October 26, 2016

National Organic Standards Board
USDA-AMS
1400 Independent Ave. SW
Washington, D.C. 20250
Re: AMS-NOP-16-0049

Docket # AMS-NOP-16-0049

Dear National Organic Standards Board Members:

The following comments are submitted to you on behalf of The Cornucopia Institute, whose mission is to support economic justice for family scale farming.

HANDLING SUBCOMMITTEE

Carrageenan - 2018 Sunset

SUMMARY

The Cornucopia Institute **opposes** the relisting of carrageenan at 205.605(a) Nonagricultural (Nonorganic) substances allowed as ingredients in or on processed products labeled as ''organic'' or ''made with organic (specified ingredients or food group(s))" because **of decades of publicly funded scientific research showing biological reactivity in human cells, causing harm to human health**. Carrageenan also lacks essentiality.

We are encouraged by the Handling Subcommittee's recent vote to remove carrageenan, but have submitted the following comments to directly respond to inaccurate statements made by the carrageenan lobby and the NOSB Handling Subcommittee.

Rationale:

- Carrageenan is nonessential. **Every organic product containing carrageenan has a certified organic alternative, being produced by one or more competitors.**

- **It is an undisputed fact that degraded carrageenan is present within all food-grade carrageenan.** The industry-funded Marinalg Working Group found that bioactive, low-molecular-weight carrageenans (poligeenan) were present in

all samples of food-grade carrageenan.[1] Marinalg is the industry's trade lobby group.

- Poligeenan also emerges as an inevitable by-product of higher-molecular-weight carrageenan, due to breakdown of carrageenan into di-galactose subunits from digestion (i.e., mechanical effects, acid, heat, and bacteria).[2,3]

- Not all of ingested carrageenan is excreted. Effects of carrageenan include an immune response and the inflammatory cascade. These processes do not require carrageenan to be absorbed, but just to interact with the intestinal mucosa. (Tobacman personal communication)

- The industry-funded McKim studies do not show that experiments from public institutions are not reproducible. McKim performed different experiments, with different methods, using different cell lines, different concentrations of carrageenan, and different time periods. (Tobacman personal communication)

- The 2005 European Commission's recommendation that no more than 5% of food-grade carrageenan fractions should have molecular weight below 50 kDa[4] has not been met by the industry.[5,6]

- The accusations that research showing glucose intolerance is all from one research team and has not been replicated is **simply not true**. In fact, some of the industry reports, including older studies in primates, demonstrate elevated blood sugars in the experimental animals.[7]

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[1] Marinalg International (2006) Technical Position on Measurements Related to Meeting the EC Molecular Weight distribution Specification for Carrageenan and PES. (Formally available online, but later removed by the company. Appendix B in Cornucopia's carrageenan report www.cornucopia.org).

[2] Uno Y, Omoto T, Goto Y, Asai I, Nakamura M, and Maitani T (2001) Molecular weight distribution of carrageenans studies by a combined gel permeation/inductively coupled plasma (GPC/ICP) method. *Food Additives and Contaminants* 18: 763-772.

[3] Pittman KA, Goldberg L, and Coulston F (1976) Carrageenan: the effect of molecular weight and polymer type on its uptake, excretion and degradation in animals. *Food and Cosmetics Toxicology* 14(2):85-93.

[4] European Committee Scientific Committee on Food. Opinion on Carrageenan. Expressed on 5 March 2003. Available online: http://ec.europa.eu/food/fs/sc/scf/out164_en.pdf. Last accessed March 23, 2016.

[5] www.coruncopia.org (reports tab)

[6] Marinalg International (2006) Technical Position on Measurements Related to Meeting the EC Molecular Weight distribution Specification for Carrageenan and PES. (Formally available online, but later removed by the company. Appendix B in Cornucopia's carrageenan report www.cornucopia.org).

[7] McKim JM, Baas H, Rice GP, Willoughby JA, Weiner ML, Blakemore W. (2016) Effects of carrageenan on cell permeability, cytotoxicity, and cytokine gene expression in human intestinal and hepatic cell lines. *Food and Chemical Toxicology* 96:1-10.

