

Carrageenan

New Studies Reinforce Link to Inflammation, Cancer and Diabetes



CORNUCOPIA
INSTITUTE

Updated Report by The Cornucopia Institute | April 2016

The Cornucopia Institute wishes to thank Dr. Joanne Tobacman for her invaluable support in creating this report.

This report was made possible by generous financial contributions from:

Forrest and Frances Lattner Foundation

Wallace Genetic Foundation (original study funding)

And the thousands of family farmers and their “urban allies” who fund our work with their generous donations.

The Cornucopia Institute is dedicated to the fight for economic justice for the family-scale farming community. Through research and education, our goal is to empower farmers and eaters in the good food movement, both politically and through marketplace initiatives.

Cornucopia’s Organic Integrity Project acts as a corporate and governmental watchdog, assuring that no compromises are made to the credibility of organic farming methods and the food it produces in the pursuit of profit. We actively resist regulatory rollbacks and the weakening of organic standards to protect and maintain consumer confidence in the organic food label.

The Cornucopia Institute

P.O. Box 126
Cornucopia, WI 54827
608-625-2000 voice
866-861-2214 fax

cultivate@cornucopia.org
www.cornucopia.org

Design and layout by Draft Horse Studio | drafhorsestudio.com
Cover photos source: istockphoto.com

Note: This version, updated October 2016, includes layout and cosmetic changes only. No content has been changed from the previous 2016 version.

Copyright © 2016, The Cornucopia Institute

Table of Contents

Contents

Executive Summary	4
A Summary of the Science on Carrageenan	9
Consumer Responses: Carrageenan & GI Symptoms	11
Myths and Truths: Carrageenan in Food	13
What is Carrageenan Doing in Organic Food?	17
NOSB 2018 Sunset Review of Carrageenan	19
Food Manufacturers' Responses to Scientific Data about Carrageenan	21
Industry Confirms, then Hides Poligeenan in Food-grade Carrageenan	22
Consumers: Taking Action	23
Appendix A: Scientific Findings 1969–2016	25
Appendix B: Marinalg Working Group on Molecular Weight Distribution Specification for Carrageenan	32
Endnotes	41

Executive Summary

CARRAGEENAN IS A COMMON FOOD ADDITIVE extracted from red seaweed. For the past four decades, scientists have warned that the use of carrageenan in food is not safe. Animal studies and in-vitro studies with human cells have repeatedly shown that food-grade carrageenan* causes gastrointestinal inflammation and higher rates of intestinal lesions, ulcerations, and even malignant tumors. In fact, roughly 3,855 research papers show that carrageenan induces inflammation, most of which test the effectiveness of anti-inflammatory drugs.¹

In the past decade, researchers have successfully identified several ways in which food-grade carrageenan causes harm. The chemical structure of carrageenan—unique chemical bonds not found in other seaweeds or gums—affects the body in several ways. Most notably, it triggers an immune reaction, which leads to inflammation in the gastrointestinal system. Prolonged inflammation is a precursor to more serious diseases, including cancer.

What is carrageenan?

Carrageenan is derived from specific seaweeds, which are processed with alkali into a widely used “natural” food ingredient. When processed with acid instead of alkali, carrageenan

* In this report, we use the term “food-grade carrageenan” and “undegraded carrageenan” interchangeably, to distinguish it from “degraded carrageenan” which has a low molecular weight and has been used in thousands of studies to predictably cause inflammation and disease in laboratory animals.



Carrageenan is a common food additive extracted from red seaweed. It is often found in chocolate milk, among other processed foods and beverages.



Many individuals experiencing gastrointestinal symptoms (ranging from mild “belly bloat,” to irritable bowel syndrome, to severe inflammatory bowel disease) have noticed that eliminating carrageenan from the diet leads to profound improvements in their gastrointestinal health.

Which foods commonly contain carrageenan?

DAIRY: whipping cream, chocolate milk, ice cream, sour cream, cottage cheese, “squeezable yogurt” marketed to children

DAIRY ALTERNATIVES: soy milk, almond milk, hemp milk, coconut milk, soy desserts, soy pudding

MEATS: sliced turkey, prepared chicken

NUTRITIONAL DRINKS: examples include Ensure™, SlimFast™, Carnation Breakfast Essentials™ and Orgain™

PREPARED FOODS: canned soup, broth, microwaveable dinners, frozen pizza

SUPPLEMENTS: chewable vitamins



is degraded to a low molecular weight, and is called “degraded carrageenan” or poligeenan. Degraded carrageenan is such a potent inflammatory agent that scientists routinely use it to induce inflammation and other disease in laboratory animals to test anti-inflammation drugs and other pharmaceuticals.

Degraded carrageenan is not allowed in food, but scientists have raised concerns for decades that the use of food-grade (undegraded) carrageenan also causes harm. A convincing body of scientific literature shows negative effects caused by food-grade carrageenan. Moreover, scientists are concerned that the acidic environment of the stomach may actually “degrade” food-grade carrageenan once it enters the digestive system, thus exposing the intestines to this potent and widely recognized carcinogen.

These scientific findings, coupled with the food industry’s extensive use of carrageenan, raise serious questions for consumers.

Why is carrageenan in processed foods and beverages?

Though carrageenan adds no nutritional value or flavor to foods or beverages, the food industry uses it in a wide variety of applications; its unique chemical structure makes it useful for several reasons.

Carrageenan serves as a substitute for fat, and as a thickener of nonfat or low-fat foods or dairy replacements. It recreates a fatty “mouthfeel” in products such as low-fat or nonfat dairy (e.g., low-fat cottage cheese, low-fat sour cream) and plant-based dairy substitutes (e.g., soy milk, coconut milk).

