# FMC BioPolymer

**FMC Corporation**
1735 Market Street
Philadelphia, PA 19103
USA

3 May, 2012

National Organic Standards Board
USDA-AMS-NOP
1400 Independence Ave. SW
Room 2648-So.
Mail Stop 0268
Washington DC 20250-0268

Electronic Submission to www.Regulations.gov

Subject: Docket ID: AMS-NOP-12-0017
Comments: Sunset – carrageenan
Technical Evaluation Report (October 3, 2011)

FMC Corporation is one of the major producers of carrageenan. We have over 50 years of experience and technical expertise in carrageenan. We appreciate the opportunity to submit comments to the NOSB with regard to the Sunset of carrageenan as a § 205.605 (a) - Nonagricultural (nonorganic) substance allowed as an ingredient in or on processed products labeled as "organic" or "made with organic (specified ingredients or food group(s))" - nonsynthetic .

We read with interest the Carrageenan Handling/Processing Technical Evaluation Report compiled by ICF for the National Organic Program. The report contains some inaccuracies and lacks some significant information. We are limiting our comments to three sections in which we believe the inaccuracies are significant enough to mislead a reviewer to draw erroneous conclusions about the production and safety of carrageenan. The three sections of interest are:

- The recommendation to classify carrageenan as a synthetic substance
- The discussion of alleged reported effects upon human health
- The discussion on environmental impact of cultivation practices

FMC

**Re: recommendation to classify carrageenan as a synthetic substance**
*(Comments provided by William R. Blakemore, President – Hydrocolloid Technology, Celtic Colloids Inc.)*

Carrageenan is extracted from specific red seaweed species under alkaline conditions to preserve the molecular weight of the extract by avoiding degradation, because acidic conditions rapidly destroy the carrageenan molecules.

Carrageenan is composed of copolymers of up to at least twelve different ideal structures; the three primary ones being kappa, iota, and lambda. These ideal carrageenan structures do not occur as pure natural polymers; thus carrageenan is comprised of at least two of these ideal structures. The primary differences between these ideal carrageenan structures are the amount and position of ester sulphate groups and presence of 3:6-anhydrogalactose.

Kappa Carrageenan

Kappa carrageenan, as found in red seaweed, is a copolymer of ideal kappa carrageenan (70%) and ideal mu carrageenan (30%). When extracted in mild alkali (pH 8), commercial kappa carrageenan comprises ideal kappa carrageenan (75%) and ideal mu carrageenan (25%), which is a small change in the ratio of these two ideal structures. Thus, the action of alkali on native kappa carrageenan simply changes the ratio of the two primary structures by converting ideal mu carrageenan to ideal kappa carrageenan.

When extracted in stronger alkali (pH 11-12), the ratio of these two ideal structures changes so that commercial kappa carrageenan comprises ideal kappa carrageenan (90-95%) and ideal mu carrageenan (5-10%).

No new structures are created by the extraction of kappa carrageenan in alkali; only the ratio of the two natural ideal structures has been changed.

Iota Carrageenan

The overview above for kappa carrageenan can be directly applied to commercial iota carrageenan, in this case the components being ideal iota carrageenan and ideal nu carrageenan, and including the same percentages in nature and under mild and stronger alkaline conditions.

Again, no new structures are created by the extraction of iota carrageenan in alkali; only the ratio of the two natural ideal structures has been changed.

Lambda carrageenan

Lambda carrageenan is a copolymer of ideal lambda carrageenan (95%) and ideal theta carrageenan (5%). The extract is always extracted in mild alkali (pH 8) to preserve this molecular composition, commercial lambda carrageenan comprising ideal lambda carrageenan (90%) and ideal theta carrageenan (10%), which is a small change in the ratio of these two ideal structures. Thus, the action of mild alkali on native lambda carrageenan simply results in a slight change of the ratio of the two primary structures by converting ideal lambda carrageenan to ideal theta carrageenan.

No new structures are created by the extraction of lambda carrageenan in alkali; only the ratio of the two natural ideal structures has been changed.

References

Blakemore, W.R. & Harpell, A.R., "Food Stabilisers, Thickeners and gelling Agents", Edited by A. Imeson, Chapter 5, Carrageenan, 2010, Wiley Blackwell, UK, ISBN 978-1-4051-3267-1.

