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Protecting Dignitary Interests of Biobank Research Participants: Lessons from *Havasupai Tribe v Arizona Board of Regents*

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I. INTRODUCTION

Since the explosion of research in human genetics some 40 years ago, legal and ethical experts have found it increasingly difficult to balance societal interests in the advancement of medical science with participants' interests, concerns and expectations. The landmark decision in *Moore v Regents of the University of California*[1]—which ruled that tissue donors do not possess property rights in their excised tissue—as well as widespread fears that genetic information may be used for insurance or employment discrimination, have put ownership and confidentiality issues at the forefront of the debate.[2] However, factors beyond the commonly anticipated risks must be taken into account when evaluating current tissue research practices, especially as we have entered a new era of research using large biobanks.

Recently, a lawsuit in which the Native American Havasupai tribe objected to research that had been done on their blood samples and to results that were stigmatising and disruptive to their self-understanding, has put the spotlight on a kind of harm that is frequently overlooked in current debates. The case under consideration, *Havas-*

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1 *Moore v Regents of the University of California*, 793 P 2d 479, 489–92 (Cal 1990) (holding that a patient whose cell line was patented without his permission had no cause of conversion because he did not retain a sufficient property interest in his cells once they were extracted from his body).

2 Ted T Ashburn, Sharon K Wilson and Barry I Eisenstein, 'Human Tissue Research in the Genomic Era of Medicine: Balancing Individual and Societal Interests' (2000) 160(22) *Archives of Internal Medicine* 3377, 3378–81. For an excellent overview of current biobank research issues, see Bernice Elger *et al* (eds), *Ethical Issues in Governing Biobanks: Global Perspectives* (Ashgate, 2008); Jane Kaye and Mark Stranger (eds), *Principles and Practice in Biobank Governance* (Ashgate, 2009). For some thought-provoking examples of biobank research that infringes on human dignity and autonomy, see Lori B Andrews and Dorothy Nelkin, *Body Bazaar: The Market for Human Tissue in the Biotechnology Age* (Crown, 2001); Donna L Dickenson, *Property in the Body: Feminist Perspectives* (Cambridge University Press, 2007).

upai Tribe v Arizona Board of Regents, reveals that biobank research can lead to so-called 'dignitary harms', which involve infringement on the autonomy, privacy or moral integrity of the research participants. In this article, we provide several illustrations of such harms and argue that they should be taken seriously and that both the regulatory and the legal framework should be revised to more adequately protect the interests of biobank research participants.

We begin with a discussion of the details of the Havasupai case, relying heavily on the so-called Hart Report.[3] Subsequently we provide some examples of 'non-obvious' tangible harms which may occur in the context of biobank research. This is followed by an investigation into the meaning, relevance and possible manifestations of (intangible) 'dignitary harm'. The next part of the paper considers the Code of Federal Regulations and identifies major flaws which are exposed by the Havasupai case. We proceed to show that biobank research participants seeking redress under present tort doctrine will be left without a remedy, because courts have not recognised a duty of special care outside the therapeutic setting and have not considered dignitary harms to be compensable injuries. In the final part of the paper we suggest two ways in which current tort doctrine could be modified to better protect the dignity of biobank research participants—one involving an expansion of existing remedies and the other concerning the development of a distinct dignitary tort. By way of conclusion, we summarise some of the main implications of the Havasupai case for present-day biobank research practices and the regulatory and legal frameworks that govern them.

II. BACKGROUND TO THE HAVASUPAI CASE

The Havasupai are a Native American tribe, inhabiting a vast (760 km²) reservation at the bottom of the Grand Canyon, Arizona. Today, the tribe counts about 650 members, nearly all living in or around the remote village of Supai.[4] Since the 1960s, the Havasupai have experienced a rapid increase in the incidence of type 2 diabetes.[5] Dozens of

3 As will be explained in more detail below, the Hart Report set out the investigative findings of attorneys Stephen Hart and Keith Sobraske, who were appointed by the Arizona Board of Regents to 'investigate the circumstances surrounding the collection of blood samples and other data from members of the Tribe and any and all subsequent uses of the data and the samples or their derivatives'. See Stephen Hart and Keith Sobraske, *Investigative Report Concerning the Medical Genetics Project at Havasupai* (23 December 2003), Investigative Assignment and Scope of Investigation, 4 http://cnhp.montana.edu/conference/HartReport.pdf.

4 Official website of the Havasupai Tribe, www.havasupai-nsn.gov/index.html.

5 The Havasupai tribe has the fourth highest prevalence of diabetes of any population in the world (46%), three times higher than the statistical average for Native Americans (16%) and more than six times higher than the statistical average for non-Hispanic whites (7%). It is one of the leading causes of death in Havasupai adults. See National Diabetes Information Clearinghouse, *National Diabetes Statistics* (NDIC 2011), http://diabetes.niddk.nih.gov/dm/pubs/statistics/DM_Statistics.pdf.

Havasupai diabetics have had their lower limbs amputated or have been forced to leave the canyon for dialysis.[6]

Because diabetes had such a devastating effect on their community, in July 1989 tribal leaders approached John Martin, an anthropology professor from Arizona State University (ASU), to look into its causes. After spending more than a year in Supai in the early 1960s and writing his PhD on the Havasupai, Martin had developed a strong relationship with them. He had written extensively on their customs and traditions and made a good academic career out of it.[7] Since the Havasupai, like other Native Americans, were deeply suspicious of exploitation by outsiders and considered their bodies to be sacred, the special trust placed in Martin proved crucial to overcoming the reluctance of tribe members to participate in the project.[8]

Martin suspected that the diabetes epidemic was related to genetics and diet, and he contacted genetics professor Therese Ann Markow and nutrition professor Linda Vaughan, both from ASU. Markow was not an expert on diabetes. However, she was ASU's only human geneticist at the time and a rising star, known for her success in winning research grants. Whilst approached to study diabetes, Markow was interested in the prospect of studying the high incidence of schizophrenia that the Havasupai allegedly also suffered from. She would later claim that Martin had lured her into the diabetes project by mentioning that the incidence of schizophrenia was seven times higher than normal and that he could provide her with genealogical and demographic reports dating from 1896.[9] During the preparatory meetings, Markow expressed a desire to include schizophrenia, but was told by Martin that the Havasupai would be unlikely to be interested, at least at this point. However, Markow almost immediately submitted an application to the National Alliance for Research on Schizophrenia and Depression for a grant to study schizophrenia among the Havasupai.[10]

Markow, Martin and Vaughan designed a diabetes project that they proposed at a meeting of the Havasupai Tribal Council in March 1990: an educational pilot program (for which funding had already been obtained); a summer school at ASU for about 10 Havasupai women, educating them about diabetes and the role of good nutrition in prevention; collection and analysis of blood samples to identify individuals susceptible to the disease; and tests to determine whether there was a clear genetic cause.[11]

6 Amy Harmon, 'Indian Tribe Wins Fight to Limit Research of Its DNA', *New York Times* (22 April 2010), A1.

7 Hart and Sobraske (n 3) Witness Interview Summaries, 153–4.

8 According to his assistant Daniel Benyshek, John Martin was the 'only reason why the project worked at all'. Because he had developed a lot of trust, 'over the course of many informal talks, community and Council meetings, Martin was able to engender unusually high support for the project'. *Ibid*, 26.

9 *Ibid*, 8, 132, 168. See also Paul Rubin, 'Indian Givers', *Phoenix New Times* (27 May 2004), www.phoenixnewtimes.com/2004–05–27/news/indian-givers.

10 She had understood that, as a small, genetically isolated population, the Havasupai would offer her a unique chance to discover rare gene variants.

11 Hart and Sobraske (n 3) Witness Interview Summaries, 27–28, 158–9, 218–19. Recently, a link had been reported between a genetic variant and the high rate of type 2 diabetes among the Pima, a Native American tribe from Arizona. See Robert C Williams *et al*, 'HLA-A2 and Type 2 (Insulin Independent) Diabetes Mellitus in Pima Indians: An Association of Allele Frequency with Age' (1981) 21(5) *Diabetologia* 460.

In May 1990, after careful deliberation, the Havasupai Tribal Chair wrote to Martin to confirm that the diabetes project could proceed. However, Markow had already obtained funding for the schizophrenia research, without informing the Havasupai.[12]

In June 1990, before funding was obtained for the diabetes study, blood draws started on more than 100 Havasupai. Except for Markow and Kevin Zuerlein, the young psychiatrist she had appointed to coordinate the draws, all parties concerned were convinced that they were participating only in diabetes research. The first series of blood draws was in fact paid for with money from the schizophrenia grant.[13] Moreover, Zuerlein was instructed to surreptitiously scan the medical files in the tribal clinic for records of psychiatric distress.[14] Markow insisted on securing a general informed consent from Havasupai blood donors. Surprisingly, Martin—who meanwhile had learned that Markow had obtained funding to study schizophrenia and claims to have told her again that the Havasupai simply would not be interested—was agreeable to this.[15]

The consent form was kept deliberately vague, stating that the purpose of the project was to 'study the causes of behavioral/medical disorders'.[16] However, in all dealings with the tribe, only diabetes research was mentioned and individual donors were convinced that research would be limited to this topic.[17] The ASU Institutional Review Board approved Markow's schizophrenia study in January 1991 and her diabetes study in March 1991, months after work on these projects had begun.[18]

In July 1991, a second series of blood draws was initiated, which proceeded intermittently until the summer of 1994 and involved an additional 130 members of the Havasupai.[19] According to Daniel Benyshek, an assistant of Martin who coordinated these blood draws, no written informed consent was sought.[20] He would later claim to have been advised by Charlotte Beauty, the Havasupai nurse performing the blood draws, that the written consent documents would confuse the tribal members and that

12 Hart and Sobraske (n 3) Investigative Findings, 23–24.

13 *Ibid*, 45.

14 Hart and Sobraske (n 3) Witness Interview Summaries, 239.

15 *Ibid*, 155.

16 Hart and Sobraske (n 3) Investigative Findings, 58.

17 *Ibid*, 50–52.

18 *Ibid*, 24.

19 According to Benyshek's records, more than a third of tribe members donated blood specimens. The Hart Report could only ascertain 208 Havasupai blood donors. See Hart and Sobraske (n 3) Witness Interview Summaries, 25, 30, 175; Investigative Findings, 2.

20 Hart and Sobraske (n 3) Witness Interview Summaries, 31, 35. When confronted with Benyshek's statement, Markow reacted in a curious way. She indicated that he had obtained written consent forms from every participant but that she had lost the file containing them when she moved from ASU to the University of Arizona (UA) in the mid-1990s. However, in the same interview she said that she was surprised when she learned that Benyshek had not obtained signed consents and that she felt that he must have been aware of the need to secure them. *Ibid*, 139. None of the researchers working on the genetics project could remember ever having seen signed consent documents pertaining to the second series of blood draws. *Ibid*, 19, 63, 76, 179, 202–3.

providing purely oral information would be more convincing. The information Benyshek provided to the tribal members focused only on diabetes and emphasised that, with a view to better treatment and prevention, blood samples would be analysed in order to understand how diabetes passed from one generation to another.