Carrageenan can also serve as a stabilizer for beverages that separate, and must be stirred or shaken before use to redistribute the particles. Addition of carrageenan allows beverages like chocolate milk and nutritional shakes to be consumed without first shaking or stirring.

Scientists are concerned that the acidic environment of the stomach may “degrade” food-grade carrageenan once it enters the digestive system, thus exposing the intestines to this potent and widely recognized carcinogen.

Though carrageenan adds no nutritional value or flavor to foods or beverages, the food industry uses it in a wide variety of applications.

Carrageenan is also used in meats, especially processed deli meats and prepared chicken. It is sometimes injected as a brine in precooked poultry to improve tenderness and maintain juiciness. It is added to low-sodium or low-fat deli meat (e.g. sliced turkey) as a binder.

It is found in many processed foods, even some certified organic frozen pizzas and nutritional bars. And, many varieties of canned pet food contain carrageenan.

Why is carrageenan harmful?

The unique chemical structure of carrageenan triggers an innate immune response in the body, recognizing it as a dangerous invader. This immune response leads to inflammation.

For individuals who consume carrageenan on a regular or daily basis, the inflammation will be prolonged and constant, a serious health concern as a precursor to more serious diseases. In fact, the medical community has long recognized that inflammation is associated with over 100 human diseases, including inflammatory bowel disease, rheumatoid arthritis, and arteriosclerosis. Inflammation is also linked to cancer.

Many individuals experiencing gastrointestinal symptoms (ranging from mild “belly bloat,” to irritable bowel syndrome, to severe inflammatory bowel disease) have noticed that eliminating carrageenan from the diet leads to profound improvements in their gastrointestinal health.

Researchers are exploring other ways in which carrageenan is harmful. Scientists have recently found that contact with carrageenan reduces the activity of certain beneficial enzymes in human cells.² And, a recent study exposing mice to carrageenan in drinking water showed impaired insulin action and profound glucose intolerance—precursors to diabetes.³

How long have scientists been concerned about the use of carrageenan in food?

Starting in the late 1960s, research showed that the type of carrageenan used in food caused gastrointestinal disease in laboratory animals, including an ulcerative colitis-like disease, intestinal lesions, and colon cancer.

“The rising incidence and prevalence of ulcerative colitis across the globe is correlated with the increased consumption of processed foods, including products containing carrageenan. Since carrageenan has been found to cause colitis in animal models of ulcerative colitis we felt it would be important to perform a well-controlled dietary study to determine whether carrageenan causes exacerbations (flare ups) of ulcerative colitis in patients in clinical remission.”

—Dr. Stephen Hanauer, MD, Chief, Section of Gastroenterology, Hepatology and Nutrition, and Joseph B. Kirsner, Professor of Medicine and Clinical Pharmacology, University of Chicago School of Medicine

“Carrageenan exposure clearly causes inflammation; the amount of carrageenan in food products is sufficient to cause inflammation; and degraded carrageenan and food-grade carrageenan are both harmful.”

—Dr. Joanne Tobacman, MD, Associate Professor of Clinical Medicine, University of Illinois at Chicago

“[Dr. Tobacman] explained that all forms of carrageenan are capable of causing inflammation. This is bad news. We know that chronic inflammation is a root cause of many serious diseases including heart disease, Alzheimer’s and Parkinson’s diseases, and cancer. All told, I recommend avoiding regular consumption of foods containing carrageenan.”

— Dr. Andrew Weil

“There is a need for extreme caution in the use of carrageenan or carrageenan-like products as food additives in our diet.”⁵

—Written in 1981 by Dr. Raphael Marcus and Dr. James Watt, Department of Pathology, University of Liverpool, United Kingdom

Since eliminating carrageenan from my diet, I have had no problems with stomach cramps, body aches or extreme bloating. I am extremely careful not to ingest even the smallest amount, as it will cause me hours of suffering.

—Kim DeLaroque, Warren, Manitoba, Canada

My wife always wondered why I had diarrhea, and I just told her it was normal and that I'd always had it. These symptoms were from carrageenan.

—Jeff Pokorny, Bend, Oregon

Before I identified carrageenan as the cause of my symptoms, I was afraid to go out anywhere, because I never knew when I would be “hit” with a sudden bout of diarrhea and nausea.

—Diane Jordan, Ottawa, Ontario, Canada

In 1981, two prominent researchers conducted a literature review of the science published since the late 1960s, and raised concerns about the widespread use of carrageenan in the diet. The researchers wrote in the journal *Cancer Detection and Prevention*: “[U]ndegraded carrageenan is still widely used throughout the world as a food additive. Its harmful effects in animals are almost certainly associated with its degradation during passage through the gastrointestinal tract. There is a need for extreme caution in the use of carrageenan or carrageenan-like products as food additives in our diet.”⁴

In the two decades between 1981 and 2001, more published research studies showed harmful effects of consuming food-grade carrageenan. In 2001, the official journal of the National Institute of Environmental Health Sciences, which is part of the National Institutes of Health, published a review of the scientific literature. Its author, Dr. Joanne Tobacman, concluded: “The widespread use of carrageenan in the Western diet should be reconsidered” due to evidence that “exposure to undegraded as well as to degraded carrageenan was associated with the occurrence of intestinal ulcerations and neoplasms.”⁶

Meanwhile, carrageenan manufacturers and the food industry commissioned scientists to perform similar studies.⁷ As is to be expected when a profitable industry faces scientific scrutiny from publicly funded research, the carrageenan manufacturers and food industry even commissioned scientists to publish criticisms of the prior scientific findings pointing to harm.⁸

In recent years, publicly funded scientists have moved beyond animal studies, which repeatedly point to harm, and have conducted studies using human cell cultures to identify the biological mechanisms by which carrageenan causes inflammation. One of these mechanisms has now been identified: a particular immune pathway, activated by other “natural” poisons, such as pathogenic bacteria (including *Salmonella*).⁹

It is time for consumers to take action and pressure the food industry to remove this harmful ingredient from our food supply.

