Public health and carrageenan regulation: a review and analysis

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Abstract

The status of carrageenan in the regulatory sphere influences how and where it may be used, with implications for seaweed farmers, carrageenan manufacturers and consumers. Over the period 1935 to the present the status of carrageenan has been effected by changes in the regulatory environment that reflect new understandings about carrageenan, health and health risks as well as broader trade, social and political changes. This paper reviews regulatory progress from the 1930s to the present. It reflects, in particular, the shifting priorities in public health and their effects on the regulatory status of carrageenan. Four case studies of public controversies about carrageenan safety are discussed in relation to regulatory responses and their public health significance. It is concluded that current assessments of risk associated with carrageenan have, in some contexts, failed to take into account the full spectrum of safety assessments that have been carried out and the maturing of food additive regulations thereby allowing a myth of risk to continue.

Key words: carrageenan, degraded carrageenan, health risk, poligeenan, public health, food regulation

Introduction

Carrageenan is approved and widely used as a food additive (Bixler, 1996; Shah et al., 2003). Despite official sanction for use in food, over the last 50 years, carrageenan has been subjected to intense scrutiny for potential health risks associated with human consumption. Controversy and debate about carrageenan and human health have periodically flared in academic literature and the media (see for example Borthakur et al., 2007; Chapman, 2001; Cohen et al., 2002; Marcus et al., 1969; Shah et al., 2003; Tobacman, 1998, 2001; Tobacman et al., 2001a; Tomarelli et al., 1974).

Regulatory authorities, and independent scientific advisory committees, have maintained the position that carrageenan is safe for human consumption. Carrageenan is approved for use by the Food and Drug Administration (FDA) in the United States (Food and Drug Administration, 2006) by the European Parliament and Council (Commission Directive, 1995), and by the Joint World Health Organization and by the Food and Agriculture Organization Expert Committee on Food Additives (Cohen et al., 2002). Yet in some jurisdictions precautionary measures have been instigated that place restrictions on where and how carrageenan may be used: Carrageenan is not permitted for use in infant formula in Europe (European Parliament and Council, 1995) but is permitted for use in the US (Food and Drug Administration, 2004).

The Scientific Committee on Food (SCF) of the European Commission recently endorsed a molecular weight distribution limit on carrageenan that is more restrictive than is the case in the US (Scientific Committee on Food, 2003a). At the same time, the SCF acknowledges ‘‘there is no evidence … that exposure to low molecular weight carrageenan from the use of food-grade carrageenan is occurring.’’ This precautionary approach provides a rationale for adverse public and government response in Europe that is not necessarily matched elsewhere. This example illustrates the regulation of carrageenan is not uniform internationally; and controversy on the use of carrageenan has not been resolved to the satisfaction of all (Borthakur et al., 2007).

Legislative action in relation to food safety issues is progressive (Merrill, 1997). This paper reviews the history of carrageenan from the time that it began to be industrially manufactured for food use in the US to the present. While differences still exist, there has been a growing move in recent years towards international harmonisation of food

regulation through the Codex Alimentarius system and the EU Commission (Garrett et al., 1998; Livermore, 2006; Millstone et al., 2002; Veggeland et al., 2005).

Four examples are discussed in which carrageenan use in foods has been associated with risks to human health: carcinogenicity and ulceration in the 1960s; baby formula concerns in the 1980s, more recently controversy surrounding the publications of Dr. Joanne K. Tobacman and the appearance of weak mutagen in carrageenan.

Carrageenan as a regulated food additive in the US

Until the late 1930s, what is now recognised as carrageenan (extract) was not widely used as a substance added to food and the term carrageenan did not exist in regulations for foods. Decoctions of the seaweed *Chondrus crispus* had a long history of safe use in herbal and pharmaceutical preparations (See for example Council of the Pharmaceutical Society of Great Britain, 1911; Felter et al., 1898). Decoctions were made by macerating the seaweed with water or milk. The gelling properties of *Chondrus crispus* had also been utilised for centuries in food products, such as the dessert blancmange (Stanley, 1987). In 1862 Stanford coined the term "carrageenin" for the extract of *Chondrus crispus*; the spelling was later changed to carrageenan by the American Chemical Society to reflect the use of –an as an affix denoting the presence of a polysaccharide (McHugh, 2003).