Soon after it started, the diabetes-genetic study was put on the backburner. Analysis of the blood samples and the medical files of the Indian Health Service clinic in Supai had shown that the Havasupai indeed had an extremely high incidence of type 2 diabetes, affecting 38 per cent of men and 55 per cent of women over the age of 35. However, the ASU researchers concluded that the incidence of diabetes had risen too quickly to be related to genetics.[21] With hopes of finding an answer seemingly lost, the genetic diabetes research was essentially abandoned without the tribe members being informed about the conclusions that were reached. Martin, Vaughan and Benyshek instead concentrated on nutritional factors, suggesting that the high-fat, sugar-laden diet of the Havasupai contributed to childhood obesity and the onset of type 2 diabetes.[22]

After the research on genetic markers for diabetes ended in 1991, Markow and her collaborators continued to conduct research on samples from and data regarding tribal members. Over the following years, a good deal of research was conducted in Markow's main field of interest, schizophrenia. Beginning in September 1991, her doctoral assistant, Christopher Armstrong, analysed the Havasupai blood samples, hoping to find a genetic variation that could be associated with the development of schizophrenia. However, while Armstrong claimed to have found a genetic variation that could be relevant, he was unable to link this finding with the incidence of schizophrenia among the Havasupai.[23] Moreover, the medical files that Zuerlein had reviewed in the Havasupai clinic did not reveal unusual levels of psychiatric distress.

Apart from the schizophrenia study, Havasupai data were also used to conduct research regarding two other topics that the tribe members had not validly consented to. In 1993, a paper was published by Markow and Martin reporting that indicators of inbreeding among the Havasupai were among the highest reported for any group.[24] The inbreeding study involved 36 Havasupai handprints that were collected by Benyshek

21 Kevin Zuerlein, John F Martin, Linda Vaughan and Therese A Markow, 'NIDDM: Basic Research Plus Education' (1991) 338(8777) *Lancet* 1271.

22 Linda A Vaughan, Daniel C Benyshek and John F Martin, 'Food Acquisition Habits, Nutrient Intakes, and Anthropometric Data of Havasupai Adults' (1997) 97(11) *Journal of the American Dietetic Association* 1275; Daniel C Benyshek, John F Martin and Carol S Johnston, 'A Reconsideration of the Origins of the Type 2 Diabetes Epidemic among Native Americans and the Implications for Intervention Policy' (2001) 20(1) *Medical Anthropology* 25; Daniel C Benyshek, 'The Nutritional History of the Havasupai Indians of Northern Arizona: Dietary Change and Inadequacy in the Reservation Era and Possible Implications for Current Health' (2003) 26(1–2) *Nutritional Anthropology* 1.

23 Hart and Sobraske (n 3) Witness Interview Summaries, 11. Sixty-nine tribal blood samples were used in the context of Armstrong's PhD research on the general etiology of schizophrenia. *Ibid*, 140, 242.

24 Therese A Markow and John F Martin, 'Inbreeding and Developmental Stability in a Small Human Population' (1993) 20(4) *Annals of Human Biology* 389.

during the second series of blood draws. As with the blood draws, no informed consent was obtained. Rather unconvincingly, Martin later suggested that inbreeding research could yield important insights into developmental instability patterns that might play a role in diabetes.[25]

Until 1993–4, the genetic research on the Havasupai focused exclusively on behavioural and medical disorders. Although, diabetes aside, the ASU researchers' communications with the Havasupai tribe members were too misleading for their consent to be truly informed, this kind of research still fell under the scope of the project described in the *written* consent document signed by the participants in the first series of blood draws. However, that was no longer the case when, a few years later, the focus changed to population migration. After Markow had moved from ASU to the University of Arizona (UA) and had taken the Havasupai blood samples with her, she provided samples to UA researchers with a keen interest in ancient population migration theory.[26] The samples were analysed to trace the origins of the tribe by comparing DNA of its members with that of other groups. By showing that it was probable that the Havasupai's ancestors had reached America by crossing the Bering Straits, conclusions were reached that were inconsistent with the beliefs of most Havasupai tribal members.[27] For this use of the samples, no permission was sought from the tribe or from any Institutional Review Board.

Markow also sent some of the blood samples to researchers from other universities, despite the fact that the written consent form had stipulated that no information on the Havasupai would leave ASU. When later confronted about this, she insisted that, since those samples were coded and individual donors could not be identified, no information had left ASU.[28]

Apart from Armstrong, none of the researchers involved seemed to have any moral qualms about the ways the Havasupai samples and data were used and whether these uses were authorised. On numerous occasions in 1996 and 1997, Armstrong commu-

25 Hart and Sobraske (n 3) Witness Interview Summaries, 152.

26 *Ibid*, 144–5.

27 In 1997, UA researchers published a paper concerning 10 Havasupai samples; this paper supported the hypothesis of a single wave of migration into the New World instead of the three-wave migration model that was dominant at the time. See Tatiana M Karafet *et al*, 'Y Chromosome Markers and Trans-Bering Strait Dispersals' (1997) 102(3) *American Journal of Physical Anthropology* 301. In 1999, another paper was published concerning the same samples; this paper supported the possibility of two waves of migration. See Tatiana M Karafet *et al*, 'Ancestral Asian Source(s) of New World Y-Chromosome Founder Haplotypes' (1999) 64(3) *American Journal of Human Genetics* 817. Finally, in 2004, the same research team published a paper in which no use was made of Havasupai samples; this paper suggested one wave of migration occurring no more than 17,000 years ago. See Stephen L Zegura, Tatiana M Karafet, Lev A Zhivotovsky and Michael M Hammer, 'High-Resolution SNPs and Microsatellite Haplotypes Point to a Single, Recent Entry of Native American Y Chromosomes into the Americas' (2004) 21(1) *Molecular Biology and Evolution* 164. However, despite a vast body of research, considerable disagreement remains within the research community as to the number and timing of the early migration waves into the Americas.

28 Hart and Sobraske (n 3) Witness Interview Summaries, 138. The researchers concerned all confirmed that the samples they received did have a code system with identification numbers and that they had no access to any names or pedigree information. *Ibid*, 67, 90, 126, 194.

nicated to Markow that she was guilty of research misconduct. He also notified ASU officials.[29] However, although Armstrong was rebuked by ASU's lawyer for having made 'serious and defamatory allegations' against Markow, no further action was taken by ASU until March 2003, when, invited by Martin, a tribal leader attended a PhD defence in ASU concerning diabetes-related research on Havasupai blood samples but also mentioning the population migration research.[30] Shocked by this, the Havasupai issued a 'banishment order' to forbid ASU employees from setting foot on their reservation. ASU's President was informed about the Havasupai complaints and was asked to make reparations, but did not react until it came to his attention that the tribe intended to hold a press conference to publicise the matter.[31] ASU then suggested to the tribe that a jointly selected independent investigator be appointed to investigate what had happened. The tribe accepted and signed a Joint Confidentiality and Cooperative Investigation Agreement with ASU. However, because ASU unilaterally selected Phoenix attorneys Stephen Hart and Keith Sobraske to perform the investigation, the Havasupai declined to lift their banishment order. As a result, Hart and Sobraske had to rely exclusively on interviews with 34 academics and officials from ASU and elsewhere.[32]

In December 2003, Hart and Sobraske issued their final report, finding no firm evidence of research misconduct but listing important issues concerning the administration of the project and especially the scope of the consent.[33] The report uncovered numerous studies and projects carried out at various universities and laboratories throughout the United States, resulting in at least 23 scholarly articles and dissertations involving Havasupai blood samples. Only eight of these publications dealt with diabetes, whereas the others focused on schizophrenia, inbreeding and population migration.[34] The Hart Report also revealed that the principal researchers held contradictory views on the nature of their original project. According to Martin and Vaughan, the project was only about diabetes, notwithstanding the fact that the informed consent form referred more generally to 'behavioral/medical disorders'. Markow, on the other hand, maintained that the project included the study of any medical or behavioural disorder. She considered that pressing medical problems that Martin had told her about, such as schizophrenia, fell under the umbrella of the project and that the informed consent form was formulated to encompass all diseases affecting the Havasupai tribe.[35]

29 *Ibid*, 15–16, Investigative Findings, 28–29.

30 In response to a request by Martin, the chapter mentioning the Havasupai was removed from the dissertation and an article based on this chapter was withdrawn prior to publication. See Hart and Sobraske (n 3) Witness Interview Summaries, 85, 102.

31 *Havasupai Tribe v Arizona Board of Regents*, 204 P 3d 1063, 1067 (Ariz Ct App 2008).

32 Hart and Sobraske (n 3) Investigative Findings, 4, 49.

33 *Ibid*, 2–3.

34 *Ibid*, 70–145. See also Larry Hendricks, 'Havasupai Tribe Files $50M Suit against ASU', *Arizona Daily Sun* (16 April 2004), www.ipcb.org/issues/human_genetics/htmls/havasupai.html.

35 Hart and Sobraske (n 3) Investigative Findings, 58–59, 83, 117–18, Witness Interview Summaries, 132, 136–7, 155.

The Havasupai were very upset to learn how their blood samples had been handled by ASU researchers—particularly how they had been used for unauthorised studies with potentially extremely undesirable effects on their community.[36] The Havasupai objected to the schizophrenia research, claiming that it could stigmatise their tribe. They were offended by the inbreeding paper, because apart from stigmatisation it caused major concern based on their cultural belief that inbreeding brings harm to one's family. Further, they were shocked by the population migration study, because its conclusions contradicted their belief that they had originated in the Havasu canyon and were assigned to be its guardian.[37]

The Havasupai filed several notice-of-claim letters. They contended that the improper use of their blood samples had invaded both their personal privacy and the 'cultural and religious privacy' of the tribe, and had caused them severe harm, extreme distress and emotional trauma. In addition, they claimed that this misconduct had resulted in a growing mistrust of medical care, because many tribe members now feared going to the health clinic, seeking medical attention, and providing blood samples for medical diagnosis or treatment.[38]

When no settlement was reached, two separate lawsuits were filed in February and March 2004, one by 52 tribe members who had participated in the blood draws and the other by the Havasupai tribe, on its own behalf and *in parens patriae*. These lawsuits were directed at the Arizona Board of Regents (ABOR), the governing body of Arizona's public university system supervising ASU and UA, and at Markow, Martin and Benyshek. The plaintiffs requested a halt to all use and transfer of the blood samples, genealogy information and handprints, the prevention of any further publication or sharing of that information, and the return of all remaining samples. Claims were filed alleging breach of fiduciary duty, lack of informed consent, fraud and misrepresentation, fraudulent concealment, intentional infliction of emotional distress, negligent infliction of emotional distress, conversion, violation of civil rights, negligence, negligence per se, and gross negligence, for a total of $60 million in damages.[39] A long procedural battle ensued, ending before the Court of Appeals of the State of Arizona in November 2008, when it became clear that the substantive case would have to be heard in court unless a settlement was reached.[40] In April 2010, after more than six years of legal battle and $1.7 million spent by ABOR on legal costs, a settlement was indeed reached. ABOR agreed to pay the plaintiffs $700,000 and to return all remaining blood samples as well as docu-

36 Havasupai blood donors were appalled to learn that many of their blood lines had died during a freezer malfunction due to negligent maintenance. See Hart and Sobraske (n 3) Witness Interview Summaries, 11–12, 145–6.

37 Harmon (n 6).

38 *Tilousi v Arizona Board of Regents*, 2007 WL 4934760 (Ariz App Div 1), No 1 CA-CV07-0801, Plaintiffs-appellants' opening brief, 7–8, 21, appendix 1.

39 *Ibid*, appendix 1–4; *Havasupai Tribe* (n 31) 1068–70.