In 2008, Dr. Tobacman, the author of the 2001 *Environmental Health Perspectives* review, urged the Food and Drug Administration (FDA) to prohibit the use of carrageenan in food. The FDA, relying primarily on industry-funded research and failing to review additional studies published since 2008, denied the petition in 2012.

Scientists in other countries as well have been urging regulators to take action for over three decades. But, whenever government agencies have raised concerns (especially in the European

Union), they have come under intense pressure from the international trade-lobby group, Marinalg International, and from the food manufacturing industry, to continue allowing carrageenan in food.

It is time for consumers to take action and pressure the food industry to remove this harmful ingredient from our food supply.

Who is affected by carrageenan?

Many individuals who have lived for years, sometimes decades, with gastrointestinal discomfort or disease—ranging from mild bloating to serious ulcerative colitis—have noticed that eliminating carrageenan from the diets dramatically improves their gastrointestinal health.

But the absence of noticeable gastrointestinal symptoms does not signify that an individual is unaffected by carrageenan. Research shows carrageenan predictably causes inflammation. Low-grade inflammation of the intestines may go unnoticed; nevertheless, chronic low-grade inflammation in the body is profoundly unhealthy. Scientists are increasingly concerned about the negative effects of low-grade inflammation on overall health, especially as it often leads to more serious diseases down the road.

“The episodes—which included pain, nonstop throwing up, and sweats/chills—were intolerable. If I had not stopped ingesting carrageenan, I would have outrageous medical bills and be unable to eat without fear of such an episode.”

—Kyla L., Morgantown, West Virginia

“I no longer have Irritable Bowel Syndrome flare ups and am now able to do things I couldn’t do previously. Before, I was afraid to go on overnight camping trips, day canoeing trips, or Kendo seminars, because the pain would literally incapacitate me, and now, after eliminating carrageenan from my diet, it’s not an issue.”

—Katie M., St. Louis, Missouri

A Summary of the Science on Carrageenan

FOOD-GRADE CARRAGEENAN (“undegraded”) is distinguished from “degraded” carrageenan, which has a lower molecular weight. For decades scientists have used degraded carrageenan to induce gastrointestinal inflammation in laboratory animals in order to test the effectiveness of new anti-inflammation drugs.^{10 11 12 13 14} This type of carrageenan is specifically classified as a “possible human carcinogen” by the International Agency for Research on Cancer of the United Nations.¹⁵

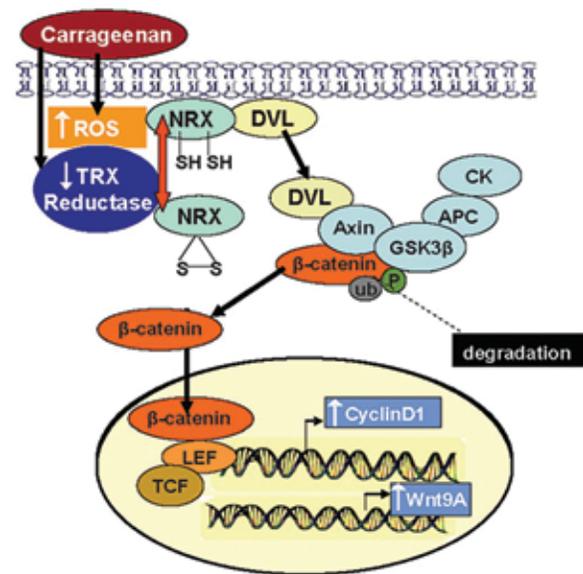
Food manufacturers claim that only degraded carrageenan is harmful, and that food-grade carrageenan is safe. Both independent scientists and the carrageenan manufacturers’ own data¹⁶ have disproved this claim.

While pharmaceutical scientists indeed use non-food-grade, degraded carrageenan to test new pharmaceuticals, a separate track of scientific inquiry has investigated food-grade carrageenan for its effects on human health.

Since 1969, dozens of studies of food-grade carrageenan have been published in peer-reviewed academic journals.[†] Results from these scientific experiments, cited in Appendix A, unequivocally point to harmful effects from food-grade carrageenan in the diet. Studies from the 1960s, 1970s, and 1980s link food-grade carrageenan to higher rates of digestive diseases, including colon cancer, in laboratory animals. In 2001, a review published in the official journal of the National Institute of Environmental Health Sciences questioned the safety of food-grade carrageenan, based on an examination of the extant scientific literature.¹⁷

Numerous studies have been published identifying carrageenan’s unique chemical structure and how it triggers an immune response in the body, which is similar to the effects of pathogenic bacteria like *Salmonella*.

Effect of Carrageenan on Wnt Signaling Pathway



In the colon, carrageenan activates Wnt signaling, a group of signal transduction pathways made of proteins that pass signals from outside of a cell through cell surface receptors to the inside of the cell. Carrageenan’s effect on Wnt signaling enables uncontrolled proliferation and tumorigenesis with the potential for polyp formation and colorectal cancer.

In response to that 2001 review, scientists set out to explore the ways in which carrageenan affects the body. As of the publishing of this report, April 2016, researchers have identified three biological mechanisms by which food-grade carrageenan negatively affects the human body. Numerous studies have

[†] Articles in peer-reviewed journals are accepted for publication only after expert scientists, who were not involved in the study, have reviewed them.

been published identifying carrageenan's unique chemical structure and how it triggers an immune response in the body, which is similar to the effects of pathogenic bacteria like Salmonella.¹⁸

Another concern is that degraded carrageenan (poligeenan) is commonly found in food-grade carrageenan. In response to a European Commission request¹⁹ to ensure that contamination with carcinogenic degraded carrageenan be kept to levels below 5%, the carrageenan manufacturers tested samples of food-grade carrageenan at six different laboratories.²⁰ Test results varied widely from laboratory to laboratory, suggesting that even the carrageenan manufacturers have no reliable way of determining the levels of contamination with degraded carrageenan in their food-grade products.²¹

Eight of the 12 samples of food-grade carrageenan contained higher than 5% degraded carrageenan, according to at least one of the laboratories. The highest level of degraded carrageenan found in a sample was 25%. All samples contained at least some degraded carrageenan, according to the majority of laboratories.