Despite knowledge of the properties of carrageenan-bearing seaweed in the mid nineteenth century, it was almost a further century before a commercial industry based on the extracting carrageenan from certain seaweeds developed. In the US in 1937 ground *Chondrus crispus* was found to stabilise dairy-produced chocolate milk. Three years later the Chicago based dairy company, Krim-ko, established a small plant near Boston to manufacture a water extract of *Chondrus* for chocolate milk and junket (Chapman, 1950; Lewis et al., 1988). Algin Corp of America in Rockland, Maine (later to become Marine Colloids, Inc and later still FMC Biopolymer) commercialized carrageenan extraction in the US in the 1950s. About the same time production of carrageenan began in Denmark and France.

Chondrus crispus (carrageenin) was regulated in food regulations in the US first as a GRAS substance, defined as a substance generally recognised as safe following the 1958 Miller amendment to the US Food and Drug Act of 1938 (See Table 1 for a chronology of regulation of carrageenan). Under the Miller amendment the FDA divided substances added to food into regulated food additives and substances that were GRAS either due to their history of use in food prior to the 1st January 1958 (the so-called grandfather clause) or on the basis of a consensus of expert opinion. The

Miller amendment prohibited the use of any new food additives considered inadequately tested for safety.

Table 1 Summary of US Regulation of Carrageenan

Year	Event	Status of carrageenan	Stated aims
1906	Federal Pure Food and Drugs Act and Federal Meat Inspection Act	Extract not yet developed. Carrageenan-bearing seaweeds little valued as food in US however long history of use in Ireland and elsewhere.	Regulates safety and quality of food. Defines official recipes for some products/prohibits food 'adulteration'.
1938	Federal Food, Drug and Cosmetics Act	1937, Krim-ko company, Chicago used ground Chondrus as ingredient for chocolate milk suspension. Not regulated.	Replaces Pure Food Act. Among provisions, labelling requirements were increased to include some 'truthful' listing of ingredients and additives on some products. Full ingredient listing not required on 'standardised products'.
1958	Food Additives Amendment Also Delaney clause	21CFR182.7255 Carrageenin (Chondrus extract) classified 'Generally Recognised as Safe' due to long history of use in foods.	Provides for a pre-market approval system for ingredients 'added to food'. Delaney clause gives FDA powers to ban food additives found to induce cancer in 'people or animals'. Classifies over 10,000 substances as food additives.
1960		MCInc. petition FDA to expand GRAS list. Carrageenan listed as a food additive under 21CFR172.620	Expanded list of carrageenan-bearing seaweeds. Carrageenan defined according to species list of eight seaweeds.
1969	White House Conference on Food, Nutrition and Health	1972 FDA review: molecular weight limitations proposed	Recommends a review of GRAS substances following FDA's ban of the artificial sweetener cyclamate as a potential carcinogen under the Delaney clause.
1973	FDA regulations for nutritional labelling of food introduced	1979 FDA move away from issuing molecular weight requirement and through Food Chemical Codex adopted water	Voluntary for most foods, required for foods with added nutrients.

		viscosity test to mimic molecular weight.	
1990	Nutrition Labeling and Education Act	Carrageenan used for fat-replacement in meat (under auspices of USDA)	Requires mandatory labelling of nutrition of all processed foods, plus increased 'clarity' of ingredients labelling.

Chondrus extract was grandfathered by the 1958 Amendment to the GRAS status through its previous uses. Under the GRAS listing Chondrus extract (carrageenin) was permitted for use in food under section 21CFR182.7255 of the US Code of Federal Regulations as harmless under prescribed conditions of use. However, for Marine Colloids Inc., the status of Chondrus extract limited production capability. The wording of the GRAS legislation allowed just one seaweed species from which carrageenan could be derived: *Chondrus crispus*.