40 *Havasupai Tribe* (n 31) 1081.

ments containing research derived from the blood samples. In addition, ABOR initiated a five-year collaborative project in the areas of education, clinical care and tourism.[41]

The importance of the Havasupai case cannot easily be overstated. By way of *obiter dictum* from the Arizona Court of Appeals, the fact that 'dignitary interests' must be taken into account when evaluating biobank research was for the first time explicitly acknowledged in this case. Indeed, research participants may have interests that go beyond the safety and confidentiality considerations that most often dominate the ethical and regulatory debates. The next section discusses a few examples of 'non-obvious' (and hence easily overlooked) tangible harm. This is followed by an overview of (intangible) 'dignitary' harms that may occur. We provide illustrations from the Havasupai and other cases and explain why such harms need to be taken seriously.

III. 'NON-OBVIOUS' TANGIBLE HARMS

Discussions of the ethical and legal issues in biobank research frequently only consider potential harms of a physical or informational nature to be relevant. The risk of physical harm is usually regarded as minimal. As regards the risk of informational harm, it is indeed true that inappropriately disclosed personal health information that derives from biobank samples may expose sample providers to insurance or employment discrimination and hence to economic harm.[42] However, the actual extent of this kind of discrimination remains a matter of speculation, especially after the Genetic Informa-

41 Communication by the Arizona Board of Regents, https://azregents.asu.edu/palac/newsreleases/Havasupai-ABOR-Lawsuit.htm.

42 In *Norman-Bloodsaw v Lawrence Berkeley Lab*, 135 F 3d 1260, 1267, 1275 (9th Cir 1998), seven (former) administrative and clerical employees filed suit against their employer for violating their right to privacy because employment was conditioned on mandatory preplacement examinations involving non-consented-to genetic testing for syphilis, sickle cell traits and pregnancy. The Court of Appeals stated that 'it goes without saying that the *most basic* violation possible involves the performance of unauthorized tests' and ruled that the District Court erred in dismissing the plaintiffs' privacy claims. In *Equal Employment Opportunity Commission v Burlington Northern and Santa Fe Railway Company*, Civ No 01-4013 (ND Iowa 2001), the Equal Employment Opportunity Commission filed a petition alleging a violation of the Americans with Disabilities Act in relation to the employer's request that employees who developed carpal tunnel syndrome undergo physical examinations involving non-consented-to genetic testing to identify a genetic defect allegedly predisposing individuals to this type of condition. Before the case was heard, the defendant announced that it would cease its genetic testing program and a settlement agreement was reached. See Press Release, Equal Employment Opportunity Commission, 'EEOC Settles ADA Suit against BSNF for Genetic Basis' (18 April 2001), www.eeoc.gov/eeoc/newsroom/release/4–18–01.cfm. For further background, see Patricia A Roche, 'The Genetic Revolution at Work: Legislative Efforts to Protect Employees' (2002) 28(2–3) *American Journal of Law and Medicine* 271; Ashley M Ellis, 'Genetic Justice: Discrimination by Employers and Insurance Companies Based on Predictive Genetic Information' (2003) 34(4) *Texas Tech Law Review* 1071; Kimberly G Fulda and Kristine Lykens, 'Ethical Issues in Predictive Genetic Testing: A Public Health Perspective' (2006) 32(3) *Journal of Medical Ethics* 143; Louise M Slaughter, 'Genetic Testing and Discrimination: How Private Is Your Information?' (2006) 17(1) *Stanford Law & Policy Review* 67.

tion Non-Discrimination Act came into effect.[43] Moreover, an exclusive focus on these types of harm may push other risks out of sight. For instance, while the possibility of physical harm arising from biobank research is usually rejected out of hand, it is quite conceivable that research participants could suffer *indirect physical harm* when they are exploited, and consequently lose their trust in the medical profession. The Havasupai case is an appropriate example, because, as was emphasised during the proceedings, the improper use of their samples left many blood donors afraid of going to the health clinic, seeking medical attention, and providing further blood samples for medical diagnosis or treatment.[44]

Yet other tangible harms may arise—even harms affecting a whole community—from certain forms of research. In the case of Native American tribes that enjoy extensive sovereignty, being labelled with a stigmatising condition could result in downgrading the community's bond rating, making it more difficult to obtain financing.[45]

Another concern, which was explicitly voiced by one of the Havasupai leaders, is that legal entitlements might be threatened when, as was the case with the population migration study, genetic tests reveal that the tribe did not originate in its current location.[46]

IV. DIGNITARY HARM

The Concept of Dignitary Harm

Apart from the abovementioned 'non-obvious' but potentially formidable tangible harms, biobank research can also lead to severe *intangible* harms. Our focus here is on

43 See Allen Buchanan, 'An Ethical Framework for Biological Samples Policy' in National Bioethics Advisory Commission (ed), *Research Involving Human Biological Materials: Ethical Issues and Policy Guidance*, vol 2 (NBAC, 2000) B1, B6; Henry T Greely, 'Genotype Discrimination: The Complex Case for Some Legislative Protection' (2001) 149(5) *University of Pennsylvania Law Review* 1483, 1490; Jeffrey S Morrow, 'Insuring Fairness: The Popular Creation of Genetic Antidiscrimination' (2009) 98 *Georgetown Law Journal* 215, 225. The Genetic Information Non-Discrimination Act (Pub L 110-233, 122 Stat 881), prohibiting health insurance and employment discrimination on the basis of genetic information, was signed into law by President Bush on 21 May 2008 and came into effect on 21 May 2009 (for health insurance companies) and 21 November 2009 (for employers): www.gpo.gov/fdsys/pkg/PLAW–110publ233/pdf/PLAW–110publ233.pdf.

44 *Havasupai Tribe* (n 31) 1069.

45 In 1979, findings of a research study examining the alcohol intake of the Inupiaq residents of Barrow were misinterpreted by reporters as showing that they were irresponsible alcoholics. As a result, the Inupiaq community's bond rating was reduced and funding for key projects denied. See EF Foulks, 'Misalliances in the Barrow Alcohol Study' (1989) 2(3) *American Indian and Native Alaska Mental Health Research* 18; Carol E Kaufman and Saumya Ramarao, 'Community Confidentiality, Consent, and the Individual Research Process: Implications for Demographic Research' (2005) 24(2) *Population Research and Policy Review* 149, 155.

46 Harmon (n 6); JL McGregor, 'Population Genomics and Research Ethics with Socially Identifiable Groups' (2007) 35(3) *Journal of Law, Medicine and Ethics* 356, 363.

so-called 'dignitary harms'. In the context of the topic of this paper, these are at issue when research participants are not respected as persons but are denied respect for their humanity and used merely for the ends of others. Irrespective of other, palpable negative effects that may result from biobank research, these harms arise from the fact that participants were not treated with the dignity and respect they deserve.[47] More specifically, dignitary harms involve infringement on the autonomy, privacy and moral integrity of research participants. As persons, they have an inalienable right to decide for themselves and to act upon their decisions without outside interference; they are entitled to a personal sphere free from public attention and intrusion; and they deserve respect for who they are and for the values, preferences and commitments they subscribe to.

Why Should We Care about Dignitary Harms?

As has been forcefully argued by bioethicist Julian Savulescu with regard to the use of leftover body material for research purposes:

> Each mature person should be the author of his or her own life. Each person has values, plans, aspirations, and feelings about how that life should go. People have values which may collide with research goals … To ask a person's permission to do something to that person is to involve her actively and to give her the opportunity to make the project a part of her plans. When we involve people in our projects without their consent we use them as a means to our own ends.[48]

Even when research participants have consented to their samples being used in certain specified ways, a situation may arise where these samples are used for a purpose that was only ambiguously defined in the original consent form, and donors who did not realise the full implications of their consent should still be allowed to stop uses of their samples to which they object. This right can be illustrated with an example given by Søren Holm regarding the rights of donors of stem cell lines:

> Let us imagine that a stem cell line derived from an embryo I have donated can develop into a kind of tissue called bronchial epithelia, and let us assume further that I have consented to 'any research or medical use.' The tissue has no specific therapeutic value but it is very useful for toxicological testing of inhaled substances. It therefore becomes the de facto standard in pulmonary toxicology screening and is produced and sold in large quantities. I discover that although the pharmaceutical industry is a major user of this tissue, the largest users are Phil-

47 See Dan B Dobbs, *Law of Remedies: Damages, Equity, Restitution* (West, 2nd edn 1996) 623 ('[D]ignitary harms may cause economic harm as well as affront to personality. If so, economic damages may be recovered. However, in a great many … cases, the only harm is the affront to the plaintiff's dignity as a human being, the damage to his self-image, and the resulting mental distress').

48 Julian Savulescu, 'For and Against: No Consent Should Be Needed for Using Leftover Body Material for Scientific Purposes—Against' (2000) 325(7365) *British Medical Journal* 648, 649. A similar opinion is voiced in Rosamond Rhodes, 'Rethinking Research Ethics' (2005) 5(1) *American Journal of Bioethics* 7, 16–17.

> lip Morris and British American Tobacco. Being strongly opposed to the immoral marketing tactics of the tobacco industry, I feel aggrieved and want to stop their use of 'my' cell line. Are there any good reasons why I should not be allowed to do this?[49]

Moreover, having one's body material used for purposes one is morally opposed to may make one feel morally complicit. 'Moral complicity' refers to the idea that one can do wrong by being associated in some way with wrongdoing by others, for example by causally contributing to others' wrongdoing in a certain way or by increasing the likelihood of the wrongdoing occurring even without causing it in any way.[50] Allowing people to avoid moral complicity is an additional reason for avoiding dignitary harms in research.

The fact that dignitary harm usually cannot be proven (unlike, for example, physical harm) is not a convincing reason to disregard it. According to the majority opinion of the Arizona Court of Appeals in the Havasupai case:

> The allegations [made by the Havasupai] present information from which injury might be inferred, which injury is necessarily personal and subjective and difficult to quantify, and which injury need not be established with regard to dignitary torts because it is presumed.[51]

Especially in the case of so-called 'population isolates', the prospect of gaining novel insights into complex diseases may sometimes prove too hard to resist for researchers to give proper consideration to the interests and concerns of the target group. Consequently, research participants risk being treated merely as means for the pursuit of other people's ends and being used in research without benefiting from it.[52]

Potential Manifestations of Dignitary Harm

Sometimes dignitary harms manifest themselves as psychosocial harms, especially when information is released that is stigmatising or upsetting to the participants. In such cases, research participants run the risk of being regarded in a more negative way or even of suffering a loss of self-esteem, which may damage their relationships with others. Moreover, if research suggests a linkage between one ethnic group and the prevalence of

49 Søren Holm, 'Who Should Control the Use of Human Embryonic Stem Cell Lines? A Defence of the Donors' Ability to Control' (2006) 3(1–2) *Journal of Bioethical Inquiry* 55, 59.

50 For interesting readings on moral complicity, see Christopher Kutz, *Complicity: Ethics and Law for a Collective Age* (Cambridge University Press, 2000); Ronald M Green, 'Benefiting from "Evil": An Incipient Moral Problem in Human Stem Cell Research' (2002) 16(6) *Bioethics* 544; Helen Watt (ed), *Cooperation, Complicity & Conscience: Problems in Healthcare, Science, Law and Public Policy* (Linacre, 2006); John Gardner, 'Complicity and Causality' (2007) 1(2) *Criminal Law and Philosophy* 127.