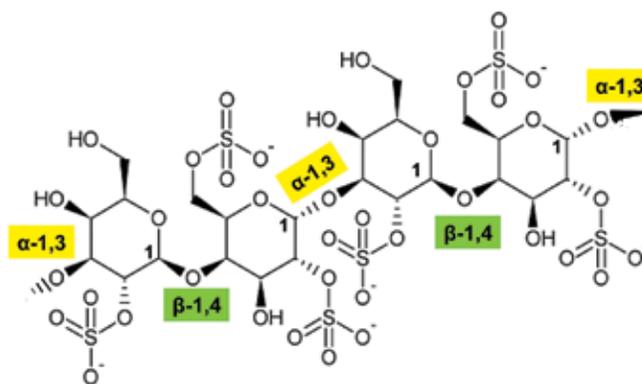
Not a single sample could confidently claim to be entirely free of the material that is classified as a "possible human carcinogen."

Yet, food manufacturers are unwilling to replace this convenient and useful stabilizing and thickening ingredient in their processed foods or to be honest with their customers about the scientific data pointing to harm. They cling to scientific knowledge about carrageenan as if it were 1968, the year before the first study was published showing higher rates of ulcerative colitis-like diseases in rats given food-grade carrageenan in the diet.

Carrageenan used in pharmaceutical studies is degraded with the use of acid hydrolysis.²² What happens to carrageenan in the stomach's acidic en-

vironment? Researchers have suggested that acid digestion may degrade carrageenan, so that it essentially transforms into a carcinogenic substance by the time it reaches the intestines. Several studies that subjected food-grade carrageenan to conditions similar to those found in the human stomach have found that some degradation occurs.^{23, 24, 25}

Further research continues. An ongoing study with ulcerative colitis patients at the University of Chicago and the University of Illinois at Chicago aims to shed light on the effects of carrageenan in the diet on gastrointestinal disease.²⁶ Additional studies currently underway are examining the link between food-grade carrageenan and diabetes.^{27,28} Clinical reports identifying symptoms in individuals are becoming more common.²⁹ The effects of carrageenan on insulin resistance is currently being studied by T.W. Jung, S.Y. Lee, and H.C. Hong.³⁰ The induction of diabetes by carrageenan in an animal model is being studied by H.S. Baek and J.W. Yoon (1991).³¹



The structure of carrageenans include alternating α -1,3 and β -1,4 glycosidic bonds and sulfations of carbons of alternating galactose residues. Research shows that the inflammatory response initiated by carrageenan may be due to exposure to alpha-gal bonds (galactose- α -1,3- galactose).

Consumer Responses: Carrageenan & GI Symptoms

INDIVIDUALS WHO HAVE SUFFERED for years from undiagnosed gastrointestinal symptoms—abdominal bloating, spastic colon, irritable bowel syndrome, and diagnosed diseases, such as ulcerative colitis—often find relief when they eliminate carrageenan from their diet.

The Cornucopia Institute developed an online questionnaire for individuals who have eliminated carrageenan from their diet, in an effort to improve their gastrointestinal health. In the first three years, 1,397 distinct individuals completed the survey and checked either “gastrointestinal symptoms completely disappeared” or “gastrointestinal symptoms improved” after eliminating carrageenan from their diet.

Responses to the online questionnaire are shared with medical researchers, and are confidential. The following individuals agreed to share their stories:

“Before I knew about carrageenan, I suffered tremendous stomach cramps, body aches and extreme bloating from eating certain foods, sandwich meat, ice cream, etc. My symptoms would last for a minimum of 24 hours, sometimes lasting for 48 hours. I had several exploratory procedures done to see if I had a blockage somewhere in my intestinal tract. I started to record a food journal and a list of ingredients of everything I ate, and suddenly discovered my symptoms were caused solely by carrageenan.”

“Since eliminating carrageenan, I have had no problems with stomach cramps, body aches or extreme bloating. I am extremely careful not to ingest even the smallest amount, as it will cause me hours of suffering. I am extremely strict about the products I purchase, and after having researched the terrible effects of this awful ingredient, I have taken extra precautions that my four children do not ingest anything that contains carrageenan.”

Kimberly DeLaroque
Warren, Manitoba, Canada

“I learned that carrageenan was bad but was not yet aware of what the symptoms were from exposure. Upon learning that it affected the lower GI, and upon recognizing that my elimination of symptoms coincided with my elimination of carrageenan from my diet, it became clear that it was likely more than coincidence that these symptoms were from carrageenan.”

“My wife always wondered why I had diarrhea, and I just told her it was normal and that I’d always had it. She also wondered why I defecated so frequently (3-6 times per day). Now I’m down to 1-2. Damn the corporations that put this junk in our food and pass it along as though it’s totally safe and ‘made from seaweed.’”