During the early part of the 1950s a rapid increase in demand, and limited supply of *Chondrus crispus*, led industry to explore other seaweed species as a source of the extract that was recognised by its chemical name carrageenan (Chopin, 1998). From the 1950s into the 1960s the industry was experiencing other changes: increased knowledge of carrageenan chemistry and improved processes for optimizing carrageenan performance in foods. Industry members became interested in how to develop the raw materials supply through the use of a broader range of seaweed species, and through increasing interest in cultivation. In 1960 Marine Colloids Inc. petitioned the FDA to alter the GRAS listing and to permit carrageenan to be defined by its chemistry, rather than the seaweed source. FDA did not accept the chemistry definition but agreed to expand the seaweeds from which carrageenan could be extracted. To effect this change the FDA moved to list carrageenan as a regulated food additive under section 21CFR172.620, with the expanded, but limited, list of seaweed species and to establish a few purity criteria. Some confusion was created when Chondrus extract (carrageenin) was still listed as GRAS, and the extract of *Chondrus crispus* - 'carrageenan' was listed as a regulated food-additive, a situation that still exists.

The 1938 Act (See Table 1) was essentially a 'policing statute' to ensure government had the authority to address dangers associated with foods or constituents of food that were considered 'injurious to health'(Merrill, 1997). The origins of the Act can be traced to concerns about food adulteration in the late 19th and early 20th centuries (Coveney, 2003). Following World War II significant advances in processing, preservation and packaging were developed that led to an increased interest and use

of food processing aids (Atkins et al., 2000). The 1938 Act did not require advance approval for substances added to foods and processing aids could be widely adopted. In 1952 the US Congress established a special commission, chaired by Congressman James Delaney, to consider the growing use of chemical processing aids in foods and the implications for consumer health. The resultant Food Additives Amendment (1958) was based on an assumption that anything added to food was adulterated unless it met with prior approval of the FDA, or unless there was already a long history of safe use (Merrill, 1997). Proving safety of new additives became the responsibility of manufacturers (Food and Drug Administration, 2004). The treatment of carrageenan was far from unique. Other GRAS substances came under specific regulations about this time (Food and Drug Administration, 1958; Merrill, 1997).

The passage of food regulations transferred more and more responsibility from the Federal Government as enforcer of honesty and fairness, to focus on pre-market controls. Regulation of new substances added to food provided a scientifically verified guarantee of safety that was not the case for GRAS category, however it also increased the surveillance of potential health risks by requiring manufacturers to prove, using scientific evidence, (usually from animal feeding studies) that any new additive was safe for human consumption.

The development of food regulations in the US was a prelude to similar actions in Europe and in the FAO/WHO Codex Alimentarius; although occurring somewhat later and usually by-passing the GRAS concept.

Four Case Studies of Public Health Controversy

Case I: The origin of concerns and regulatory action: Ebimar

In the mid 1960s a UK company Glaxo (now GlaxoSmithKline Beecham) began to market a pharmaceutical product called *Ebimar* in France. It was based on 'carrageenin' which had been found to reduce the pain associated with peptic ulcers (Anderson et al., 1965; Bixler, 1996; Piper et al., 1961). It was thought that stomach acids, including pepsin, contributed to the formation of ulcers (Anderson et al., 1965). Sulphated polysaccharides occurring naturally in the gastric mucous were found to inhibit the formation of pepsin. 'Carrageenin' was proposed as a cheap and natural alternative to other synthetic sulphates of polysaccharides that had been proposed as treatment agents.

At the doses required, the carrageenan was extremely viscous and difficult to consume in quantities thought necessary to produce a positive health benefit. It is

well known that the viscosity of these solutions [carrageenin] could be reduced or destroyed by controlled heating with dilute mineral acid followed by purification. C16, the polygalactose sulfate component of Ebimar, was the product of this technology.