Therkelsen, G.H., "Industrial Gums", Third Edition, Edited by Whistler, R.L. & BeMiller, J.N., Chapter 7, Carrageenan, 1993, Academic Press, USA, ISBN 0-12-746253-8.

**Re: alleged reported effects upon human health from use of petitioned substance.**
*(Comments provided by Myra L. Weiner, Ph.D., D.A.B.T., Fellow, A.T.S. Principal, TOXpertise LLC)*

We are not aware of any confirmed reported effects upon human health due to the use of carrageenan in food.

The ICF Technical Evaluation Report (TER) discusses specific *in vivo* (in the living body of an animal) and *in vitro (*outside the living body/artificial environment*)* studies. It is unclear how or why these studies were selected. Regardless, the TER makes some assumptions based on limited and incorrect information in the literature, namely that food grade carrageenan may cause human health effects from its use in food. The TER incorrectly states that the presence of low molecular weight polymer in food- grade carrageenan or the degradation of food-grade carrageenan to low molecular weight material, called "degraded carrageenan", has the potential to cause the same or similar adverse effects as those reported for "degraded carrageenan". To demonstrate our point, we refer to lines 571- 582:

> *"Today, both concern and debate exists over human health hazards from not only direct use of degraded carrageenan in foods, but also based on the idea that acid hydrolysis in the stomach following consumption of non-degraded carrageenan could result in formation of degraded carrageenan, which could then potentially promote colon cancer (Tobacman, 2001, Carthew, 2002). (Lines 571-574) In 2001, Joanne K. Tobacman published a review of 45 studies dated from 1969 through 1997, that showed that exposure to degraded and/or undegraded carrageenan was associated with intestinal lesions such as lacerations and neoplasms in several different animal models, including ferret, guinea pig, monkey, mouse, rat and rabbit (Tobacman, 2001). (Lines 574-578) Animal studies published since 1997 that were not included in Tobacman's review have shown conflicting results. While some studies have verified that carrageenan is associated with induction or promotion of gastrointestinal tract inflammation, ulcerations and / or neoplasms in animal models (e.g. Benard et al, 2010 and human tissues (e.g. Borthakur et al, 2007; Bernard et al, 2010), other studies have contradicted this finding (e.g. in vivo: Weiner et al, 2007; and in vitro: Tobacman and Walters, 2001). (Lines 579-582)* (TER page 13 of 18)

Comments:

1. **Line 571-574:** Degraded carrageenan (poligeenan) is not used directly in foods. In the assessment of carrageenan, a distinction must be made between the extracts used in the food industry (carrageenan) and poligeenan (often referred to in the literature as "degraded carrageenan"). Poligeenan uses red seaweed extract or carrageenan as a starting material. The starting material is extensively acid-hydrolyzed for extended periods of time at high temperatures and low pH. Poligeenan is the accepted name assigned by the US Adopted Names (USAN) Council. (Note: the USAN is sponsored by the American Medical Association, the US Pharmacopoeial Convention and the American Pharmacist Association.) USAN describes poligeenan as having a molecular weight of 10,000 – 20,000 and it is assigned CAS No. 53973-98-1. Poligeenan is used as a dispersing agent for

medical imaging. This distinction is essential because of the great differences in physical and toxicological properties between these two separate substances. Carrageenan has high molecular weight and exhibits textural functionality at concentrations as low as 0.01% in some systems. Poligeenan has no gelling properties whatsoever, even at a 10% concentration. Poligeenan does not have the functional properties to act as a direct food additive. It is not a food additive.