Jeff Pokorny
Bend, Oregon

“I wrote extensive food journals for at least a year—what I ate, the ingredients, and the effects which occurred. There were several Emergency Room visits where I didn’t know what was wrong, and I needed fluids and sometimes medication because I couldn’t stop vomiting. It was painful, and I became severely dehydrated. I had several tests done including a barium upper GI and a gastrointestinal nuclear scan. Those tests came out OK, but the barium drink used for the x-rays had carrageenan and I was vomiting profusely after ingestion (since I had to fast) and it occurred pretty much as soon as the drink hit my small bowel. At the point of this test, I realized what had to be the cause of my GI distress—mostly due to the food journals commonality, but also that precise moment. Discovering this reaction was a long, horrible process and I felt like my own science experiment every time I ate.”

“The episodes—which included pain, nonstop throwing up, and sweats/chills—were intolerable. If I had not stopped ingesting carrageenan, I would have outrageous medical bills and be unable to eat without fear of such an episode.”

Kyla L.,
Morgantown, West Virginia

“I discovered that carrageenan caused my gastrointestinal symptoms after correlating my stomach upsets with the consumption of ice cream and prepared coffee shop drinks. Since I was not lactose intolerant, I started looking for common ingredients and noticed carrageenan in the ice cream, creamer and coffee shop smoothies. When I removed things with carrageenan from my diet, there were no more problems.”

“I no longer have Irritable Bowel Syndrome flare ups and am now able to do things I couldn’t do previously. Before, I was afraid to go on overnight camping trips, day canoeing trips, or Kendo seminars, because the pain would literally incapacitate me, and now it’s not an issue.”

Katie M.,
St. Louis, Missouri

“Before I identified carrageenan as the cause of my symptoms, I was afraid to go out anywhere, because I never knew when I would be ‘hit’ with a sudden bout of diarrhea and nausea. Had no idea what was wrong with me. I was even starting to have anxiety attacks over my health.”

“Now that I have eliminated carrageenan from my diet, I can finally lead a normal life. I can enjoy myself again, not afraid to travel, get on an airplane, bus or train. No more feeling nausea or having diarrhea almost every day.”

“I don’t trust any foods with cream, soups, etc., and will not try any sauces. I am still very nervous about what I eat, but what a difference this has made on my life.”

Diane Jordan
Ottawa, Ontario, Canada

Myths and Truths: Carrageenan in Food

MYTH: Carrageenan is natural and therefore safe.

TRUTH: Not all natural substances are safe. Many species of plants and seaweed contain substances that are very potent, either as medicine or poison. Other “natural” materials with powerful effects on the human body include tobacco, poison ivy, and rhubarb leaves, which are poisonous.

Carrageenan has a unique chemical structure that leads to prolonged inflammation and other negative health effects. Its effect on the body is similar to the effect of certain pathogenic bacteria such as *Salmonella*, which are also “natural.”

The health impacts from consuming food-grade carrageenan are well documented in the scientific literature (see Appendix A).

MYTH: Food processors only use undegraded carrageenan, which is safe.

TRUTH: In recent decades researchers concerned with the effects of carrageenan in the diet have used undegraded, food-grade carrageenan. These studies point to harmful effects.

When the carrageenan manufacturers’ trade group tested 12 samples of food-grade carrageenan, it found every sample was considered contaminated with degraded carrageenan (classified as a “possible human carcinogen”) by at least one of the testing laboratories. Food processors have an ethical obligation to their customers to take these test results seriously. Their claims that food-grade carrageenan is safe cannot be backed by recent scientific studies or other test results.

MYTH: The controversy around carrageenan is due to the work and activism of one scientist.

TRUTH: This is an especially sinister myth aimed at discrediting a publicly funded, independent researcher. These claims, perpetuated by corporate agribusiness and trade lobbyists, refer to Dr. Joanne Tobacman, a Harvard-educated physician-scientist who is a researcher and associate professor at the nation’s largest medical school, the University of Illinois at Chicago. The majority of her publications have been funded by the National Institutes of Health and the Veterans Administration’s Merit Grants. She has also received financial assistance from the Broad Medical Foundation, a private foundation that seeks to advance scientific understanding about gastrointestinal diseases, and the American Diabetes Association.

Singling out independent scientists who have the moral courage to speak out, and painting their work as an aberration from the dominant scientific paradigm, is a popular tactic with corporations who are unwilling to accept scientific evidence that the products they sell are harmful.

However, while a popular tactic, it is a weak defense of carrageenan, since it has no basis in reality. Concern about the use of carrageenan in food began in the 1970s, three decades before Dr. Joanne Tobacman became involved.

Before Dr. Tobacman’s 2001 review article, dozens of studies by numerous different teams of scientists had raised concern about carrageenan. Scientists from the following institutions have been involved, or are currently involved, in studying the harmful effects of carrageenan: University of Chicago Medical School, Sorbonne University (France), University of Iowa, University of Liverpool (UK), Michigan State University, and Rensselaer Polytechnic Insti-

tute., University of Tuebingen (Germany), Louisiana State University School of Medicine, Division of Endocrinology and Metabolism, Department of Internal Medicine at the Korea University Guro Hospital, University of Massachusetts Medical School, and Technion Israel Institute of Technology.

Studies by these authors were all peer-reviewed, reviewed by other scientists who examined research methodology and the validity of conclusions. Studies were published in different journals at different times, which means they were scrutinized by different editors and reviewers.

To claim that one researcher is responsible for the controversy may be a useful sound bite for those wishing to defend carrageenan, but it is an inaccurate and weak defense of carrageenan's safety. The body of literature, authored by numerous scientists, calling out carrageenan as a possible threat to human health dates back well into the 1960s.

MYTH: Scientific studies pointing to carrageenan's harmful effects have been discredited.

TRUTH: Scientists have been employed or commissioned by carrageenan manufacturers and the food industry to defend the continued use of carrageenan, and they do indeed criticize, and attempt to discredit, the studies pointing to carrageenan's harmful effects.