Given the limited knowledge of peptic ulcer causation, there was a correspondingly weak understanding of how or why the product worked. In the late 1960s, Marcus and Watt, two researchers under contract to the developers of Ebimar, undertook research to establish the mechanism through which low molecular weight carrageenan worked. During animal experimentation with both hydrolysed (C16) and unhydrolysed carrageenan, the latter being the type used in foods, Marcus and Watt (1969) discovered that, at very high doses, both could produce ulcerations in the cecum of the guinea pig, but ulcerations were more severe with the degraded form. Furthermore, the dose below which food-type carrageenan caused no further ulcers still showed considerable ulceration with C16. Marcus and Watts went on to speculate this ulceration as a precursor to the disease ulcerative colitis.

This is a good point to introduce some nomenclature that is common knowledge today among scientists and regulators, but was a source of confusion in the 1960s and continues to be one for the general public. C16 today would be called "poligeenan" a name provided by the US Adopted Name Council (USAN). While carrageenan is the raw material for producing poligeenan, the two different polymers have different properties and uses. Poligeenan with an average molecular weight of about 20,000 daltons has none of the food functions of carrageenan whose average molecular weight is never lower than 100,000 daltons and is usually much higher. The only application today for poligeenan is as a component of an X-ray imaging diagnostic product. Carrageenan for food use contains a very small fraction with a molecular weight in the range of that of poligeenan. Any suggestion that carrageenan with a small amount of low molecular weight matter could have the same ulcerating effect of poligeenan assumes equivalence between the substances.

Watt and Marcus concluded that the "…significance of our results in relation to human ulcerative colitis is at present only speculative and must await more comprehensive investigation" (Marcus et al., 1969, p. 188S). In 1969, carrageenan use in food was already widespread and as Marcus and Watt reported, at the time of their publication there had been 'no reports of adverse effects' associated with carrageenan usage (Marcus et al., 1969, p. 187S).

One effect of the Marcus and Watt publication was further surveillance and concern about carrageenan safety. Under FDA guidelines it was the responsibility of industry

to prove carrageenan safe. Industry members conducted further studies involving other animal species. In 1972, the FDA reviewed carrageenan safety in light of Marcus and Watt's research and all the studies that had been generated as a result of their findings (Informatics Inc., 1972)

On the basis of the Informatics report, the FDA arranged a meeting with health professionals and industry representatives to discuss a motion to modify the regulations for carrageenan in light of concerns about ulcerations found in the Watt and Marcus studies. It was agreed that the issue was of little significance to human health. Nevertheless, precautionary measures were proposed to limit the molecular weight to a minimum of 100,000 and to seek further animal studies to confirm this decision. Since 1969 scientific assessments of carrageenan have included short-term and long-term generational studies involving different dosages of degraded and non-degraded forms, and various animal studies including rats, mice, rabbits, rhesus monkeys, squirrel monkeys, pigs, gerbils, baboons, hamsters, ferrets, chick embryos and dogs (Cohen et al., 2002; Greig, 1999; JECFA, 1974, 2001), While much of the above work was going on in the United States, various of the toxicology studies were also carried out in Europe.

All of the studies supported the safety of carrageenan for use in foods. Regulatory authorities saw no reason to question the safety of carrageenan as long as the average molecular weight was 100,000 daltons or higher.

Regulations were modified to insure that carrageenan used in foods would meet this limit, and a simple water viscosity measurement was adopted for this purpose.
As a further precautionary measure, Europeans limited the 'Acceptable Daily Intake' of 75mg/kg body weight/day, an amount well above any average daily intake of even a diet high in carrageenan content (Bixler, 1994). More recently JECFA increased the ADI to "not specified" meaning the use of carrageenan in foods allowed was for technical functionality reasons and the amount used did not have to be numerically specified (JECFA, 2001).