If acid hydrolysis of higher molecular weight food-grade carrageenan does occur in the gastrointestinal tract, any lower molecular weight fragments of carrageenan resulting from such degradation have not been found to cause any toxicity to test species *in vivo* (Weiner *et* al, 2007). The animal toxicology studies in which food-grade carrageenan was administered in the diet to animals at up to 5% of the diet (a limit dose under FDA guidance) on a subchronic and chronic basis failed to show any evidence of intestinal inflammation or other adverse effects. Carrageenan is a soluble fiber. Chronic administration of carrageenan in the diet to numerous species did not result in adverse effects, other than soft stools or diarrhea. These effects are commonly seen when bulking agents or dietary fibers are fed at high doses. No evidence of tumor promotion or colon cancer has been found due to carrageenan in animal dietary feeding studies *in vivo* (Cohen and Ito, 2002). This important review of carrageenan and processed eucheuma seaweed by Cohen and Ito (2002) was not included in the ICF document. The information contained in the Cohen and Ito (2002) paper was submitted to, and reviewed by, the Joint FAO/WHO Expert Committee on food Additives (JECFA) at its 57$^{th}$ meeting in 2001. As a result of that review, the JECFA assigned carrageenan an ADI of "not specified". An ADI of "not specified" is used to refer to a food substance of very low toxicity that, on the basis of the available data (chemical, biochemical, toxicological and other) and the total dietary intake of the substance arising from its use at the levels necessary to achieve the desired effects and from its acceptable background levels in food, does not, in the opinion of the Committee, represent a hazard to health. (IPCS JECFA glossary of terms).

2. **Line 574-578:** It is not appropriate to refer to the effects from exposure to "degraded and / or undegraded carrageenan" together as was done in the Technical Evaluation Report (TER) and in the review by Tobacman, 2001. As noted previously, degraded carrageenan (poligeenan) and food-grade carrageenan are two totally different substances with very different toxicological properties. In cases where the authors refer to such biological effects due to "degraded and / or undegraded carrageenan", a more careful evaluation of the test materials in the animal studies shows that the intestinal lesions stated (ulcerations, neoplasms) were reported only in studies where degraded carrageenan (poligeenan) was the test substance. Such effects were not found when food-grade carrageenan was the test substance in animal dietary feeding studies. Such generalizations tend to

become repeated in the literature without thorough review of the original references, leading to misunderstandings of the two different materials.

In addition, the JECFA concluded the following (Benford *et al*, 2008):
*"At its fifty-first meeting, the Committee concluded that such breakdown is probably of limited toxicological significance since, if native carrageenan were sufficiently degraded to cause ulceration or tumour growth,* ***this would be detected in feeding studies.***" Page 79.

No such effects of carrageenan, as described for pure degraded carrageenan (poligeenan), have been reported in the animal studies on food-grade carrageenan.

3. **Lines 579**-582: The study quoted as verifying an association of carrageenan with induction or promotion of gastrointestinal tract inflammation, ulcerations and/or neoplasms refers to Benard *et al*, 2010. The Benard et al 2010 study title states that degraded carrageenan was used. Therefore, the results of this study are not relevant to food-grade carrageenan. The other reference, Borthakur *et al*, 2007 is an *in vitro* study. The authors conclude that carrageenan activates an inflammatory pathway *in vitro*; however, the study provides only limited dose-response data and has limited demonstration of reproducibility. In addition, the use of spontaneously immortalized human colon epithelial cells may not be a good model of human colon cells. This model has not been verified with humans. Studies in animals have not demonstrated activation of inflammation *in vivo*. When carrageenan is ingested in food, it becomes bound to proteins in the food and is less accessible to the intestinal epithelial cells compared to the addition of carrageenan directly to cell cultures. Thus, the cell cultures do not accurately mimic the human exposure to carrageenan in food. It is speculative and hypothetical to conclude, as Borthakur *et al* (2007) does, that carrageenan might have a role in intestinal inflammation and possibly inflammatory bowel disease. There is simply no evidence to support this suggestion.

   The TER correctly states that the *in vivo* 90-day dietary study in which rats were fed carrageenan (Weiner *et al*, 2007) contradicts the work of Benard *et al* (2010) which used degraded carrageenan. The Weiner et al, 2007 study is significant because it used a carrageenan sample specifically altered to contain a low molecular weight tail of 7% (mean) carrageenan to maximize any potential effects of the lower molecular weight fraction on the gastrointestinal tract. (Note: The 7% (mean) low molecular weight fraction is 40% greater than the 5% specification proposed by the European Commission's Scientific Committee for Food in March, 2003). "There were no treatment related effects on body weights, urinalysis, hematology, or

clinical chemistry parameters, or on organ weights or ophthalmic, macroscopic or microscopic findings. The gastrointestinal tract appeared normal in detailed histopathological evaluation using the Swiss roll technique." (Weiner et al, 2007).