After two University of Liverpool scientists published a review study and two letters in *The Lancet* in 1980 and 1981, the journal published a letter in response, defending the safety of carrageenan. The letter's author was Herbert J. Sarett, a Vice President at Mead Johnson, a corporation that manufactures infant formula, including ready-to-feed infant formula containing carrageenan.³²

After the publication of Dr. Joanne Tobacman's 2001 review, the journal *Environmental Health Perspectives* published a letter criticizing the study; the letter's author was an employee of Unilever,³³ a Dutch-based multinational corporation with \$18 billion in annual food sales. Unilever owns Slimfast,[™] a nutritional drink that contains carrageenan.³⁴

Studies cited by the food industry, used to refute publicly funded studies, have been, for the most part, performed by corporate scientists. These studies have been performed by scientists at FMC Corporation, a \$3.4 billion chemical corporation and leading carrageenan manufacturer,³⁵ and San-Ei Gen FFI, Inc., a Japanese company that markets carrageenan, in addition to other food additives, such as artificial sweeteners and colors.³⁶

In contrast, within publicly funded, university-affiliated scientific circles, concerns about the harmful effects of both degraded and undegraded carrageenan are taken very seriously.

As just one example, in 2011, researchers at the Harvard School of Public Health wrote: "[Studies] suggest that both native [i.e. undegraded] and degraded carrageenan may have a pronounced effect on the exertion of an inflammatory pressure on colonic mucosal cells including colonic epithelial cells and monocytes/macrophages."³⁷

MYTH: Carrageenan is safe because the Food and Drug Administration (FDA) allows its use, and rejected a citizen's petition by a preeminent researcher requesting carrageenan's removal from our food supply.

FACT: The FDA allows the use of artificial sweeteners such as aspartame, synthetic food dyes (artificial colors), and genetically engineered foods, despite scientific research questioning the safety of these ingredients.

When the FDA declared in 2012‡ that it would not

‡ It is not unusual for the FDA to take four years to respond to a citizen petition. In fact, many petitions have languished with the agency for much longer. Since the FDA denial letter came just weeks after the NOSB vote on carrageenan, which raised public awareness about carrageenan's health concerns, it seems likely that the carrageenan industry exerted pressure on the FDA to move forward with denying the citizen petition. Cornucopia has filed a Freedom of Information Act request with the FDA to determine what, if any, role corporate lobbyists played in the regulatory agency's decision.

act on the citizen petition requesting to discontinue the use of carrageenan in food, the agency did not perform a thorough analysis of the scientific literature. Dozens of studies pointing to potential harmful effects of food-grade carrageenan were never identified or considered by the FDA before it reached its conclusion that “the existing literature does not provide support for [the] requested action.” The FDA’s letter contained twenty citations, including only one additional study that points to harm. The agency seemingly cherry-picked, considering research performed and funded by the carrageenan/food industry, while ignoring disturbing publicly funded, peer-reviewed studies.

Considering the size of the industry that profits from either the manufacture of carrageenan or its use in foods and beverages, industry trade lobby groups will likely fight for continued FDA approval. Since, given its track record, it is unlikely that the FDA will act in the public’s interest in the near future, it is up to consumers to protect themselves and their families, carefully read labels, and stop buying foods containing carrageenan. This will pressure the food industry to make changes voluntarily, as happened with trans fats and “pink slime” (a food ingredient used as a filler in ground beef, containing meat residues and antimicrobial chemicals).

MYTH: Carrageenan is safe because other regulatory agencies, including the European Union, allow it in food.

TRUTH: Pointing to regulatory agencies is another common tactic used by agribusiness and biotechnology corporations to defend their products.

Many food substances that are recognized by the medical and scientific communities to be harmful are allowed by regulatory agencies overseas, including trans fats, artificial sweeteners like aspartame, and synthetic food dyes that have been linked to neurological harm in children. Claiming an ingredient is safe because it is allowed in other countries is a convenient tactic because it avoids a discussion about scientific data.

In fact, no single regulatory authority has unequivocally pronounced carrageenan to be safe, although every decision is inevitably celebrated by the car-

rageenan manufacturers as indisputable “proof” of carrageenan’s harmlessness.

When the United Nation’s Joint FAO/WHO Expert Committee on Food Additives (JECFA) reviewed carrageenan and approved its continued use, the carrageenan trade group Marinalg hailed the decision as confirmation of carrageenan’s safety.³⁸ In fact, the committee had raised concerns. An excerpt from the JECFA 68th meeting:

A recent in vitro study indicates that carrageenan (with an average molecular weight of 1000 kDa) induces inflammation in human intestinal epithelial cells in culture through a Bc110-mediated pathway that leads to NF- κ B and IL-8. Carrageenan may be immunogenic owing to its unusual 1,3-galactosidic link, which is part of its disaccharide unit structure. This study suggests that carrageenan might have a role in intestinal inflammation and possibly inflammatory bowel disease, since Bc110 resembles NOD2 (the gene that activates NF- κ B), of which some mutations are associated with genetic susceptibility to Crohn disease (Borthakur et al., 2007)

One new study conducted in mice showed that carrageenan enhanced the tumorigenicity of a carcinogen, MNU, confirming the results of studies previously evaluated by the Committee at its fifty-seventh meeting.

Proliferative and inflammatory effects were observed in one new study in mice administered kappa-carrageenan in the drinking-water at concentrations of 1% and 4%.³⁹

[Emphasis added]

Despite these concerns, JECFA allows the use of carrageenan.

When the European Commission’s Scientific Committee on Food reviewed safety data on carrageenan, they concluded that food-grade carrageenan is not safe unless the amount of degraded carrageenan is kept to a minimum.

The committee declared that levels of degraded carrageenan in food-grade carrageenan should be kept at levels below 5%.⁴⁰ This decision prompted the laboratory testing of food-grade carrageenan by the industry, which revealed that no food-grade carrageenan sample could confidently be shown to be free from degraded carrageenan at concentrations below 5%. Results from this testing have been removed from the internet, but available below in Appendix B.