While the above work should have settled the carrageenan safety for food processors, it did not. In 1984 labelling of food additives using the E number system came into effect among members of the European Economic Community. In the UK, additives had not previously been listed on food products. E numbers on food labels revealed additives to supermarket shoppers for the first time. The E numbers were widely interpreted by the public as new chemicals being added to food, rather than as existing additives being declared (London Food Commission, 1988, p. 39). In May 1986 eighty-nine MPs from across all parties signed a motion to seek a ban on all

unnecessary additives in children's food. In January 1987 the Ministry of Agriculture, Fisheries and Food (MAFF) in the UK made public a survey of public attitudes to food additives. The survey revealed that one third of the British public could not see any justification for using additives at all (MAFF, 1987). The survey was significant in demonstrating the failures of policy communication about food additives, but also was linked to a more general decline of public trust in food policy and regulation (Lang, 1999). With increasing public concern about additives, and a declining trust in public institutions, government regulators in the UK were under intense public scrutiny. Consumer groups were particularly active in voicing concern about baby foods and pre-schoolers diets (Bixler, 1996).

Case II Infant formula and carrageenan

As already noted above, no foodstuff attracts more attention about safety than infant formula used in the first 4-6 months of a human life. It is considered particularly important because it may be the sole source of nutrition for infants over an important period of their physical development. Infant formula became a key policy concern early in the twentieth century along with population-based measures indicating declining rates of breastfeeding in industrialised countries, and increased scientific understanding of the importance of nutrition (Murphy, 2004; Wolf, 2003). Carrageenan had been used in the US since the late1950s in liquid infant formulas to prevent fat separation and thereby assure more uniform nutrition. However, Marcus and Watt's research generated sufficient concern to warrant further investigation.

In the FDA's1972 review of carrageenan, the use of carrageenan in liquid infant formula was considered, and it was decided the benefits of using carrageenan noted above outweighed any risk to the infant. Even though the terms of the 1958 Food Additive Amendment did not permit any public health benefits to be taken into account in determining the safe use of additives, practical considerations made it hard for regulatory authorities to exclude benefits in a risk assessment.

In Europe carrageenan is not permitted as a food additive for baby formula. The ban can also be traced to more general concerns about food additives that emerged in the 1980s. In 1992 the UK Food Advisory Committee in MAFF commissioned an extensive report on additives in baby milk and weaning formulas and concluded about carrageenan that:

"Although there is no direct evidence of harm from carrageenan in infants and no toxicologically significant effects were seen in infant baboons fed carrageenan in

commercial infant formulae for 16 weeks, high levels of reassurance are needed to permit additives in infant formulae. The Committee could not exclude the possibility of absorption of carrageenan by the immature gut or the possibility that absorbed material might affect the immune system in the infant. The Committee does not therefore consider carrageenan acceptable for use in infant formulae (European Commission, 1992)."

The decision to ban the use of carrageenan in infant formulae, because of the 'high levels of assurance' needed, was subsequently reaffirmed by the EC-SCF (Scientific Committee on Food, 2003b). The SCF suggested that because there was insufficient information on the effect of carrageenan on the immature gut of babies, its use was inadvisable but they had 'no objection to its use to the use of carrageenan, for technological reasons, in foods for older infants, such as follow-on formulae (SCF, 1983) and weaning foods'(Scientific Committee on Food, 2003b, p. 90).

Industry has continued to support the benefits of using carrageenan in liquid infant formula and has sought to quantify risk and unequivocally assure safety to infants. New information has been provided to JECFA for their 2007 review of carrageenan.

Case III The 'Tobacman' controversy

Concerns about the use of carrageenan in food were not altogether assuaged despite the precautionary approaches adopted by various regulatory agencies and even though poligeenan, a suspected human carcinogen, is not and never has been used as a food additive. Poligeenan exists today specifically for diagnostic use only. The small amount of low molecular weight material present naturally in carrageenan is considered of no safety consequence by regulatory authorities. This is noteworthy because from time to time, academic researchers revisit the toxicity of poligeenan in relation to food grade carrageenan. The most recent and vocal researcher to enter this arena is Dr. Joanne K. Tobacman, currently at the University of Illinois in Chicago.