51 As summarised in Judge Thomson's dissenting opinion: see *Havasupai Tribe* (n 31) 1081.

52 Ernest Wallwork, 'Ethical Analysis of Research Partnerships with Communities' (2008) 18(1) *Kennedy Institute of Ethics Journal* 57, 67. Even if the research in question concerns a condition that members of the studied group suffer from, there is no guarantee that the research will yield any benefit to them, because any product or intervention that is developed on the basis of the research may be inaccessible or unaffordable or even ineffective for them.

a psychiatric condition, or a socially unacceptable practice like inbreeding, individuals may suffer psychosocial harms simply by being members of that group.[53] In the Havasupai case, for instance, information gleaned from donated biological samples reinforced the racial stereotype that Native Americans are unusually susceptible to certain types of disease.

Perhaps even more detrimental than external stereotyping is the risk of cultural harm, which may eventually lead to community disruption.[54] Biobank research that undermines cultural and spiritual beliefs may indeed be devastating to the self-understanding of the community. In the Havasupai case, the self-representation of the group was severely disturbed in at least three ways. The schizophrenia study was based on the presumption that the alleged high incidence of schizophrenia may have originated with a tribal shaman living in the late nineteenth century, clearly suggesting that one of the most important historical spiritual leaders of the Havasupai was insane.[55] The inbreeding study, for its part, touched on a major taboo, because according to the cultural beliefs of the tribe this kind of behaviour brings misfortune to one's family.[56] But what really shook the community to its foundations was that the tribe's origin myth was discredited when the population migration study showed that the tribe had not originated in the Grand Canyon but had entered North America from Siberia. By upsetting the Havasupai's historical narrative, their sense of themselves and of their community was severely undermined, because their identity, spiritual traditions and way of life were founded upon it.[57]

Dignitary harm can also result from violations of trust. In the Havasupai case, despite promises that the blood samples would remain with the ASU researchers, the fact that the researchers sent samples to researchers at other institutions and that the latter researchers also published papers that stigmatised the Havasupai was disrespectful, as the ASU researchers violated the trust that tribe members had placed in them.

Further, biobank sample providers and their relatives may suffer dignitary harm if their cell lines are immortalised, patented or commercialised without their knowledge or approval,[58] or if samples that they invest with religious significance are tampered with,

53 Mats G Hanson, 'Balancing the Quality of Consent' (1998) 24(3) *Journal of Medical Ethics* 182, 185; Buchanan (n 43) B7; Robert F Weir, 'The Ongoing Debate About Stored Tissue Samples' in National Bioethics Advisory Commission (n 43) F1, F12–F13.

54 Rebecca Tsosie, 'Cultural Challenges to Biotechnology: Native American Genetic Resources and the Concept of Cultural Harm' (2007) 35(3) *Journal of Law, Medicine and Ethics* 396, 403.

55 Hart and Sobraske (n 3) Witness Interview Summaries, 8; Rex Dalton, 'When Two Tribes Go to War' (2004) 430(6999) *Nature* 500, 501.

56 Harmon (n 6).

57 Harmon (n 6); Rubin (n 9); Howard Fischer, 'Havasupai Blood Lawsuit Reinstated', *Azdailysun* (28 November 2008), http://azdailysun.com/news/article_2921c286–4454–57eb–926b–11e795134f8f.html; Leslie E Wolf, 'Advancing Research on Stored Biological Materials: Reconciling Law, Ethics, and Practice' (2010) 11(1) *Minnesota Journal of Law, Science and Technology* 99, 126.

58 As was the case with Henrietta Lacks and John Moore. On the case of Henrietta Lacks, see Rebecca Skloot, *The Immortal Life of Henrietta Lacks* (Crown, 2010); Gail Javitt, 'Why Not Take All of Me? Reflections on *The Immortal Life of Henrietta Lacks* and the Status of Participants in Research Using Human Specimens'

lost or not returned after the research is finished. In the Havasupai case, for instance, the tribal belief that blood continues to retain the essence of the individual and must be buried after death to let the spirits rest, explains the interest of the tribe in having the remaining blood samples returned.[59]

Important Lessons from the Havasupai Case

The Havasupai case seems to offer at least three valuable lessons for current biobank research practices. First, researchers need to ensure that they understand and fully consider the interests and concerns of their research participants. Admittedly, many research projects can lead to unforeseen results, meaning that the potential harms to participants are poorly understood before the research starts and hence may be underestimated, by both researchers and participants.[60] Likewise, investigators tend to anticipate only the types of harms that they consider they themselves might experience, and are unlikely to recognise unique kinds of harm that their research participants might experience.[61] Culturally specific harms may seem trivial or superstitious to researchers, and hence not worth acknowledging.[62] However, researchers have to take local cultural sensitivities seriously instead of relying only on their own judgment. After all, whether or not an investigator acknowledges the validity of a particular risk, it is up to the potential research participants to decide whether the research is justified according to their own values and principles. Respect for their autonomy requires that they may decide to participate in the light of their own values and beliefs, irrespective of the point of view or expectations of the researcher. The advancement of scientific knowledge (and cer-

(2010) 11(2) *Minnesota Journal of Law, Science and Technology* 713. On the Moore case, see Karen G Biagi, '*Moore v Regents of the University of California*: Patients, Property Rights, and Public Policy' (1991) 35(2) *St Louis University Law Journal* 433; Helen R Bergman, 'Case Comment: *Moore v Regents of the University of California*' (1992) 18(1–2) *American Journal of Law and Medicine* 127; Russell Korobkin, '"No Compensation" or "Pro Compensation": *Moore v Regents* and Default Rules for Human Tissue Donations' (2007) 40(1) *Journal of Health Law* 1; Patricia Roche, 'The Property/Privacy Conundrum over Human Tissue' (2010) 22(3) *HEC Forum* 197.

59 Michael Kiefer, 'Havasupai Tribe Ends Regents Lawsuit with Burial', *Arizona Republic* (22 April 2010), www.azcentral.com/arizonarepublic/local/articles/2010/04/22/20100422arizona-havasupai-tribe-regents-lawsuit.html. For information regarding a very similar case involving the Nuu-chah-nulth tribe of British Columbia, Canada, see Rex Dalton, 'Tribe Blasts "Exploitation" of Blood Samples' (2002) 420(6912) *Nature* 111; David Wiwchar, 'Nuu-chah-nulth Blood Returns to West Coast', *Ha-Shilth-sa* (16 December 2004), http://caj.ca/wp-content/uploads/2010/mediamag/awards2005/%28David%20Wiwchar,%20Sept.%2012,%202005%29Blood2.pdf.

60 Fred Beauvais, 'Obtaining Consent and Other Ethical Issues in the Conduct of Research in American Indian Communities' (1998) 14(1–2) *Drugs and Society* 167, 176–7; National Bioethics Advisory Commission (n 43) 55.

61 McGregor (n 46) 362–3.

62 In the Havasupai case, principal researcher Markow stated that it had not occurred to her that the research might have been upsetting to the tribe members. When confronted with allegations that her research project had resulted in severe harm, she called these claims 'hysterical'. See Hart and Sobraske (n 3) Witness Interview Summaries, 143. See also Fischer (n 57).

tainly of academic careers) is not so important that it should trump the interests of the research participants.[63]

Secondly, the Havasupai case exposes as an illusion the standard conviction that ethical issues disappear when samples are anonymised. There is considerable doubt as to whether anonymisation can truly be achieved, since DNA has greater identifying power than commonly thought.[64] *Even if* sample providers *cannot* be identified, though, it is incorrect to assume that they cannot be harmed.[65] Indeed, if samples are individually unidentifiable, research findings can still be connected to a specific community in case of research involving closed groups. Moreover, even if a sample could be made totally anonymous, research could still result in a dignitary harm if it conflicted with the moral values and beliefs of the sample provider.[66] As was clear from the Havasupai lawsuit, anonymising the samples would not have eliminated the objections of the donors.[67]

Finally, the example of the Havasupai shows that so much might be at stake for the participants that they should be allowed a right to withdraw consent and have their samples returned or destroyed. Only by withdrawing consent can they be enabled to call a halt to possible infringements on their dignity, and only by having their samples returned can they prevent further research that might be objectionable or—if religious significance is invested in the sample—restore the physical integrity of the tissue source.

V. LIMITATIONS OF FEDERAL REGULATIONS IN PREVENTING DIGNITARY HARMS IN BIOBANK RESEARCH

Apart from revealing that biobank research may lead to so-called dignitary harms that must be taken into account in evaluating research practices, the Havasupai case also exposes the limitations of current regulatory safeguards in preventing this kind of harm. More specifically, it reveals manifest flaws in the federal guidelines governing biobank

63 McGregor (n 46) 365. Clearly, there may be exceptional cases of overwhelming public health interests where the interests of individuals have to come second to those of the population as a whole, such as in the case of a serious epidemic.

64 Zhen Lin, Art B Owen and Russ B Altman, 'Genomic Research and Human Subject Privacy' (2004) 305(5681) *Science* 183; Dov Greenbaum, Jiang Du and Mark Gerstein, 'Genomic Anonymity: Have We Already Lost It?' (2008) 8(10) *American Journal of Bioethics* 71, 73; Amy L McGuire and Richard A Gibbs, 'No Longer De-Identified' (2006) 312(5772) *Science* 370, 371; William W Lowrance and Francis S Collins, 'Identifiability in Genomic Research' (2007) 317(5838) *Science* 600, 601; Matthias Wjst, 'Caught You: Threats to Confidentiality Due to the Public Release of Large-Scale Genetic Data Sets' (2010) 11 *BMC Medical Ethics* 21, 23.

65 National Bioethics Advisory Commission (n 43) 60–61.

66 MB Kapp, 'Ethical and Legal Issues in Research Involving Human Subjects: Do You Want a Piece of Me?' (2006) 59(4) *Journal of Clinical Pathology* 335, 337.

67 Henry T Greely, 'Human Genomics Research: New Challenges for Research Ethics' (2011) 44(2) *Perspectives in Biology and Medicine* 221, 224–5; Michelle M Mello and Leslie E Wolf, 'The Havasupai Indian Tribe Case: Lessons for Research Involving Stored Biologic Samples' (2010) 363(3) *New England Journal of Medicine* 204, 206.

research in the US, as set forth in the Code of Federal Regulations. This Code establishes requirements for the protection of human participants in federally funded research and is adopted by numerous federal agencies as a Common Rule.[68] Inspired by the moral principles enshrined in the Nuremberg Code, the Declaration of Helsinki and the Belmont Report, its provisions aim to protect the safety, welfare and dignity of human research participants.

The Code of Federal Regulations requires researchers to obtain informed consent from research participants and approval of the research protocol by an Institutional Review Board (IRB)—an ethics committee set up to oversee research involving human participants. As a rule, potential research participants have to be provided with a written consent form that includes easily understandable information about the exact purpose of the research, the reasonably foreseeable risks and benefits, and the confidentiality procedure that will be followed.[69] Before the research can go ahead, an IRB has to review the protocol to ascertain that adequate information will be given and that the anticipated benefits of the research justify its risks.[70] However, federal regulations allow for waiver of informed consent when the IRB determines that the research involves no more than minimal risk to the participants, the waiver will not adversely affect the rights and welfare of the participants, and the research could not practicably be carried out without it.[71] Research is in fact completely exempt from IRB review and consequently from the obligation to obtain informed (re)consent if it involves only the collection or study of existing data or specimens which are publicly available, or where the information is recorded by the researcher in a way that participants cannot be identified directly or through identifiers linked to them.[72] In its guidance from 2004 and 2008, the US Office for Human Research Protection (OHRP) indicated that research aiming to obtain private information or specimens that are not individually identifiable would not trigger legal obligations to obtain informed consent or to seek IRB review. The OHRP specified that private information or specimens are to be considered not individually identifiable when they cannot be linked to specific individuals by the investigator directly or indirectly through coding systems.[73]

To what extent did the Havasupai research violate these federal regulations? Apart from infringing basic research requirements, Markow took advantage of the fact that some provisions on informed consent left room for interpretation. Admittedly, the purpose of the research project, as set forth in the oral script and the written consent form

68 45 CFR § 46 (2009) (Code of Federal Regulations, Public Welfare, Protection of Human Subjects), www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html.