- Despite what the carrageenan lobby claims, older studies also distinguish between high and low-molecular-weight carrageenan, as evidenced in the review of carrageenan research published in *Environmental Health Perspectives*, showing molecular weights with each study.[8]

- **The positions taken by regulatory agencies have been influenced by aggressive lobbying and industry-funded reports about carrageenan — by law, the NOSB needs to take a more critical approach.** The NOSB should practice the *precautionary principle* — there is ample reason to err on the side of caution.

- Questions about the relevance of studies using high-molecular-weight carrageenan in water are unfounded — carrageenan is often added to liquid products with high water contents. (Tobacman personal communication)

- The 2016 TR states that, "carrageenan can be avoided by sensitive individuals as it is included in the label, thereby making it easy to avoid." This is incorrect. With this logic, all "sensitive" consumers would have to be knowledgeable about carrageenan's inflammatory characteristics. Furthermore, when carrageenan is a "secondary" ingredient, as in condensed milk, milk powders, chocolate, and cream, it is often not listed on the label.

- The statement made by the NOSB subcommittee that "only some people are sensitive" is inaccurate. **Carrageenan is bioactive and inflammatory (and a potential carcinogen, due to long-term exposure) in all individuals, not just those who exhibit acute symptoms due to the galactose-alpha-1,3-galactose bond, which humans do not make.** Therefore, the effects of carrageenan occur in all individuals and are independent of the molecular weight, although more harmful effects are observed with lower-molecular-weight carrageenans (present in all food-grade carrageenan).

- The industry has also tried to discount studies in human colonic epithelial cell line NCM460, routinely used in many cell culture studies (not just investigating carrageenan), because it enables survival in culture. This is not an issue! All of the studies had controls that were **not** exposed to carrageenan for comparison, and data were analyzed by appropriate statistics. (Tobacman personal communication)

[8] Tobacman JK (2001) Review of Harmful Gastrointestinal Effects of Carrageenan in Animal Experiments. Environmental Health Perspectives 109(10):983-994.

- Studies have also shown inflammation in normal human colonic epithelial cells from colon surgery specimens, from other established rodent and human intestinal cell lines, and in mouse models.[9]

- The lack of more "dose-response" studies has been erroneously criticized in reports funded by the industry; several dose-response studies have been performed. **The amount of carrageenan exposure in many of the experiments that demonstrate inflammation is less than what is consumed in the typical diet.** (Average carrageenan consumption of 250 mg/day. Levels of daily consumption of carrageenan in the diet may be much higher, on the order of 18-40 mg/kg/d). (Tobacman personal communication)

- The 2016 TR failed to examine at least 16 pertinent, peer-reviewed, and published studies (and two letters submitted to the Lancet). Thus, the Handling Committee was unable to consider these findings.

New Studies Since the Spring 2016 NOSB Meeting:

- Bhattacharyya S, Shumard T, Xie H, Dodda A, Feferman L, Halline A, Goldstein JL, Hanauer SB (2016) Mo1792 Effects of the No Carrageenan Diet on Ulcerative Colitis Disease Activity: A Pilot and Feasibility Study. *Gastroenterology* 105(4):S777. **Summary of findings**: An association between carrageenan intake and earlier relapse in ulcerative colitis was found. Restriction of dietary carrageenan consumption benefits patients with ulcerative colitis.

- Fahoum L, Moscovici A, David S, Shaoul R, Rozen G, Meyron-Holtz EG, and Lesmes U. (2016) Digestive fate of dietary carrageenan: Evidence of interference with digestive proteolysis and disruption of gut epithelial function. *Molecular Nutritional Food Research.* **Summary of findings**: Food grade carrageenan may reduce protein and peptide bioaccessibility, disrupt normal epithelial function, promote intestinal inflammation and compromise consumer health.

DISCUSSION

Carrageenan is a direct food additive with an **average** molecular weight of 200-800 kDa, and may be referred to as "undegraded" or "native" carrageenan in the literature. However, **average molecular weights are misleading, because all carrageenan contains some detectable percentage of degraded carrageenan (degraded carrageenan is used to study inflammation, cancer and anti-inflammatory drugs)**. The kappa, iota, or lambda formation of carrageenan is defined by the number and position of sulfate groups, but all types are used in foods.