In *Environmental Health Perspectives* (EPH, 2001*),* a journal on environmental factors and human health, Dr. Tobacman reviewed all scientific literature relating to carrageenan safety (Tobacman (2001). The article reviewed 45 existing animal studies on poligeenan and carrageenan in relation to safety for food use. Critiques of the paper note how Dr. Tobacman ascribes results for poligeenan feeding studies to carrageenan and the disregard for how the method of administration to the animals can effect the results (Carthew, 2002; Cohen et al., 2002).

A consequence of this confusion of two different materials is exemplified in a quote from the author's interview of Dr. Tobacman in December, 2003.

'I guess that underlying this issue is the consideration about how much data are sufficient to make a judgement about carcinogenicity? Many animal studies demonstrating ulcerations and neoplasms from carrageenan (sic) exposure were completed decades ago. What evidence and how much evidence does it take to lead to changes in policy and behaviour? '(Tobacman, 2003, pers. Comm., 3 December).

For Tobacman, rather than proving safety, the weight of evidence from past studies suggested that carrageenan in foods is a risk. As already discussed, shifts in regulatory policy in the 1950s required manufactures to produce 'data' as evidence of safety. Her concern was also fuelled by a clause in the 1958 Amendment that related specifically to carcinogenicity – the so-called 'Delaney clause'. The 'Delaney clause' was introduced as an additional clause to the Food Additives Amendment in 1958 and mandated that:

'…no additive shall be deemed safe if it is found to induce cancer when ingested by man or animal, or if it is found, after tests which are appropriate for the evaluation of

the safety of food additives, to induce cancer in man or animal…' (Quoted in Dean, 1989, p. 6)

Tobacman's opponents have continued to stress that she is mixing up the suspected carcinogenicity of poligeenan with the lack of any such toxicity of carrageenan (Cohen et al., 2002; Weiner et al., 2007).

The application of the Delaney clause may also be evaluated in a contemporary policy context. Merrill's (1997) review of regulatory policy demonstrates that the regulatory authorities did not anticipate, at the time the amendment was drafted, that the clause would be applied to a vast range of substances as subsequently occurred.

'In 1958, neither advocates nor opponents of the policy, including FDA officials, believed it would have broad application, for only a handful of chemicals had then been shown to be animal carcinogens' (Merrill, 1997, p. 322)

Knowledge of cancer-producing substances in the 1950s was largely confined to polycyclic aromatic hydrocarbons; at that time not even cigarette smoke was accepted as carcinogenic (Weisburger, 1994). Not surprisingly, the 'zero risk' tolerance applied to 'new' chemicals with potential carcinogenic effects (new including regulated food additives not considered GRAS) has been extremely controversial (Merrill, 1997; Noah, 1999; Noah et al., 1998; Vogel, 2001; Weisburger, 1994). Some argue that zero risk is necessary to protect the health of the public, others that carcinogens occur naturally in many foods and are of little risk (Ames et al., 1997, 1998). Noah (1999, p. 34) suggests that the Delaney clause is used with less rigidity in food and drug law in the contemporary period because its wording preceded the development of more sensitive testing technologies and new medical knowledge about cancer. Where there is 'reasonable certainty of no harm', the Delaney clause is no longer used.

A second paper, Tobacman et al. (2001) in the journal *Medical Hypotheses* used an epidemiological technique known as a 'time-trend' analysis to correlate the increased use of carrageenan in the twentieth century with the increased incidence of breast cancer. The authors wrote that 'although time-trend correlations represent a weak form of evidence, when significant positive correlations are found, they can support further evaluation' (Tobacman et al., 2001a, p. 596).