69 45 CFR § 46.116(a) (2009).

70 45 CFR § 46.109 (2009) and 45 CFR § 46.111(a)(1)–(2) (2009).

71 45 CFR § 46.116(d) (2009).

72 45 CFR § 46.101(b)(4) (2009).

73 Office for Human Research Protections (OHRP), *Guidance on Research Involving Coded Private Information or Biological Specimens* (16 October 2008), www.hhs.gov/ohrp/policy/cdebiol.html.

used during the first blood draw series, was defined broadly enough to include behavioural disorders such as schizophrenia. However, contrary to Markow's opinion,[74] this did not mean that the Havasupai had adequately consented to the study of schizophrenia. After all, informed consent is not simply a signature on a form, but rather a process of information exchange. The scope of consent is defined on the basis of the overall information provided to the potential research participants.[75] Since in both the discussions with the tribal council and the communication with the individual participants only diabetes research was mentioned, the fact that the scope of the project was defined more broadly in the consent form was not decisive. Moreover, the meaning of the consent form must be viewed from the perspective of the research participant, not from the viewpoint of the researcher.[76] If research participants understood the vaguely formulated project description to encompass only the study of diabetes, then no valid consent could be inferred for research that, while formally within the scope of the definition, went beyond this interpretation.

Aside from the inadequate disclosure of information, doubts can be raised about the manner and context in which information was conveyed. More likely than not, the presentation of the scope of the project was not adapted to the capacities of the blood donors. Most of the Havasupai who were approached to give blood had no tertiary education, and many were barely literate in English.[77] As became apparent during the second blood draw series, when the number of educated and motivated contributors diminished drastically, the information presented in the consent form proved too confusing. Potential donors were very hesitant to participate and only agreed to do so after the research purpose was explained to them in the simplest of terms and the written consent form was dropped altogether.[78]

The Havasupai case is not only an example of biobank research misconduct in which researchers disregarded the rules or bent them to their own advantage. More importantly, the wide variety of unanticipated harms that participants were confronted with serves as a caution that current federal regulations may be inadequate. Indeed, while intended to protect the interests of research participants, some of its provisions inadvertently leave the door open for similar infringements.

The regulations concerning secondary research on samples which are not individually identifiable may prove especially problematic. As noted earlier, this kind of research is exempt from IRB review and, consequently, from the obligation to (re-)obtain informed consent. The rationale presumably is that no harm can be done if individual

74 Hart and Sobraske (n 3) Witness Interview Summaries, 17, 19, 136–7.

75 Editorial, 'Culture Clash on Consent' (2010) 13(7) *Nature Neuroscience* 777. See also Tom L Beauchamp and John F Childress, *Principles of Biomedical Ethics* (Oxford University Press, 6th edn 2009) 77–97.

76 See eg Courtney S Campbell, 'Research on Human Tissue: Religious Perspectives' in National Bioethics Advisory Commission (n 43) C1, C13–C14.

77 Rubin (n 9).

78 Hart and Sobraske (n 3) Witness Interview Summaries, 31.

participants remain anonymous. However, as was clearly demonstrated in the Havasupai case, major harm may befall research participants when their samples are coded but are known to originate within a particular population. In those circumstances, research that yields findings that are stigmatising and disruptive may result in severe collective harm, reflecting negatively on all group members. It is highly disturbing to realise that even if the ASU researchers had followed the regulations by the book, the population migration research, which proved most damaging for the participants, could have gone ahead. To prevent such an outcome occurring again, the National Bioethics Advisory Commission (NBAC) has recommended that researchers should consult with representatives of the relevant groups and that IRBs should not grant exemption for secondary research on samples which are not individually identifiable if a significant risk of group harm may be expected.[79]

A related regulatory weakness concerns the minimal risk standard that IRBs have to consider when balancing the risks and benefits of research that is not exempt under the Common Rule. If the IRB deems the risk of harm to be minimal and expects no adverse effects on the rights and welfare of the participants, it can allow research to proceed without informed consent. While the concept is defined in the Code of Federal Regulations,[80] there is considerable confusion about what really constitutes minimal risk, leading to a widely varying application. As noted earlier, researchers and IRB committees tend to detect only the types of harms that they consider they themselves might encounter. Consequently, IRB review is in danger of underestimating the importance of a range of factors that may prove crucial for participants from a culturally distinct environment. As was demonstrated in the Havasupai case, several tangible and dignitary harms that are not generally recognisable to the research community must be factored into the ethical reasoning to adequately protect research participants with different values and beliefs. In order to obtain a satisfactory level of protection, various precautionary measures have been proposed. As we mentioned earlier, the NBAC has recommended consultation with representatives of relevant vulnerable groups to help evaluate the study design. More far-reaching proposals include continuous involvement of group representatives throughout the stages of study design, implementation, and dissemination of results.[81] Some commentators advocate appointing a group representative to the IRB, analogously

79 National Bioethics Advisory Commission (n 43) vii, 73, Recommendation 17. See also Wolf (n 57) 148–9.

80 45 CFR § 46.102(i) states: '*Minimal risk* means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.'

81 eg Sally M Davis and Raymond Reid, 'Practicing Participatory Research in American Indian Communities' (1999) 69(4 Suppl) *American Journal of Clinical Nutrition* 577S, 757S–758S; Richard R Sharp and Morris W Foster, 'Community Involvement in the Ethical Review of Genetic Research: Lessons from American Indian and Alaska Native Populations' (2002) 10 *Environmental Health Perspectives* 145, 147; Wallwork (n 52) 69. For the philosophical rationale behind the need for more active involvement of participants, see Michel Callon, Pierre Lascoumes and Yannick Barthe, *Acting in an Uncertain World: An Essay on Technical Democracy* (MIT Press, 2009).

to the Common Rule provision on the inclusion of a prisoner representative to help reviewing research involving prisoners.[82] The most sweeping suggestions even call for community informed consent to be obtained in addition to the individual informed consent.[83]

Other, related objections can be raised against the fact that the Common Rule allows research participants to grant blanket consent for future, unspecified research. From a moral point of view, blanket consent is totally inappropriate. Respect for autonomy requires that research participants should know the purposes their samples will be used for and should have the right to authorise or reject the use in each case. To make an informed decision, they must have a clear picture of the harms that may befall them. Allowing blanket consent amounts to a lack of respect for the autonomy of participants because they are not provided with the information necessary to make an informed choice. In addition, there is a major risk of abuse if researchers may do as they please without considering the interests of the research participants. As the case of the Havasupai clearly shows, general trust in biobank researchers may be totally unwarranted.

On the other hand, obtaining fresh informed consent for each new research use of human body material would be very costly and unpractical, and would significantly slow the pace of biobank research. An intermediate solution appears to be the only way to make research on stored samples feasible without compromising the dignity of participants. As recommended by the NBAC, presenting potential research participants with a multilayered consent form, that describes a wide range of possible uses and emphasises the risks and benefits of each use, could be preferable.[84] In this regard, it could be noted that a regulatory framework seems to be developing in which the traditional emphasis on autonomy is superseded by a dedication to trust. More specifically, increased public engagement and the development of comprehensive governance structures for biobanks have been proposed as new mechanisms to ensure that ethical principles, including the dignity of biobank participants, are respected. Although the development of more appropriate governance structures is to be applauded, it is not inconceivable that consent requirements will be unduly relaxed merely because it is thought that the interests of research participants will be sufficiently protected by additional institutional

82 See McGregor (n 46) 365. For the proposal to appoint a prisoner representative to the IRB, see 45 CFR § 46.304(b) (2009) (Composition of Institutional Review Boards where prisoners are involved).

83 See Henry T Greely, 'Informed Consent and Other Ethical Issues in Human Population Genetics' (2001) 35 *Annual Review of Genetics* 785, 789–95; C Weijer and EJ Emanuel, 'Protecting Communities in Biomedical Research' (2000) 289(5482) *Science* 1141, 1143.

84 National Bioethics Advisory Commission (n 43) 64, Recommendation 9. See also Timothy Caulfield, Ross EG Upshur and Abdallah Daar, 'DNA Databanks and Consent: A Suggested Policy Option Involving an Authorization Model' (2003) 4 *BMC Medical Ethics* 1, 3; Eric M Meslin and Kimberly A Quaid, 'Ethical Issues in the Collection, Storage, and Research Use of Human Biological Materials' (2004) 144(5) *Journal of Laboratory and Clinical Medicine* 229, 231; Bjørn Hofmann, Jan H Solbakk and Søren Holm, 'Consent to Biobank Research: One Size Fits All?' in Jan H Solbakk, Søren Holm and Bjørn Hofmann (eds), *The Ethics of Research Biobanking* (Springer, 2009) 3, 17–19.

safeguards.[85] One of the main challenges for the model of trust that is currently being elaborated is to still allow research participants maximum autonomy to determine the extent of their participation.

Finally, the Havasupai case also illustrates the need to regulate in more detail the right to withdraw consent. The Code of Federal Regulations explicitly grants that research participants may discontinue participation at any time without penalty or loss of benefit.[86] However, it remains unclear what such withdrawal of consent boils down to in practice. Considerable disagreement exists concerning the right of participants to order the destruction of samples and any information gleaned from them. While it is frequently advocated that withdrawal should imply the destruction of all samples and any associated information,[87] the Havasupai example reveals that this might not be enough.[88] Where the sample itself is invested with religious significance, participants may have a real interest in having their samples returned instead of destroyed. It would not make any difference if the samples were to be made irrevocably anonymous, as is sometimes proposed instead of destruction.

As the Havasupai experienced to their detriment, protections provided under the Common Rule, even when honoured in practice, are not always adequate to avoid severe infringements on the dignity of biobank research participants. Instead of merely encouraging researchers by way of recommendations, the federal regulations governing biobank research need to be updated to guarantee due consideration of dignitary interests that researchers may find difficult to identify. The safeguards built into the Common Rule still are too much indebted to the informed consent doctrine that was originally developed in the therapeutic setting. Indeed, its provisions do not yet sufficiently address the protection of parties other than the individuals directly participating in research who might be affected. In addition, by focusing almost exclusively on health, safety and welfare risks, they lose sight of less palpable harms that can prove to be even more problematic.