[9] Borthakur A, Bhattacharyya S, Dudeja PK, and Tobacman JK (2007) Carrageenan induces interleukin-8 production through distinct Bc110 pathway in normal human colonic epithelial cells. *American Journal of Gastrointestinal Liver Physiology* 292: G829-G838.

The European Commission's recommendation that no more than 5% of carrageenan fractions should have molecular weight below 50 kDa[10] has been impossible for the industry to comply with, based on their own reports.[11] Carrageenans with molecular weights less than 50kDa are thought to cause the most severe health problems.

A number of studies by multiple researchers have identified potential human health concerns by consuming carrageenan, such as:

- The **study** by Pittman, Golberg and Coulston (1975)[12], **demonstrated that high-molecular-weight carrageenans are degraded to some extent as a result of their passage through the intestinal tract**.
- The findings of Capron, Yvon and Muller (1996)[13] showed that **after 2 hours in simulated gastric juice at pH 1.2, almost 90% of the carrageenan had a mass of less than 100 kDa and 25% had a mass of less than 20 kDa**.
- Grasso et al. (1973)[14] identified multiple pin-point caecal and colonic ulcerations in guinea pigs after being fed 5% diet of carrageenan for 45 days.
- A series of studies from many scientists [15,16,17,18,19,20] demonstrated that food-grade carrageenan **can induce a complex inflammatory cascade in human intestinal epithelial cells through an immune-response.**

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[10] European Committee Scientific Committee on Food. Opinion on Carrageenan. Expressed on 5 March 2003. Available online: http://ec.europa.eu/food/fs/sc/scf/out164_en.pdf. Last accessed March 23, 2016.

[11] Marinalg International (2006) Technical Position on Measurements Related to Meeting the EC Molecular Weight distribution Specification for Carrageenan and PES. (Formally available online, but later removed by the company. Appendix B in Cornucopia's carrageenan report www.cornucopia.org).

[12] Pittman KA, Goldberg L, and Coulston F (1976) Carrageenan: the effect of molecular weight and polymer type on its uptake, excretion and degradation in animals. *Food and Cosmetics Toxicology* 14(2):85-93.

[13] Capron IM, Yvon, and Muller G (1996) In-vitro gastric stability of carrageenan. *Food Hydrocolloids* 10(2):345.

[14] Grasso PM, Sharrat MB, Carpanini, and Gangolli SD (1973). "Studies on Carrageenan and Large-bowel Ulceration in Mammals." *Food Cosmetic Toxicology* 11:555-564.

[15] Borthakur A, Bhattacharyya S, Anbazhagan AN, Kumar A, Dudeja PK, Tobacman JK. (2012) Prolongation of carrageenan-induced inflammation in human colonic epithelial cells by activation of an NFκB-BCL10 loop. *Biochimica Biophysica Acta* 1822(8):1300-7.

[16] Bhattacharyya S, Dudeja PK, Tobacman JK. (2008) Carrageenan-induced NFkappaB activation depends on distinct pathways mediated by reactive oxygen species and Hsp27 or by Bcl10. *Biochimica Biophysica Acta* 1780(7-8):973-82.

[17] Bhattacharya, Sumit, et al. (2010) B-cell CLL/Lymphoma 10 (BCL10) Is Required for NF-kB Production by Both 316 Canonicl and Noncanonical Pathways and for Nf-kB-inducing Kinase (NIK) Phosphorylation. *Journal of Biological Chemistry* 285(1): 522-530.

[18] Borthakur A, Bhattacharyya S, Dudeja PK, and Tobacman JK (2007) Carrageenan induces interleukin-8 production through distinct Bc110 pathway in normal human colonic epithelial cells. *American Journal of Gastrointestinal Liver Physiology* 292:G829-G838.

[19] Bhattacharya S et al. (2010) Carrageenan-induced innate immune response is modified by enzymes that hydrolyze distinct galactosidic bonds. *Journal of Nutritional Biochemistry* 21: 906-913.