As a general comment, when reviewing the literature about carrageenan it is important to:

- Differentiate carrageenan from poligeenan ("degraded carrageenan")
- Understand the context of the study,
- Determine applicability of the route of exposure
- Examine the evidence from the body of relevant literature

References


Benard,C., Cultrone,, A., Michel, C., Segain, J.P. et al 2010. Degraded carrageenan causing colitis in rats induces TNF secretion and ICAM-1 upregulation in monocytes through NF-kB activation. PLoS ONE 5(1): e8666.

Borthakur, A., Bhattacharyya, S., Dudeja, P.K., Tobacman, J.L. 2007. Carrageenan induces interleukin-8 production through distinct Bcl10 pathway in normal human colonic epithelial cells. AJP-GI 292(3): G829-G838.

Cohen, S.M. and Ito, N. A Critical Review of the Toxicological Effects of Carrageenan and Processed Eucheuma Seaweed on the Gastrointestinal Tract. Critical Reviews in Toxicology, 32(5): 413-444. (2002)

European Commission Health and Consumer Protection Directorate: Scientific Committee on Food. Opinion of the Scientific Committee on Food on Carrageenan (expressed on 5 March, 2003). SCF/CS/ADD/EMU/199 Final.

IPCS JECFA glossary of terms. http://www.who.int/foodsafety/chem/jecfa/glossary.pdf

Tobacman, J.K. 2001. Review of harmful gastrointestinal effects of carrageenan in animal experiments. Environmental Health Perspectives 109: 983-994.

USAN Council. List No. 297 – New Names. Reprinted from Clinical Pharmacology and Therapeutics 44(2): 246-248, August, 1988.

Weiner, M.L. *et al.* A 90-day study on kappa carrageenan with emphasis on the gastrointestinal tract. Food and Chemical Toxicology 45(2007) 98-106.

WHO Food Additive Series: 48. Safety evaluation of certain food additives and contaminants. Prepared by the fifty-seventh meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). Carrageenan and Processed Eucheuma Seaweed (addendum). Prepared by Dr. D.J. Benford.

WHO Food Additive Series: 59. Safety evaluation of certain food additives and contaminants. Prepared by the sixty-eighth meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). Page 79

**Re: The discussion on environmental impact of cultivation practices**

*(Comments provided by Erick Ask, M.S. Marine Agronomy/Applied Phycology– FMC Corporation)*

In a discussion about the overharvesting of Gigartina in Chile, the review states that "overall biomass was reduced and individual plants were smaller, resulting in many infertile plants (Faugeron et al., 2004). This is a questionable conclusion. Harvesting too soon in the season before algae reproduces can reduce the population the next year. Harvesting does not cause infertility.

By way of clarification about seaweed farms (Lines 479-496):

a. To create a seaweed farm, vegetative propagules are tied to ropes. These ropes are anchored in one of three ways. In intertidal farms, wooden stakes are use. In floating systems both rafts and floating long lines are used.
b. In response to the discussion about invasive seaweed species and impact on coral reefs, we bring to your attention that in our experience, more than 80% of farmed carrageenophyte volume is produced in the Philippines, Indonesia and Tanzania where the species are native. The problems described with invasive issues (lines 483-496) indicate that prior to introduction, there needs to be a clear project plan with ecological studies including a survey of existing native herbivores. Fish of the family Siganidae are herbivorous and control farmed carrageenophytes lost from farms. However this Siganidae don't exist in Hawaii. The sea urchin, *Tripneustes gratilla* eats farmed carrageenophytes and does exist in Hawaii but is overfished by residents of the state of Hawaii for personal consumption. Farmed carrageenophytes were also introduced to many countries of the South Pacific in the 1970's and 80's which have not reported problems of invasive species and do have Siganidae fish and *Tripneustes gratilla* providing herbivore pressure. The TER reference to work in India fails to mention that it was subject to criticism from other marine scientists in India.