Carrageenan manufacturers have an international

trade lobby group, Marinalg International, with a mission of defending the worldwide use of carrageenan in foods. Through Marinalg, carrageenan manufacturers employ professional lobbyists charged with ensuring that regulatory agencies continue allowing carrageenan in food.

The decisions by overseas regulatory agencies (as well as the U.S. FDA) to continue to allow use of carrageenan in food testify to the power and clout of the carrageenan manufacturers' lobbyists, not to the safety of carrageenan.

MYTH: For some products, like soy milk, there are no alternatives to carrageenan for food processors.

TRUTH: On supermarket shelves, equivalent products appear side-by-side, some containing carrageenan and others without it. Food processors use gums, including guar gum and locust bean gum, as

alternatives to carrageenan. Others write "Shake Well" on the package,⁴¹ since the simplest alternative to carrageenan in products such as chocolate milk is to have the consumer shake the product right before use.

Other gums used as stabilizers and thickening agents do not share the unique chemical structure of carrageenan, and therefore do not raise the same health concerns. In 1988, Food and Drug Administration researchers compared damage to the colon in rats given carrageenan and given guar gum as an alternative. The researchers found damage to the rats given carrageenan, but no damage to the rats given guar gum in the diet.⁴²

The Cornucopia Institute has a consumer guide on its website (www.cornucopia.org, under the Scorecards tab) that provides a list of products with and without carrageenan.

What is Carrageenan Doing in Organic Food?

ORGANIC FOODS SHOULD BE A SAFE HAVEN from harmful ingredients. In fact, the Organic Foods Production Act of 1990, the law governing organic foods, requires that non-agricultural ingredients must be determined safe to human health and not deleterious to the environment before they can be added to organic foods.⁴³ Federal organic standards also require that nonorganic ingredients must be essential to producing the food (e.g., baking powder for producing organic cookies).⁴⁴ Since nearly every product on store shelves containing carrageenan can be found by another manufacturer using an alternative to carrageenan (e.g., locust bean gum, guar gum), carrageenan does not appear to be an essential food-processing ingredient.

Yet carrageenan, a nonorganic, non-agricultural ingredient, made its way into organic foods due to carelessness by government regulators, misinformation supplied by corporate “independent” scientists advising the USDA, and successful lobbying by carrageenan manufacturers and food processors.

Carrageenan made its way into organic foods due to carelessness by government regulators, misinformation supplied by corporate “independent” scientists advising the USDA, and successful lobbying by carrageenan manufacturers and food processors.

For the past two decades, food industry executives and lobbyists have managed to convince enough members of the National Organic Standards Board (NOSB)—the citizen panel that determines which non-organic ingredients can be used in organic foods—to give carrageenan its stamp of approval. Their tactics have become increasingly more manipulative and ethically questionable as it becomes clearer that scientific evidence is not on their side.

The NOSB first approved carrageenan in the mid-1990s. As required by law, the USDA had hired three “independent” contractors to perform a thorough scientific and technical review of the additive. Their job was to provide an independent review, including any concerns about the additive’s effects on

human health or the environment. In their official reports to the NOSB, the three contractors assured that no “effects on human health” had been identified.

One of the three “independent” contractors was Dr. Richard Theuer, a former corporate executive who had been a colleague at Mead Johnson of Dr. Herbert Sarett, the author of the letter published in *The Lancet* defending the safety of carrageenan in food. Another contractor was Stephen Harper, a food scientist at Small Planet Foods, which is now owned by the multi-billion-dollar corporation General Mills. The third contractor was an academic. The three scientists claimed they had found no studies raising concern about carrageenan’s effects on human health.⁴⁵ The NOSB, unaware of the concerns about this food additive, approved carrageenan for use in organics.

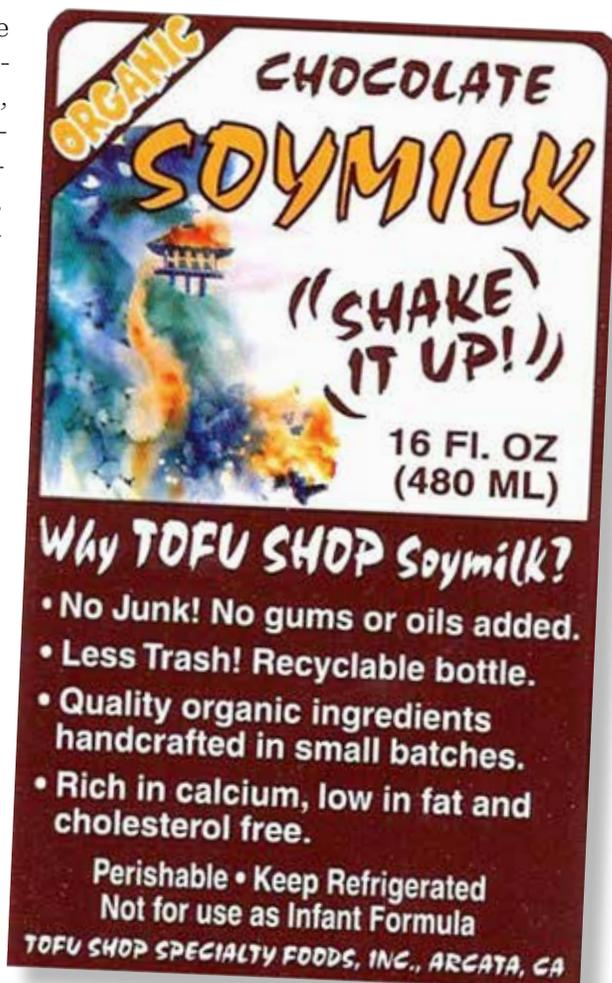
The NOSB voted on whether to relist carrageenan as an approved substance in organic foods at its meeting in May 2012. Cornucopia staff members were present at the meeting and urged the NOSB to remove carrageenan from the list of approved additives. Meanwhile, industry lobbyists presented misinformation about carrageenan’s safety and questioned the credibility of independent research commissioned by the National Institutes of Health.