[20] Bhattachayra S, Feferman L, and Tobacman JK. (2015) Carrageenan Inhibits Insulin Signaling through GRB10-mediated Decrease in Tyr(p)-ISR1 and through Inflammation-induced Increase in Ser(P)[307]-IRS1. *Journal of Biological Chemistry* 290(17): 10764-10774.

- Undegraded carrageenan is associated with intestinal ulcerations and neoplasms, due to contamination with low-molecular-weight carrageenan.[21,22,23,24,25,26,27]

Technical Reviews (TR's) should be completed by independent scientists with advanced degrees in related fields. Below are some missing studies from the 2016 Technical Review of Carrageenan. That TR was completed by two individuals with bachelor's degrees and missed many of these important peer-reviewed studies performed by multiple scientists around the world.

- Marinalg International (2006) Technical Position on Measurements Related to Meeting the EC Molecular Weight distribution Specification for Carrageenan and PES. (Formally available online, but **later removed by the trade lobby organization**. Appendix B in Cornucopia's carrageenan report www.cornucopia.org). **Summary of findings**: **Degraded carrageenan was found in all food-grade carrageenan samples, but the percentage could not be replicated across different labs.**
- Tobacman JK (2015) The Common Food Additive Carrageenan and the alpha-gal epitope. *Journal of Allergy and Clinical Immunology* 136(6): 1708-9. **Summary of findings**: The specific chemical composition of carrageenan is immunogenic due to the presence of the galactose-alpha-1,3-galactose bond, which humans do not make. Therefore, the effects of carrageenan occur in all individuals and are independent of the molecular weight of the carrageenan ingested, although more harmful effects occur from low molecular weight carrageenan.
- Coleman MR and Coleman MT (2015) "Dairy-free" dietary substitute, abdominal pain, and weight loss. *Clinical Medical Reviews and Case Reports* 2:8. **Summary of findings**: Elimination of carrageenan-containing almond milk from the diet of a patient that had substituted it for cow's milk several months prior resulted in stabilization of weight and resolution of abdominal pain.
- Jung TW, Lee SY, Hong HC, Choi HY, Yoo JH, Baik SH, and Choi KM (2014) AMPK activator-mediated inhibition of endoplasmic reticulum stress ameliorates carrageenan-induced insulin resistance through the suppression of

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[21] Nicklin S and Miller K (1984) Effect of orally administered food-grade carrageenans on antibody-mediated and cell-mediated immunity in the inbred rat. *Food Chemical Toxicology* 22(8): 615-621.
[22] Rustia M, Shubik P, and Patil K (1980) Lifespan carcinogenicity tests with native carrageenan in rats and hamsters. *Cancer Letters* 11:1-10.
[23] Pittman KA, Goldberg L, and Coulston F (1976) Carrageenan: the effect of molecular weight and polymer type on its uptake, excretion and degradation in animals. *Food and Cosmetics Toxicology* 14(2):85-93.
[24] Engster M and Abraham R (1976) Cecal response to different molecular weights and types of carrageenan in the guinea pig. *Toxicology and Applied Pharmacology* 38(2):265-282.
[25] Poulsen E (1973) Short-term Peroral Toxicity of Undegraded Carrageenan in Pigs. *Food Cosmetic Toxicology* 11:219-227.
[26] Benitz KF, Golberg L, and Coulston F (1973) Intestinal Effects of Carrageenans in the Rhesus Monkey (Macaca mulatta). *Food Cosmetic Toxicology* 11:565-575.
[27] Grasso P, Sharrat M, Carpanini MB, and Gangolli SD (1973) Studies on Carrageenan and Large-bowel Ulceration in Mammals." *Food Cosmetic Toxicology* 11:555-564.

selenoprotein P in HepG2 hepatocytes. *Molecular and Cellular Endocrinology* 382(1):66-73. **Summary of findings**: Carrageenan causes inflammation through toll-like receptor 4, which plays an important role in insulin resistance and type 2 diabetes mellitus. Carrageenan induces endoplasmic reticulum (ER) stress in a time- and dose-dependent manner.

