, Commercial Conference of the Supreme Court of Victoria/University of Melbourne, 7 September 2015)

Federal Court of Australia Practice Note CM 7, Expert witnesses in proceedings in the Federal Court of Australia, 4 June 2013

Federal Court of Australia Practice Note GPN-EXPT, Expert Evidence Practice Note, 25 October 2016

Federal Judicial Center, *Reference Manual on Scientific Evidence* (National Academy of Sciences, 2nd ed, 2000)

Federal Judicial Center, *Reference Manual on Scientific Evidence* (National Academy of Sciences, 3rd ed, 2011)

Financial Services Council, *FSC Standard No 11: Moratorium on Genetic Tests in Life Insurance* (at 21 June 2019)

Hals, Tom, 'Bayer to rethink Roundup in U.S. residential market after judge nixes $2 bln settlement' *Reuters* (online), 28 May 2021 <https://www.reuters.com/business/healthcare-

pharmaceuticals/us-judge-rejects-bayers-2-bln-deal-resolve-future-roundup-lawsuits-2021-05-26/>

Illinois Supreme Court Committee on Pattern Jury Instructions in Civil Cases, *Illinois Pattern Jury Instructions: Civil* (St Paul, West Publishing Co, 2006)

International Agency for Research on Cancer, *IARC Monographs on the Identification of Carcinogenic Hazards to Humans, Volumes 1-127*, 17 November 2020) <https://monographs.iarc.fr/agents-classified-by-the-iarc/>

Judicial Council of California, *Civil Jury Instructions* (LexisNexis, 2020) No 200

Judicial Council of California, 'Use and Cost of References in General Civil Cases: A Report to the California Legislature' (Report, August 2004)

Kwiatkowski, Carol, 'PFAS "forever chemicals" are widespread and threaten human health - here's a strategy for protecting the public' *The Conversation* (online), 9 October 2020 <https://theconversation.com/pfas-forever-chemicals-are-widespread-and-threaten-human-health-heres-a-strategy-for-protecting-the-public-142953>

National Health and Medical Research Council, *Use and Disclosure of Genetic Information to a Patient's Genetic Relatives under Section 95AA of the Privacy Act 1988 (Cth) - Guidelines for Health Practitioners in the Private Sector* (2014)

National Human Genome Research Institute, *GWAS Catalog: The NHGRI-EBI Catalog of human genome-wide association studies* <http://www.genome.gov/gwastudies>

New South Wales Law Reform Commission, 'Compensation to Relatives' (Consultation Paper No 14, May 2011)

New South Wales Workers Compensation (Dust Diseases) Board, 'Past and Future Incidence of Mesothelioma in Men in New South Wales' (Report, 2007)

Nobel Prize Outreach, *Press release: The Nobel Prize in Chemistry 2020* (7 October 2020) <https://www.nobelprize.org/prizes/chemistry/2020/press-release/>

Pollis, Andrew, 'What Oklahoma's Opioid Settlement Means for Other States, Cities and Counties Suing Purdue Pharma', *The Conversation* (online), 29 March 2019, <https://theconversation.com/what-oklahomas-opioid-settlement-means-for-other-states-cities-and-counties-suing-purdue-pharma-114469>

Review of the Law of Negligence (Final Report, September 2002) ('Ipp Report')

Romanuik, Eugene and Bruce Smith, 'Why Expert Conclaves Go So Wrong, So Badly and So Often', *Lawyers Weekly* (Online, 13 November 2015) <https://www.lawyersweekly.com.au/partner-features/17509-why-expert-conclaves-go-so-wrong-so-badly-and-so-often>

Safe Work Australia, 'Mesothelioma in Australia: Incidence 1982 to 2006, Mortality 1997 to 2007 ' (Report, May 2010)

Sand, LB, et al, *Modern Federal Jury Instructions* (LexisNexis, 2007)

Spector, Mike, and Dan Levine, 'Special Report: Inside J&J's secret plan to cap litigation payouts to cancer victims' *Reuters* (online), 5 February 2022 <https://www.reuters.com/business/healthcare-pharmaceuticals/inside-jjs-secret-plan-cap-litigation-payouts-cancer-victims-2022-02-04/>

Supreme Court of New South Wales, Practice Note SC CL 5: Supreme Court Common Law Division – General Case Management List, 29 January 2007

Supreme Court of New South Wales, Practice Note SC Gen 11: Joint Conferences of Expert Witnesses, 17 August 2005

'Text of the White House Statements on the Human Genome Project', *The New York Times* (online), 27 June 2000 <https://archive.nytimes.com/www.nytimes.com/library/national/science/062700sci-genome-text.html>

The Associated Press, 'Justice Breyer Calls for Experts To Aid Courts in Complex Cases', *The New York Times*, 17 February 1998 <https://www.nytimes.com/1998/02/17/us/justice-breyer-calls-for-experts-to-aid-courts-in-complex-cases.html>

ToxicoGenomica, 'The Litigator's Guide to Using Genomics in a Toxic Tort Case' (White Paper, ToxicoGenomica, 11 June 2018)

United States Congress, Office of Technology Assessment, Reproductive Health Hazards in the Workplace (1985)

United States Department of Veterans Affairs, *Agent Orange Settlement Fund*, 19 January 2018, <https://www.benefits.va.gov/compensation/claims-postservice-agent_orange-settlement-settlementFund.asp>

Weitzmann Institute, *GeneCards* (Web Page) <https://www.genecards.org/>

'What they said: Genome in quotes', *BBC News* (online), 26 June 2000 <http://news.bbc.co.uk/2/hi/science/nature/807126.stm>

World Health Organization, *WHO definitions of genetics and genomics* (Web Page) <https://www.who.int/genomics/geneticsVSgenomics/en/>