A further response to the Tobacman papers came from the European Commission Scientific Committee for Food. A Commission report, prepared to review and

critique Tobacman's *EPH* and *Medical Hypotheses* papers, was critical of her findings in relation to the *Medical Hypotheses* article about which it concluded that it:

…did not support the hypothesis that breast cancer may be causally related to intakes of carrageenan and other water-soluble polymers used as food additives. The Committee noted that such correlations might be found for any dietary component or chemical to which there has been increasing exposure during the twentieth century (Scientific Committee on Food, 2003a, p. 6).

Furthermore, the Commission found nothing new in Tobacman's *EPH* review that had not already been considered by the Scientific Committee for Food in determining the safety, purity criteria and ADI for carrageenan.

Although the report was critical of many of Tobacman's findings, there was one issue upon which the Committee felt further research should be undertaken – the possibility that 'native' carrageenan could create significant amounts of poligeenan either by processing techniques or by acids during digestion. Like earlier controversies over baby formula the perception of risk in Europe was deemed serious enough to warrant a response. Thus regardless of the deficiencies of Tobacman's research, or the diagnostic use of poligeenan for imaging, a precautionary approach was adopted. The Committee suggested 'if feasible, a molecular weight limit of not >5% below 50,000 should be introduced into the specification to ensure that the presence of any (low molecular weight) carrageenan [in food] is kept to a minimum' (Scientific Committee on Food, 2003a, p. 6). This specification is enforced today although no appropriate, validated analytical method is available to quantify the percentage of low molecular weight material in carrageenan.

More recently Tobacman has published on bench top experiments on the interaction of carrageenan with various organ cells (Borthakur et al, 2007). The continued focus of her research has been to implicate carrageenan as a carcinogen by association. However, what happens *in vitro* does not provide a sufficient evidence base for what occurs *in vivo*. Even if a harmful relationship could be established *in vitro*, *in vivo* studies have demonstrated that ingested carrageenan does not pass the blood – gut barrier to interact with organ cells. Moreover, recent studies contradict cancer-producing effects of carrageenan and indicate that k-carrageenan may, though the enhancement of immune systems, actually inhibit tumours (Yuan et al., 2006). Work that seeks to establish a carrageenan/carcinogen link continues to be fuelled by suspicion.

Case IV Semicarbazide - A new problem handled quickly

Semicarbazide (SEM), a weak mutagen, was used for years in Europe as an indicator for the presence of the banned veterinary antibiotic, Nitrofurazone (de la Calle et al., 2005). The association between SEM and carrageenan came to attention through a circuitous route (summarized in Table 2).

Table 2. Public health concerns and semicarbazide

Pre 1950s	Azodicarbonamide (ADC) developed for use in plastics in Germany
1993	Nitrofuran drugs used in animal husbandry banned in the European Union following findings of mutagenic potential – zero-tolerance rules applied
2002	Semicarbazide (SEM), a known metabolite of nitrofurans used as marker for nitrofuran abuse – routine analysis begins with (more) sensitive methods
2003	SEM found in foods of non-animal origin including tomato sauce, egg, high levels found in baby food
2003	Denmark issues EC alert notification 2003/201 for 'carrageen derived from see weed' from Canada, Chile, Indonesia and Tanzania in relation to SEM and nitrofurans
2003	SEM linked to packaging and ADC used for PVC gaskets (extensive use in baby food)
2003	European Food Safety Authority finds SEM has weak mutagenic activity, low risk to human health. Nevertheless concerns about high levels in baby food
2004	Evidence of natural occurrence supports finding that SEM not a specific marker for nitrofuran abuse.
2004	Seaweed Industry Association Philippines announces budget to study SEM in carrageenan. Industry begins to assess alternate methods of bleaching/halt to bleaching.
June 2005	Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food concludes issue of carcinogenicity is not of concern for human health at the concentrations of SEM encountered in food.'
2005	ADC banned from use in plastics

The EC, EFSA and the World Health Organisation have declared that, based on levels reported in food, the health risk, if any, to consumers, including infants, appears to be very small (European Food Safety Authority, 2003; World Health Organization, 2007). Nevertheless, at the time the issue came to light it created concerns that carrageenan could pose a risk to human health. The carrageenan industry through its trade organization, Marinalg International, was required to perform tests for SEM on representative commercial carrageenan products and issue a response (Marinalg International, 2003).