- Bhattacharyya S, Feferman L, and Tobacman JK (2014) Regulation of Chondroitin-4-Sulfotransferase (CHST11) Expression by Opposing Effects of Arylsulfatase Bon BMP4 and Wnt9A. *Biochim Biophys Acta* 1849(3): 342-352. **Summary of findings**: Exposure to the common food additive carrageenan, which reduces ARSB activity, reduced expression of bone morphogenetic protein (BMP)-4 in colonic epithelium and increased Wnt9A expression and Wnt/β-catenin signaling.
- Bhattacharyya S, Feferman L, and Tobacman JK (2014) Increased Expression of Colonic Wnt9A through Sp1-mediated Transcriptional Effects involving Arylsulfatase B, Chondroitin 4-Sulfate, and Galectin-3 *The Journal of Biological Chemistry* 289(25): 17564-17575. **Summary of findings**: Mechanism by which Wnt expression was increased by carrageenan exposure was unknown. Extracellular events can regulate transcription through changes in arylsulfatase B and chondroitin 4-sulfation.
- Yang B, Bhattacharyya S, Linhardt R and Tobacman JK (2012) Exposure to common food additive carrageenan leads to reduced sulfatase activity and increase in sulfated glycosaminoglycans in human epithelial cells. *Biochimie* 94(6): 1309-16. **Summary of findings**: Exposure to small amounts of food-grade carrageenan reduces the activity of sulfatase enzymes, which are critical for many vital cellular processes.
- Bhattacharyya S, Dudeja PK and Tobacman JK (2010) Tumor necrosis factor alpha-induced inflammation is increased but apoptosis is inhibited by common food additive carrageenan. *Journal of Biological Chemistry* 285(50): 39511-22. **Summary of findings**: This study examines the particular mechanisms by which food-grade carrageenan cause inflammation.
- Bhattacharyya S, Gill R, Chen ML, Zhang F, Linhardt RJ, Dudeja PK and Tobacman JK (2008) Toll-like receptor 4 mediates induction of the Bcl10- NFkappaB-interleukin-8 inflammatory pathway by carrageenan in human intestinal epithelial cells. *Journal of Biological Chemistry* 283(16): 10550-8. **Summary of findings**: Exposure of human colonic epithelial cells in tissue culture to small quantities of food-grade carrageenan was associated with changes in molecular signaling pathways that resemble the changes found in human colonic polyps. Untreated polyps can develop into colon cancer.
- Bhattacharyya S, Borthakur A, Dudeja PK and Tobacman JK (2008) Carrageenan induces cell cycle arrest in human intestinal epithelial cells in vitro. *Journal of Nutrition* 138(3): 469-75. **Summary of findings**: Exposure of human colonic epithelial cells in tissue culture to small quantities of undegraded (food-grade) carrageenan produced an increase in cell death with cell cycle arrest, effects that can contribute to ulcerations.