85 For an overview of the issues at stake and various proposals for state-of-the-art governance structures, see Matti Häyry, Ruth Chadwick, Vilhjalmur Arnason and Gardar Arnason (eds), *The Ethics and Governance of Human Genetic Databases: European Perspectives* (Cambridge University Press, 2007); Elger *et al* (n 2); Herbert Gottweis and Alan Petersen (eds), *Biobanks: Governance in Comparative Perspective* (Routledge, 2008); Kris Dierickx and Pascal Borry (eds), N*ew Challenges for Biobanks: Ethics, Law and Governance* (Intersentia, 2009); Kaye and Stranger (n 2); Graeme Laurie, 'Reflexive Governance in Biobanking: On the Value of Policy Led Approaches and the Need to Recognize the Limits of the Law' (2011) 130(3) *Human Genetics* 347; Herbert Gottweis and Georg Lauss, 'Biobank Governance: Heterogeneous Modes of Ordering and Democratization' (2012) 3(2) *Journal of Community Genetics* 61; Jane Kaye, Susan MC Gibbons, Catherine Heeney, Michael Parker and Andrew Smart (eds), *Governing Biobanks: Understanding the Interplay between Law and Practice* (Hart Publishing, 2012); Emmanuelle Rial-Sebbag and Anne Cambon-Thomsen, 'The Emergence of Biobanks in the Legal Landscape: Towards a New Model of Governance' (2012) 39(1) *Journal of Law and Society* 113.

86 45 CFR § 46.116(a)(8) (2009).

87 eg Gert Helgesson and Linus Johnsson, 'The Right to Withdraw Consent to Research on Biobank Samples' (2005) 8(3) *Medicine, Health Care and Philosophy* 315, 319–20.

88 See Wolf (n 57) 155.

In order to be better adapted to the interests of biobank research participants, the Common Rule needs to be revised in a number of ways. To begin with, the concept of harm should be broadened to account for dignitary harms to individual participants, third parties and groups, including possible harms resulting from research on anonymised samples. Furthermore, to facilitate appropriate future use of samples, the use of a multilayered consent form should be required, providing potential participants with enough options to ascertain their preferences if the purpose of secondary research might differ from the purpose of primary research. Finally, the provision that participants may at all times discontinue participation should be made more explicit by granting a right to have their samples returned or destroyed. Only such a revision of existing regulations would ensure due protection of the interests of research participants.

VI. LIMITATIONS OF CURRENT TORT DOCTRINE IN PROVIDING RELIEF FROM DIGNITARY HARMS IN BIOBANK RESEARCH

The Havasupai case reveals that present common law tort doctrines are largely unhelpful to protect research participants when dignitary harms actually occur. Theoretically, tort law offers several causes of action on which biobank research participants may proceed, including breach of informed consent, breach of fiduciary trust, and negligent infliction of emotional distress.[89] In practice, however, these remedies prove to be largely illusory.

Breach of Informed Consent

Courts have consistently declined to acknowledge claims for breach of informed consent brought by biobank research participants against researchers. In the Havasupai case, for instance, the District Court for the District of Arizona dismissed this claim because in its opinion the consent for drawing blood was not made ineffective even if it was fraudulently procured.[90] Even in cases where judges have opted for a less conservative interpretation of the informed consent doctrine, they decided that biobank research participants did not have standing to sue for breach of informed consent.

As with other torts based in negligence, the tort of informed consent requires a breach of duty, an injury and a causal connection between the duty that was breached and the injury. However, since this tort was imported from standard medical malpractice

89 On the crucial importance of the liability framework to ensure effective retrospective and prospective accountability with regard to research injuries, see Kenneth De Ville, 'The Role of Litigation in Human Research Accountability' (2002) 9(1) *Accountability in Research* 17, 19; Larry I Palmer, 'Should Liability Play a Role in the Social Control of Biobanks?' (2005) 33(1) *Journal of Law, Medicine and Ethics* 70, 76–77.

90 *Tilousi v Arizona State University Board of Regents*, 2005 WL 6199562, 2 (D Ariz) ('Plaintiffs consented to having blood drawn and were fully aware of the character of the contact. Thus their consent is not made ineffective even if defendants did make fraudulent representations to induce that consent').

theory, its significance outside the therapeutic setting remains unclear.[91] For instance, courts have been very reluctant to recognise a duty of informed consent between biobank researchers and research participants. Admittedly, in *Moore v Regents of University of California*, the Supreme Court of California acknowledged a duty of disclosure on the part of a biomedical researcher, but only because he had also been the tissue donor's treating physician and as such was obliged to inform his patient about any personal interests that might affect his medical judgment.[92] In *Greenberg v Miami Children's Hospital Research Institute*, the District Court for the Southern District of Florida explicitly questioned whether biobank researchers owe participants a duty of informed consent in the absence of a therapeutic relationship. It argued that, even if that kind of duty could be established, it would surely not include disclosure of the researcher's economic interests.[93]

Although until now no duty of informed consent has been upheld in biobank litigation, two major cases involving experimental research on human participants suggest that such a duty may indeed extend beyond the therapeutic context. In *Whitlock v Duke University* the District Court for the Middle District of North Carolina argued that because the doctrine of informed consent applies 'in therapeutic circumstances where the health care provider has as an objective to benefit the patient', informed consent would *a fortiori* be required 'by an experimental subject in the nontherapeutic context where the researcher does not have as an objective to benefit the subject'.[94] In determining the appropriate standard of care in such a context, the court explicitly sought guidance from both the Nuremberg Code and the Declaration of Helsinki, and con-

91 E Haavi Morreim, 'Medical Research Litigation and Malpractice Tort Doctrines' (2003) 4(1) *Houston Journal of Health Law and Policy* 1, 63.

92 In *Moore v Regents of the University of California*, a patient sued, among others, his treating physician for using cells removed from him in the course of his leukemia treatment to develop a patented cell line without his permission. The Supreme Court of California ruled that he had no cause of action for conversion but could recover for breach of fiduciary duty and lack of informed consent, holding that '(1) a physician must disclose personal interests unrelated to the patient's health, whether research or economic, that may affect the physician's professional judgment; and (2) a physician's failure to disclose such interests may give rise to a cause of action for performing medical procedures without informed consent or breach of fiduciary duty'. See *Moore* (n 1) 483.

93 In *Greenberg v Miami Children's Hospital Research Institute, Inc*, 264 F Supp 2d 1064, 1070 (SD Fl 2003), parents of children who donated tissue and blood samples for Canavan disease research filed suit against the research institute for developing a patented screening test without their permission. The District Court for the Southern District of Florida dismissed the plaintiffs' claim for lack of informed consent. It declined 'to extend the duty of informed consent to cover economic interests' and rejected the plaintiffs' invocation of the *Moore* ruling, stating that '[t]he allegations in the Complaint are clearly distinguishable as [the] Defendants here are solely medical researchers and there was no therapeutic relationship as in *Moore*'.

94 *Whitlock v Duke University*, 637 F Supp 1463, 1468 (MD NC 1986). In this case, a research participant who sustained severe organic brain damage during a deep-diving simulation sued the research institution for failing to obtain adequate informed consent because it had failed to warn about the risk of organic brain damage. Although the court acknowledged a 'higher level of risk disclosure applicable to nontherapeutic experimentation', it ultimately dismissed the claim because 'no genuine issue of fact exists as to whether the risk of organic brain damage unique to experimental deep diving was a reasonably foreseeable risk' (1472).

cluded that informed consent in the nontherapeutic context would have to be consistent with the Code of Federal Regulations.[95] Similarly, in *Grimes v Kennedy Krieger Institute* the Maryland Court of Appeals found that researchers involved in nontherapeutic human experimentation face a duty under certain circumstances to obtain informed consent from the participants.[96] As in *Whitlock*, the court acknowledged the authority of the Nuremberg Code and the Declaration of Helsinki and affirmed that the Code of Federal Regulations established the appropriate standard of care.[97]

However, even if the duty of informed consent is judicially enforced in the distinct context of biobank research, plaintiffs may not succeed in their claim because their injuries are not cognisable under malpractice law. Because biobank research participants will fail to prove that they suffered a visible physical injury or recognisable psychiatric illness as a direct consequence of the breach of duty, their claim for breach of informed consent will be dismissed. Anticipating this, biobank research participants have attempted to bring an additional cause of action directly under the Code of Federal Regulations. They have asserted that they are third-party beneficiaries to the contract between the research institution and the Department of Health and Human Services in which the researchers agree to abide by the Common Rule. However, as happened in the Havasupai case,[98] courts have systematically declined to extend a private right of action to enforce the terms of the Code of Federal Regulations.[99] Acknowledging that these regulations require protective measures on the part of investigators and research institutions, courts

95 *Ibid*, 1471.

96 In *Grimes v Kennedy Krieger Institute, Inc* 782 A 2d 807, 858 (Md 2001), research subjects participating in a study testing lead abatement techniques filed suit against the research institution that sponsored the study for failing to inform them about dangerous lead levels in their blood as well as for lack of informed consent. The Maryland Court of Appeals held that 'under certain circumstances, [informed consent agreements in nontherapeutic research projects] can, as a matter of law, constitute "special relationships" giving rise to duties, out of the breach of which negligence actions may arise'. The appellate court held that the trial court had erred in granting the research institution's motions for summary judgment and remanded the case for further proceedings consistent with its opinion.

97 *Ibid*, 848–51, 858.

98 The District Court for the District of Arizona dismissed the plaintiffs' cause of action for violation of 45 CFR § 46.116, ruling that 'this federal regulation regarding institutional review boards does not provide a private right of action nor does it evidence an intent to do so. A court must determine whether a statute "displays an intent to create not just a private right but also a private remedy" … The text and structure of the statute display no intent to establish a private right of action.' *Tilousi* (n 90) 2.

99 In *Wright v Fred Hutchinson Cancer Research Center*, 269 F Supp 2d 1286, 1289 (WD Wash 2002), the plaintiffs, representing 20 deceased cancer patients who had participated in a trial to prevent graft failure in bone marrow transplantation, sued the research institution for alleged use of misleading consent forms and failure to disclose conflicts of interest. The plaintiffs claimed that as a result the research institution failed to abide by the Code of Federal Regulations and breached its contract with the Department of Health and Human Services. The District Court for the Western District of Washington dismissed the plaintiffs' cause of action under the Code of Federal Regulations on the grounds that 'agency regulations cannot give rise to a private cause of action where the authorizing statute does not confer such a right' and '[b]ecause plaintiffs have not identified any statutory basis for the private rights of action they seek to assert, their claims … must fail.' See also *Washington University v Catalona*, 437 F Supp 2d 985, 1000 (ED Mo 2006).

have insisted that violations only allow the funding agency to impose penalties or even withdraw federal funds; they do not mandate enforcement through private litigation.[100] Indeed, parties that benefit from a government contract are assumed to be no more than incidental beneficiaries unless the contract explicitly focuses on them and provides them with an actionable right.[101] Since this intent is clearly absent in the Code of Federal Regulations, courts have denied biobank research participants a basis for a judicial remedy where researchers disregard the regulatory requirements for informed consent.

Breach of Fiduciary Duty

A cause of action for breach of fiduciary duty proves to be similarly ineffective in protecting biobank research participants. As was the case in the Havasupai lawsuit, biobank research participants have argued that they put special trust in their researchers and even perceive them as fiduciaries.[102] In their view, biobank researchers must be held to the highest standard of care, put the interests of their research participants before their personal interests, and at least protect them from unreasonable harm.

However, courts have emphasised that biobank researchers are not fiduciaries of their research participants for largely the same reasons that they have dismissed a duty of informed consent on their part. They have found the fiduciary doctrine to be applicable only in the strictly medical context, where a physician is acting primarily for the benefit of the patient. By contrast, in biobank research, which is typically not undertaken for the benefit of individual participants, no fiduciary duties are said to apply, except, as underscored in the *Moore* case, for researchers who have a close physician-patient relationship with their research participants.[103] The suggestion in *Whitlock* and *Grimes*, that in the context of experimental research on human beings a heightened duty may exist even outside the strict physician-patient relationship,[104] has not been followed in biobank research litigation. For instance, the *Greenberg* court clearly stated that no automatic fiduciary relationship attaches when biobank researchers accept tissue donations; such a relationship will only be established when researchers explicitly accept the trust placed in them.[105]

100 *Wright* (n 99) 1289–90.