At the time this issue arose there was a zero tolerance limits for SEM in foods, and this combined with a subsequent discovery of SEM in baby food prompted what Hoeneick et al.(2006, p. 29) describes as 'violent discussions'. The discovery of SEM in carrageenan (Hoenicke et al., 2004) demonstrated to these researchers that it was not possible to differentiate between SEM resulting from Nitrofuran abuse; SEM occurring naturally or by bleaching processes involved in producing semi-refined carrageenan (PES). Subsequently tests demonstrated that SEM had weak mutagenic activity and posed no risk to humans in the amounts likely to be consumed

(Abramsson-Zetterberg et al., 2005; AFC Panel, 2005; Hoenicke et al., 2006; Hoenicke et al., 2004).

The SEM carrageenan issue is a reminder of the constitutive power of public health regulation in initiating suspicions of risk. Combined with concerns about carrageenan associated with dated understandings of ulcerations and cancers and *potential* harm to infants in liquid infant formula, the SEM example demonstrates that understanding risk associated with carrageenan also requires an understanding of the different regulatory settings and contexts in which 'risks' emerge as public health issues. Despite all the concerns so far discussed, carrageenan is *still* regulated as safe.

Discussion and conclusion

After over fifty years of safe use of carrageenan in foods, some confusion and uncertainty in the public view still exists. One reason for this is that scientific accounts of carrageenan risk rarely demonstrate the historical, regulatory and public health contexts. Carrageenan risks are routinely taken out of context (See for example Tobacman, 2001; Tobacman et al., 2001a; Tobacman et al., 2001b).

A recent 90 day rat feeding study that was initiated to determine if a carrageenan near the lower molecular weight limit set by regulators (molecular weight of 257,000 daltons with <5% below 50,000 daltons with a range of 1.9% – 12%, determined by four different methods) would cause any toxicological responses (Weiner et al., 2006). The study concludes that carrageenan meeting regulatory purity criteria is safe for human consumption. On the basis of these findings the authors argue that the new molecular weight distribution specification for carrageenan in Europe is unnecessary. Studies of this type may help to clear up confusion from a scientific perspective, but they do not appear to resolve perceptions of safety in other contexts.

An alternative framework for assessing and communicating risk is to review issues of safety in their broader use and health contexts. For example, it is rarely mentioned that carrageenan was intentionally degraded to make C16 for use in a specific pharmaceutical product for peptic ulcer that is no longer on the market. The only use for this product today is industrial in nature (X-ray imaging diagnostics). However, renaming C16 poligeenan and the product for food use carrageenan may not be sufficient to allay public concerns. An extensive education program placing these different substances in a broader public health context may help. Without context a consumer could easily assume equivalence between carrageenan and poligeenan.

There is also the increased recognition of the potential value of carrageenan for antiviral, hypocholesterolaemic and hypoglycemic properties (Smit, 2004). If current rounds of research prove successful, carrageenan will play an important part in sexual health applications, such as microbicides for HIV/AIDs prevention and use reduce the risk of cervical cancers by inhibiting the Human Papiloma Virus (Buck et al., 2006; Fernandez-Romero et al., 2007; Population Council, 2006). This diversity of possible new uses for carrageenan across different regulatory settings provides a complex context for assessing health risks and benefits, but the positive nature of these applications will help the public and regulators to understand the potential health effects of different products.

This paper offers some insight into how various concerns within public health have influenced the risk regulatory process. At present regulation has provided support for the safe use of carrageenan in food. However, there is also the paradox that the more safety is proven, the more controversial that proof becomes.

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