- Bhattacharyya S, Borthakus A, Dudeja PK and Tobacman JK (2007) Carrageenan reduces bone morphogenetic protein-4 (BMP4) and activates the Wnt/ beta-catenin pathway in normal human colonocytes. *Digestive Diseases and Sciences* 52(10): 2766-74. **Summary of findings**: This study identified mechanisms by which food-grade carrageenan influences the development of human intestinal polyps. Untreated intestinal polyps can develop into colon cancer.
- Suzuki J, Na HK, Upham BL, Chang CC and Trosko JE (2000) Lambda-carrageenan-induced inhibition of gap-junctional intercellular communication in rat liver epithelial cells. *Nutrition and Cancer* 36(1): 122-8. **Summary of findings**: Carrageenan functions as a tumor-promoting chemical by inhibiting GJIC (Gap-junctional intercellular communication is believed to help healthy cells fight cancer). The data revealed inhibition of GJIC by carrageenan similar to that by the well-documented tumor promoter phorbol ester.
- Corpet DE, Taché S, and Préclaire M (1997) Carrageenan given as a jelly does not initiate, but promotes the growth of aberrant crypt foci in the rat colon. *Cancer Letters* 114:53–55. **Summary of findings**: Consumption of food-grade carrageenan promotes the growth of aberrant crypt foci in the rat colon. Aberrant crypt foci are abnormal glands in the colon that are precursors to polyps and are one of the earliest changes seen in the colon that may lead to cancer.
- Calvert RJ and Reicks M (1988) Alterations in colonic thymidine kinase enzyme activity induced by consumption of various dietary fibers. Proceedings of the Society for Experimental Biology and Medicine 189:45–51. **Summary of findings**: Researchers examined the reported effects of various dietary fibers on chemically induced colon carcinogenesis in rats. This study found a four-fold increase in thymidine kinase activity (a measure for malignant disease) in colonic mucosa following exposure to food-grade carrageenan. No differences were found following exposure to guar gum, a food additive used as an alternative to carrageenan.
- Arakawe S, Okumua M, Yamada S, Ito M, Tejima S (1986) Enhancing effect of carrageenan on the induction of rat colonic tumors by 1,2-dimethylhydrazine and its relation to ß-glucuronidase activities in feces and other tissues. *Journal of Nutritional Science and Vitaminology* 32:481–485. **Summary of findings**: Higher rates of tumors were found in rats fed undegraded carrageenan in the diet.
- Watt J and Marcus R (1981) Danger of carrageenan in foods and slimming recipes. *The Lancet* 317(8215): 338. **Letter to The Lancet**: Scientists repeat their concern with the use of carrageenan in food in a letter to The Lancet.
- Watt J and Marcus R (1980) Potential hazards of carrageenan. *The Lancet* 315(8168): 602-603. **Letter to The Lancet**: The authors of published research showing increased rates of ulcerative colitis-like disease in laboratory animals given food-grade carrageenan wrote the letter to The Lancet. Highly respected, The Lancet is one of the world's leading medical journals. The scientists express their concern with the safety of carrageenan in food.
- Watanabe K, Reddy BS, Wong CQ, Weisburger JH (1978) Effect of dietary undegraded carrageenan on colon carcinogenesis in F344 rats treated with

azoxymethane or methylnitrosourea. *Cancer Research* 38:4427–4430. **Summary of findings**: This study found higher rates of tumors in rats fed food-grade carrageenan in the diet.

Carrageenan is Not Essential

Many brands are now using the lack of carrageenan in their formulations as a consumer marketing tool. **Over the past five years, a number of prominent companies have announced they have, or will soon, removed carrageenan from their product lines.** These companies include WhiteWave, one of the largest marketers of organic/natural foods in the country, who has removed it from many of their products, including Tuberz yogurt for children, chocolate milk, and whipping cream.

In response to growing marketplace concern, the following companies have completely removed carrageenan from their product lines: Almond Breeze®, Amazing Grass Kidz Superfood®, Annie's®, Califia Farms®, Good Karma®, and Organic Valley®.

In other cases companies continue to defend its safety, frequently posting biased information, supplied by lobbyists to the carrageenan industry, on their websites.

The Cornucopia Institute's webpage (www.cornucopia.org), under the "Reports" tab, has the latest resources on carrageenan in products, including a buyers' guide to help families choose products without carrageenan — in every product category, there are one or more brands that offer the same product in certified organic form without using carrageenan.

CONCLUSION

The Cornucopia Institute **opposes** the relisting of carrageenan at 205.605(a), because of harm to human health and lack of essentiality. The carrageenan industry has tried for decades to retain the use of carrageenan in food products, because of its cost-effective biological reactivity with ingredients. **This same biological reactivity is what makes carrageenan harmful**.

Efforts by industry to cover up the harmful effects of carrageenan resemble similar time-tested efforts by those with other vested interests (tobacco, climate change, fracking, etc.). **This misinformation campaign must not go unchallenged. The organic sector expects and deserves better.**

The reason Congress established the power of the NOSB to review synthetic and nonorganic food ingredients and other inputs was under the assumption that there would be a higher, more rigorous standard set for organic foods, in comparison to conventional protocols.

Since all independently funded, public research illustrates the danger to human health from ingesting food-grade carrageenan and most, but not all, industry-funded research suggests the opposite, it would be generous to suggest that the current scientific literature is "mixed."

It is incumbent upon the NOSB to erro on the side of caution, operating under the *Precautionary Principle*, by excluding carrageenan from use in organic foods.