101 John Calamari and Joseph Perillo, *The Law of Contracts* (West, 4th edn 1998) 643.

102 *Tilousi* (n 90) 2.

103 *Moore* (n 1) 485 ('Accordingly, we hold that a physician who is seeking a patient's consent for a medical procedure must, in order to satisfy his fiduciary duty … disclose personal interests unrelated to the patient's health, whether research or economic, that may affect his medical judgment').

104 *Whitlock* (n 94) 1468; *Grimes* (n 96) 858. See *ibid*, 835 ('We shall hold initially that the very nature of nontherapeutic scientific research on human subjects can, and normally will, create special relationships out of which duties arise'); *ibid*, 849 ('The question becomes whether this duty of informed consent created by federal regulation, as a matter of state law, translates into a duty of care arising out of the unique relationship that is researcher-subject, as opposed to doctor-patient. We answer that question in the affirmative').

105 *Greenberg* (n 93) 1071–2 ('[A] fiduciary relationship will only be found when the plaintiff separately alleges that the plaintiff placed trust in the defendant and the defendant accepted that trust … [T]he Court

Because the element of acceptance of trust cannot be sufficiently alleged in biobank research litigation, claims for breach of fiduciary duty have consistently been dismissed.[106] Moreover, even if a fiduciary responsibility on the part of biobank researchers were automatically allocated, disgruntled research participants would find it very difficult to recover under a claim for breach of fiduciary duty. Since this cause of action sounds in negligence, plaintiffs would have to prove that they suffered physical injury or provable psychiatric injury as a direct consequence of the researchers' breach of duty. As dignitary harms are not by themselves considered to be compensable injuries under this tort, biobank research participants would most likely be left out in the cold.[107]

Negligent Infliction of Emotional Distress

With both the tort of breach of informed consent and breach of fiduciary duty inadequate to protect the autonomy and dignity of biobank research participants, a claim for negligent infliction of emotional distress may offer them some, albeit slim, hope for recovery. Because this cause of action does not rely on medical malpractice doctrine, the applicable standard of care that researchers must live up to is not restricted to the confines of the physician-patient setting. Moreover, injuries that are not ordinarily recognised in medical malpractice litigation are more likely to be acknowledged.

However, while there is indeed a tendency to recognise a broader category of harms, courts still refuse to compensate for emotional suffering unless this has resulted in lasting physical symptoms or a provable psychiatric injury. For instance, in the Havasupai case, the District Court denied the defendants' motion to dismiss the negligent infliction of emotional distress claim because the plaintiffs' complaint alleging severe emotional harm might have been adequate if they could present evidence of a long, continuous mental disturbance that might be classified as illness.[108]

We have to conclude that all three causes of action under consideration leave biobank research participants largely unprotected and, consequently, they appear too limited to

finds that Plaintiffs have not sufficiently alleged the second element of acceptance of trust by Defendants and therefore have failed to state a claim. There is no automatic fiduciary relationship that attaches when a researcher accepts medical donations and the acceptance of trust, the second constitutive element of finding a fiduciary duty, cannot be assumed once a donation is given').

106 For instance in the case under consideration. See *Tilousi* (n 90) 2 ('plaintiffs allege no facts sufficient to establish [a fiduciary relationship]. As defendants point out, plaintiffs do not even allege that any of the defendants accepted the trust and confidence of plaintiffs, but instead plaintiffs' allegations focus on Martin and Benyshek's perception that the Havasupai trusted Martin … This does not establish that defendants accepted the trust of plaintiffs').

107 Donna M Gitter, 'Ownership of Human Tissue: A Proposal for Federal Recognition of Human Research Participants' Property Rights in their Biological Material' (2004) 61 *Washington & Lee Law Review* 257, 307; Ellen W Clayton, 'Informed Consent and Biobanks' (2005) 33(1) *Journal of Law, Medicine and Ethics* 15, 18.

108 *Tilousi* (n 90) 4 ('Plaintiffs' complaint alleging continued mental and emotional harm *may* be adequate for a claim of bodily harm if plaintiffs can present evidence to establish long continued mental disturbance of the sort contemplated by the Restatement. Therefore, the motion to dismiss the negligent infliction of emotional distress claim … is denied').

be of any real significance in the specific biobank research context. In order to establish the elements of negligence necessary to sustain their tort claims, research participants would have to prove that the researcher owed them a duty of special care, that this duty was breached, that they suffered a cognisable injury, and that the researcher's breach of duty was the proximate cause of their injury. The burden on biobank research participants to prove all four elements may be practically insurmountable.[109] Even if courts were to acknowledge that biobank researchers owe their participants a duty of special care and are found to be in breach of this duty, plaintiffs would have a very hard time demonstrating that they suffered an injury that not only qualifies under present tort doctrine but had unquestionably been caused by the negligent conduct of the defendants.

VII. AVENUES FOR MODIFYING TORT DOCTRINE TO PROTECT BIOBANK RESEARCH PARTICIPANTS

It seems that existing tort law must be substantially revised to address the kinds of mistreatment that are specific to the biobank research context and which result in injuries that affect the autonomy and dignity of participants without demonstrable physical damage. Two potential avenues can be identified to achieve this goal. The first approach involves an *expansion of existing remedies*, while the second focuses on the *development of a distinct dignitary tort*.

Expanding Existing Remedies

In an attempt to offer biobank research participants an opportunity to recover for infringements on their autonomy and dignity, a three-pronged proposition to modify existing tort remedies may be considered. *First of all*, tort law should recognise a fiduciary relationship between researchers and the persons on whose body material they carry out research.[110] This would go beyond the existing position, where such a relationship is only acknowledged in the context of *therapeutic* research, as well as beyond the rulings in *Whitlock* and *Grimes*, which related to specific non-therapeutic research contexts but *not* to that of biobank research.

109 MaryJoy Ballantyne, 'One Man's Trash is Another Man's Treasure: Increasing Patient Autonomy through a Limited Self-Intellectual Property Right' (2005) 3 *Georgetown Journal of Law and Public Policy* 567, 578; Natalie Ram, 'Assigning Rights and Protecting Interests: Constructing Ethical and Efficient Legal Rights in Human Tissue Research' (2009) 23(1) *Harvard Journal of Law and Technology* 119, 157.

110 See eg Lori B Andrews, 'Harnessing the Benefits of Biobanks' (2005) 33(1) *Journal of Law, Medicine and Ethics* 22, 27; Ram (n 109) 173. Biobank research participants could even be allowed a cause of action directly under the Code of Federal Regulations, if federal legislation were to rephrase the regulatory requirements in terms of the persons benefited and establish clear and uniform rules of engagement between all parties concerned. See Javitt (n 58) 754.

Secondly, because a cause of action for breach of fiduciary duty would still fail for want of cognisable injury, the *scope of harm* actionable under the negligence doctrine must be expanded to include dignitary harms that may result from biobank research misconduct. Although in cases of biobank research litigation, courts have systematically refused to impose liability for these kinds of harms, they have allowed recovery for types of harms that are of a non-physical nature in other litigation contexts, for instance in cases involving breach of privacy or defamation. There is no reason why negligence torts could not be similarly conceived.[111] A key argument in favour of this proposal, as was suggested decades ago, is that the prime interests protected by negligence torts ought to be the individual's autonomy and dignity instead of their interest in being free of physical injury caused by negligent action.[112]

A claim for recovery for dignitary harm has already been considered in *Diaz v Hillsborough County Hospital Authority*, a case involving inadequately consented-to clinical research. The plaintiffs in this case claimed that, even though they had not suffered any physical injuries, they had been harmed by conduct that 'overrode their autonomy, treated them as less than human, and denigrated them as human beings'.[113] When the court refused to dismiss the case and certified the case as a class action, a multi-million dollar settlement was reached that was judicially approved on the basis of a right to

111 E Haavi Morreim, 'Litigation in Clinical Research: Malpractice Doctrines versus Research Realities' (2004) 32(3) *Journal of Law, Medicine and Ethics* 474, 479–80; Ram (n 109) 158–9.

112 eg Joseph Goldstein, 'For Harold Lasswell: Some Reflections on Human Dignity, Entrapment, Informed Consent, and the Plea Bargain' (1975) 84 *Yale Law Journal* 683, 691; Jay Katz, 'Informed Consent: A Fairy Tale? Law's Vision' (1977) 39(2) *University of Pittsburgh Law Review* 137, 161; Marjorie M Shultz, 'From Informed Consent to Patient Choice: A New Protected Interest' (1985) 95(2) *Yale Law Journal* 219, 276; Alan Meisel, 'A "Dignitary Tort" as a Bridge Between the Idea of Informed Consent and the Law of Informed Consent' (1988) 16(3–4) *Law, Medicine and Health Care* 210, 210–11; Aaron D Twerski and Neil B Cohen, 'Informed Decision Making and the Law of Torts: The Myth of Justiciable Causation' (1988) 3 *University of Illinois Law Review* 607, 621–2. In the meantime, the right to recover for dignitary harm in the absence of physical damage or pecuniary loss has already been acknowledged in medical malpractice litigation. See eg *Lugenbuhl v Dowling*, 701 So 2d 447, 455–6 (LA Supreme Court 1997) ('While plaintiff failed to prove physical damages or pecuniary loss, he is still entitled to an award of general compensatory damages caused by the doctor's breach of duty. In this type of case, damages for deprivation of self-determination, insult to personal integrity, invasion of privacy, anxiety, worry and mental distress are actual and compensatory … Rather, the injury was to plaintiff's personal dignity and right of privacy, an injury for which an award of damages generally is considered appropriate. The primary concern in this injury to the personality is vindication of valuable, although intangible, right, the mere invasion of which constitutes harm for which damages are recoverable').

113 In *Diaz v Hillsborough County Hospital Authority*, 2000 WL 1682918, 3 (MD Fla), a group of about 5,000 women brought a class action suit against the hospital that subjected them to research into a new method for fetal lung maturity treatment during their prenatal care. The plaintiffs claimed that, although they had signed the informed consent document informing them that they would be subjected to a treatment method that did not satisfy the regular standard of care, their consent was invalid because it was obtained in a coercive atmosphere and because the forms were written in language that they could not possibly understand. They asserted that their interest in refusing unwanted research had been violated as a result. See Stephen F Hanlon and Robyn S Shapiro, 'Ethical Issues in Biomedical Research: *Diaz v Hillsborough County Hospital Authority*' (2003) 30(2) *Human Rights* 16, 17.

recover for dignitary harm.[114] Although the court's consent decree lacks the precedent-setting force of a court ruling, the case is notable as the first litigation to have produced a substantial monetary award to biomedical research participants who did not assert a claim of physical injury.[115]

Thirdly and relatedly, the negligence doctrine could be modified to ease the burden of proof on biobank research participants to demonstrate that they suffered dignitary harm, because the difficulties in proving this kind of harm would otherwise likely be insurmountable.