Lines 497 – 514 references 3 studies discussing the environmental impact of seaweed farms on the composition of aquatic community. These studies looked only at a few locations in Zanzibar, which used the intertidal system. Zanzibar produces 5% of the world's farmed carrageenan. To better appreciate environmental impact it would be important to study the floating farms and sandy bottom farms of the Philippines and Indonesia as well as the sandy bottom farms of Zanzibar, where the majority of seaweed is farmed (no coral, no eelgrass, no native seaweed beds). In addition, in Tanzania there are about 3,500 square km of coral reef area. http://coral.unep.ch/atlaspr.htm At 12,000mt/year of dried seaweed production, farms would cover two to three square km total, or less than 0.1% of coral reef area. In addition, we must realize that if coastal inhabitants are not farming seaweed, they would still be engaged in over fishing, coral harvesting, reef gleaning and other extractive and destructive activities. Regarding stress, if farmed seaweed is always stressed it does not grow and farmers stop farming because they cannot produce a crop to sell. So, generally speaking, people farm seaweed in areas where the seaweed is healthy and productive, not producing toxic organic compounds.

The benefit of multitrophic integrated aquaculture to sustainability, as described in lines 523-531, is primarily for cleaning up the waste of fish farms. Seaweed farms can serve the same purpose, consuming inorganic nutrients, if situated to consume these nutrients from agriculture and urban runoff. Such nutrient loads have been shown to cause wild seaweed blooms that

smother coral reefs. In all these cases, the seaweed farms serve the additional role as nutrient sink and primary water treatment.

In its discussion of waste and effluent from the manufacture of carrageenan, the review states that "the act of farming seaweed can result in a number of secondary environmental impacts, such as increased pollution on beaches and physical damages to reefs, coastal ecosystems, and mangroves (Zemke-White and Smith, 2006). " We respectfully bring to your attention that there are now over 100million Filipinos and 240million Indonesians. Pollution and habitat destruction are more to do with human population growth and the demands they place on the ecosystem, not seaweed farms.

With regard to the use of plastics (lines 543 – 544), we recognize that plastics are an issue and the farming communities know it. FMC is working with the Philippine Dept. of Science and Technology on recycling waste farm ropes to see if we can implement appropriate technology to recycle this waste.
http://www.swapp.org.ph/attachments/article/293/Municipal%20SWM%20Technologies%20-dost%20itdi.pdf

With regard to the impact on mangroves (lines 544-550), over the last twenty years there has been a large effort made to reforest mangroves and manage these forests by local communities in SE Asia and the Western Indian ocean. For example http://www.bohol-philippines.com/panadtaran-mangrove-association.html . Admittedly, there are problems but these problems can be solved with effort, education and guidance.

References

Conklin K. A. Kurihara and A. Sherwood. (2009). A molecular method for identification of the morphologically plastic invasive algal genera Eucheuma and Kappaphycus (Rhodophyta, Gigartinales ) in Hawaii. Journal of Applied Phycology 21(6) pp. 691-699.

Conklin E. and J. Smith (2005) Abundance and Spread of the invasive Red Algae, Kappaphycus spp., in Kane'ohe Bay, Hawaii and an Experimental Assessment of management options biological Invasions Journal of Applied Phycology 7(6) pp. 1029-1039

A Tewari, K. Eswaran, P.V. Subba Rao and B. Jha (2006) is Kappahycus alvarezii heading towards marine bioinvasion? Current Science 90(5) pp. 619-620.

Conclusions

The extraction of carrageenan in alkali avoids degradation of the molecular structure. Use of alkali simply changes the ratio of the natural ideal structures present in the seaweeds . No new molecular components are created. The continued listing of carrageenan as "nonsynthetic" is appropriate.

The weight of the evidence from numerous animal feeding studies continues to demonstrate that carrageenan is safe for use in food for human consumption.

There is insufficient basis to reclassify carrageenan as a synthetic because there is not yet agreement within the NOSB on the criteria to be used to make such a determination. This is evidenced by the Material Committee's Extractants and Solvents Discussion Paper of March 21, 2012 which is only scheduled for discussion at the upcoming May 2012 NOSB meeting.

Carrageenan remains safe and suitable for use in food and warrants relisting as a 7 CFR 205.605(a) - Nonagricultural (nonorganic) substance allowed as an ingredient in or on processed products labeled as "organic" or "made with organic (specified ingredients or food group(s) – nonsynthetic.

Sincerely,

Eunice M. Cuirle

Eunice M. Cuirle
Manager, Global Regulatory Affairs