Introducing a New Dignitary Tort

A second avenue for improving protection of the autonomy and dignity of biobank research participants would be for the courts to accept a distinct dignitary tort.[116] The need for an explicit recognition of a genomic tort claim based on an interest in dignity has been forcefully advocated by several commentators.[117] Relying on a conception of human dignity as essentially empowering,[118] they persuasively argue that persons should have the ability to control the flow of genetic information about themselves. Such a claim of the right to control personal genetic information could emerge either as part of a broad concept of privacy or as emanating from a proprietary interest that individuals might

114 *Diaz*, *ibid*, 3; Ana Iltis, 'Lay Concepts in Informed Consent to Biomedical Research: The Capacity to Understand and Appreciate Risk' (2006) 20(4) *Bioethics* 180, 183 fn 17; Morreim (n 91) 78–79.

115 Carl H Coleman, 'Duties to Subjects in Clinical Research' (2005) 58(2) *Vanderbilt Law Review* 387, 447; Hanlon and Shapiro (n 113).

116 Apart from initiating new types of claims, research participants now tend to sue not only the primary researcher and others directly involved in the research project, but also academic institutions and even individual members of the IRBs. For an in-depth analysis of the recent evolution of research litigation, see Michelle M Mello, David M Studdert and Troyen A Brennan, 'The Rise of Litigation in Human Subjects Research' (2003) 139(1) *Annals of Internal Medicine* 40, 42; David B Resnik, 'Liability for Institutional Review Boards: From Regulation to Litigation' (2004) 25(2) *Journal of Legal Medicine* 131, 135; Randi Z Shaul, Shelley Birenbaum and Megan Evans, 'Legal Liabilities in Research: Early Lessons from North America' (2005) 6(4) *BMC Medical Ethics* 1, 1–2.

117 See Graeme Laurie, *Genetic Privacy: A Challenge to Medico-Legal Norms* (Cambridge University Press, 2002); Roger Brownsword, 'An Interest in Human Dignity as the Basis for Genomic Torts' (2003) 42(3) *Washburn Law Journal* 413.

118 Brownsword and others have made it clear that, with the advent of the technological era, the concept of 'human dignity as empowerment' has been supplemented by the concept of 'human dignity as constraint'. The argument in favour of recognising a dignitary genomic tort is founded on the former, in that it is based on respect for the autonomy of persons. For the distinction between these conceptions of human dignity, see eg Deryck Beyleveld and Roger Brownsword, *Human Dignity in Bioethics and Biolaw* (Oxford University Press, 2001); Daniela-Ecaterina Cutas, 'Looking for the Meaning of Dignity in the Bioethics Convention and the Cloning Protocol' (2005) 13(4) *Health Care Analysis* 303; Roger Brownsword, 'Genetic Engineering, Free Trade and Human Rights: Global Standards and Local Ethics' in Daniel Wüger and Thomas Cottier (eds), *Genetic Engineering and the World Trade System* (Cambridge University Press, 2008) 287; Roger Brownsword, 'Human Dignity, Biolaw, and the Basis of Moral Community' (2010) 21(4) *Journal International de Bioethique* 21.

have in their genetic information.[119] Taking into consideration that accepting proprietary rights in relation to genetic information is likely to entail recognition of proprietary rights to the very tissue or samples that hold genetic information—an assumption that is deeply contested—a non-property approach focusing on the right to privacy may be most promising. In either case, a genomic tort claim based on an interest in dignity would give a cause of action both when genetic information has been obtained and passed on without the authorisation of the subject of the information and when genetic information has been obtained about which the subject of the information may wish to remain ignorant.[120] Such a general dignitary tort could even serve as the backbone for the development of more specific genomic torts, such as a tort relating to the violation of the right to prohibit or restrict access, or a tort relating to the violation of the right not to know.[121] Covering at the same time unauthorised outward transmission and unwanted inward transmission of genetic information, this approach would offer a judicial remedy for all injustices suffered by the Havasupai tribe.

A similar way to circumvent the difficulties of recovering for non-physical harms under present tort doctrine could be the introduction of a dignitary cause of action based directly on international ethics codes. Recently, plaintiffs in several cases involving clinical research and human experimentation have adopted this tactic by filing a separate action for breach of the 'right to be treated with dignity'.[122] For instance, in *Robertson v McGee* and *Wright v Fred Hutchinson Cancer Research Center*, the plaintiffs claimed that the Nuremberg Code and the Declaration of Helsinki, which set the minimum acceptable standards for conducting research on human participants, are essentially world statutes that create a 'right of every human subject to be treated with dignity' on the part of all citizens of the United States.[123] Anticipating that the court would deny them a private right of action under these international research ethics codes, the plaintiffs asserted that these documents are evidence that the United States recognises that certain rights are fundamental under the due process clause of the Fourteenth Amendment and that violation of these rights will give rise to liability under § 1983 of the Civil Rights Act.

119 Laurie (n 117) 84, 225–6; Brownsword (n 117) 444, 462.

120 Brownsword (n 117) 417.

121 *Ibid*, 486.

122 Mello, Studdert and Brennan (n 116) 41; Richard S Saver, 'Medical Research and Intangible Harm' (2006) 74 *University of Cincinnati Law Review* 941, 974–6.

123 In *Robertson v McGee*, 2002 WL 535045, 2–3 (ND Okla 2002), research participants and representatives of deceased research participants in a melanoma vaccine trial filed a lawsuit against, among others, the principal investigator and the hospital. Just as in *Wright v Fred Hutchinson Cancer Research Center*, the claim for lack of informed consent, alleging failure to disclose all relevant risks during the consent procedure, was supported by a separate claim for breach of the right to be treated with dignity. The case was eventually dismissed for lack of jurisdiction. See www.sskrplaw.com/files/robertson_complaint.pdf. See also *Wright* (n 99) 1288, www.sskrplaw.com/files/wright_complaint.pdf. Similar actions for breach of the right to be treated with dignity were filed in *Berman v Fred Hutchinson Cancer Research Center*; *Aderman v Trustees of the University of Pennsylvania*; *Beth Wade v Oregon Health and Science University*; *Guckin v Nagle* and *Steubin v Kornak*: see www.sskrplaw.com/lawyer-attorney-1472350.html.

However, in both cases the court rejected the plaintiffs' due process claim because the defendants' alleged actions in failing to obtain informed consent were in direct contravention of state procedures that were themselves in accord with the protections guaranteed by the Constitution and because tort law provided adequate post-deprivation remedies for the defendants' alleged conduct.[124]

Indeed, until now the courts have not been receptive to allowing a dignitary cause of action based on the Nuremberg Code or Declaration of Helsinki. As indicated by *Whitlock* and *Grimes*, these international ethics codes are at most considered useful instruments in defining the standard of care that researchers have to observe under a standard negligence theory of liability.[125]

If a 'right to be treated with dignity'—whether as part of a broad concept of privacy or based on international ethics codes—were to be recognised, research participants who have not been physically harmed would have a distinct dignitary tort with which to sue researchers, without having to establish the elements of negligence.[126] To begin with, it would no longer be necessary to demonstrate that the researchers were subject to a fiduciary duty that had been breached. Moreover, biobank research participants would no longer have to prove that they suffered a cognisable injury. Since a breach of the 'right to be treated with dignity' would automatically result in compensable injury, an explicit judicial recognition that infringing on the dignity of biobank research participants constitutes damage in itself, would no longer be necessary.

However, creating a 'dignitary tort' would also appear to have significant drawbacks. If a 'dignitary tort' were to be recognised by the courts, it would inevitably extend beyond the sphere of research on human body material. Therefore it would be difficult to prevent it from interfering with ordinary human interactions.

To ensure that the likelihood of dignitary harms occurring in the context of research on human subjects is reduced or avoided, it would seem necessary to follow the first avenue we identified, involving creating appropriate statute law and amending the Code of Federal Regulations, as argued above.

In order to provide research participants with access to appropriate redress when dignitary harm *does* occur, existing tort remedies should be modified. First, a *fiduciary relationship* between researchers and the persons on whose body material they carry out research should be recognised. Second, dignitary harms should be acknowledged to be *actionable* harms.[127] Third, since dignitary harm may not result in physical injury or

124 *Robertson* (n 123) 3–4; *Wright* (n 99) 1294.

125 *Whitlock* (n 94) 1470–1; *Grimes* (n 96) 834. See also *In re Cincinnati Radiation Litigation*, 874 E Supp 796, 821–2 (SD Ohio 1995); *White v Paulsen*, 997 F Supp 1380, 1383–4 (ED Wash 1998); *Heinrich v Sweet*, 62 F Supp 2d 282, 321 (D Mass 1999).

126 De Ville (n 89) 23; Resnik (n 116) 159.

127 In this regard, the opinion voiced by the appellate court in the Havasupai case seems to offer a signpost. By way of *obiter dictum*, the judges considered that dignitary torts such as those alleged by the Havasupai tribe do not require proof of physical manifestation of emotional suffering or distress, because these torts

emotional distress, the required burden of proof as to the *existence*, but not necessarily the extent, of dignitary harm, should be low.[128]

VIII. CONCLUSION

With human tissue research entering the era of large-scale genomic biobanking, new ethical and legal challenges arise in reconciling societal interests relating to the production of scientific knowledge with the interests and concerns of research participants. As the Havasupai case painfully illustrates, this delicate act of reconciling different sorts of interests and concerns should not be restricted to the safety, ownership and confidentiality considerations that dominate much of the present discussions. Indeed, especially but not exclusively in research on vulnerable populations, important so-called dignitary interests may also come into play. The Havasupai case holds particularly valuable lessons regarding appropriate consent requirements, the level of protection offered by anonymisation procedures, and the scope of participants' right to withdraw consent.

The challenges arising from the emerging field of biobank research are in urgent need of more adequate consideration. In order to reduce the likelihood of research participants suffering dignitary harm, the Code of Federal Regulations needs to be revised along the lines suggested above. This on its own, however, will not allow research participants to obtain redress in relation to any harm they suffer. Therefore, other steps are necessary. Since we believe the creation of a distinct new 'dignitary tort' to be fraught with problems, we recommend instead an expansion of the availability and extent of existing tort remedies. First, a fiduciary relationship between researchers and the persons on whose body material they carry out research should be recognised. Second, dignitary harms should be acknowledged to be actionable harms. Third, the required burden of proof as to the existence of dignitary harms should be low.

have to be considered damage in themselves. As regards dignitary torts, the Court of Appeals emphasised that injury need not be established because it is presumed. See *Havasupai Tribe* (n 31) 1081. The majority explicitly referred to the fact that, in dignitary torts such as invasion of privacy, cognisable injury is presumed. In addition, they referred to Dan Dobbs's contention that a dignitary tort is said to be damage in itself. Expanding on the concept of dignitary torts, Dobbs writes that 'a violation of a dignitary right is harm in itself. Here the idea does not seem to be that the plaintiff really has pecuniary loss and that the only problem is proving it. Nor does it seem to be that the plaintiff has actual substantial emotional harm that is unproven. Rather the idea seems to be that some rights are "valuable" in an important although intangible way, even if their loss does *not* lead to either pecuniary loss or compensable emotional harm. The invasion of such a right *is* harm for which damages are recoverable.' Dobbs (n 52) 625. Since the case was eventually settled, it remains unclear whether these considerations would have been legally decisive if the case had been fully litigated.

128 Lowering the burden of proof as to the *existence* of dignitary harm(s) would make it easier for the complainant to be heard in full trial. Clearly, the size of any award made by the court would have to be based upon the *extent* and severity of the dignitary harm(s) as established by testimony.