One of the NOSB members took an active role in assisting the carrageenan manufacturers. At one point, she read lengthy excerpts from a document

written by Marinalg, the carrageenan manufacturers' trade lobby group, defending the safety of carrageenan. But, before reading these lengthy excerpts, the Board member introduced the excerpts as "being from JECFA, a United Nations/FAO body" when, in fact, they were written by the industry's lobby group.

It is unclear whether this board member intentionally misled her fellow NOSB members, or whether she herself was misled by the carrageenan manufacturers' lobbyists with whom she collaborated. However, when this well-documented error was brought to her attention, she refused to correct the public record.

During the meeting, scientists with different perspectives presented oral testimonies. A scientist from FMC Corporation, a multi-billion-dollar chemical corporation that also manufactures pesticides and industrial chemicals, in addition to carrageenan, defended carrageenan's safety. A scientist representing Marinalg International, the trade lobby group for carrageenan manufacturers, also defended carrageenan. Meanwhile, Dr. Joanne Tobacman, employed by the nation's largest medical school, presented publications that were funded primarily by public institutions,



The easy alternative to carrageenan: shake the product before drinking.

including the National Institutes of Health, and urged the removal of carrageenan from organic foods and beverages. The NOSB voted, by a one-vote margin, to reapprove the use of carrageenan in organic foods.⁵

Sadly, even one of the NOSB members who was appointed as a "public interest/consumer" representative voted to approve carrageenan, despite strong opposition from every public interest and consumer group.

Several NOSB members with clear conflicts of interest voted to approve carrageenan after they failed to recuse themselves from voting, as the NOSB's policies require. One Board member who voted in favor of carrageenan was employed by Whole Foods Market, which produces and markets a wide variety of products containing carrageenan under its 365 Organic brand. Another NOSB member who voted in favor of carrageenan was employed by Organic Valley, which uses carrageenan in several of its products. In fact,

prior to the meeting, the CEO of Organic Valley spoke directly with several NOSB members to lobby for carrageenan's approval and, during the meeting, a representative of the company presented formal testimony asking for carrageenan's continued use.

⁵ According to federal law, synthetics and non-organic ingredients used in organics "sunset" every five years unless the NOSB votes to reapprove their use.

NOSB 2018 Sunset Review of Carrageenan

FEDERAL LAW REQUIRES THE NOSB to review all synthetic and non-organic materials approved for use in organics every five years to determine whether they still qualify under the Organic Foods Production Act (OFPA) of 1990. In order for the material to be maintained on the National List of Allowed and Prohibited Substances in organic production, each material must be evaluated against all three OFPA criteria: 1) impact on human health and the environment; 2) essentiality to organic production; and, 3) compatibility and consistency with OFPA.

Carrageenan will be reviewed at both 2016 NOSB meetings for Sunset in 2018. The vote for carrageenan's 2018 sunset will occur at the November, 2016 meeting. Cornucopia has concerns that the published scientific research on carrageenan is not being presented accurately to the NOSB in the 2016 limited scope Technical Evaluation Report (TR). There are additional concerns with the review conducted by the handling subcommittee. Our concerns with these documents are as follows:

1. The 2016 TR fails to discuss the undisputed fact that degraded carrageenan is present within food-grade carrageenan. Attempts by the industry to reliably measure the amount of degraded carrageenan in food-grade carrageenan were posted online and results proved that poligeenan is present in food-grade carrageenan. Fortunately, The Cornucopia Institute downloaded these documents before they were subsequently removed by the industry lobby (Appendix B).
2. Most of the positions taken by regulatory agencies have been influenced by industry-funded reports about carrageenan. These are often based on a single study in which critical points are obfuscated. As an example, the recent infant pig feeding study,⁴⁶ on which the Joint FAO/WHO Expert Committee on Food Additives (JECFA) partially based its decision, there were several flaws including: 1) use of infant pigs in which the innate immune response to carrageenan is expected to be less than in humans, since pigs make the alpha-1,3-galactosyltransferase enzyme and the galactose-alpha-1,3-galactose bond of carrageenan is not immunogenic in the pig; 2) onset of the study was after ingestion of maternal colostrum and maternal feeding for an unspecified, and variable number of days in the study animals; 3) antibiotics and iron supplements were given pri-

or to and throughout the 28-day carrageenan feeding; 4) several "incidental" deaths occurred with no explanation; 5) soft and/or watery feces were increased in the carrageenan-treated animals; 6) glycosuria occurred in 4 of the 12 animals that received 2250 ppm carrageenan; 7) rectal weight was significantly reduced in males that received 2250 ppm carrageenan; 8) weights, which were reported without ranges or standard deviations, were unusually high (all over 10 kg) at Study Day 28, suggesting that the animals were at least 5 weeks old, and therefore had entered the study closer to the age of weaning, expected to be at day 19.4 after birth; 9) histopathology demonstrates differences between control and carrageenan-treated tissues, including increased inflammatory infiltrate in the lamina propria and reduced colonic haustrations; and, 10) absence of any long-term data [Tobacman, personal communication].

In the Benitz feeding studies that were used by the WHO to study the intestinal effects of carrageenans in the Rhesus monkey 47, there were many similar flaws, including prolonged recovery periods following exposure to carrageenan. Recovery periods were up to twenty-four weeks, obscuring the impact of carrageenan-feeding on the intestinal pathology. Even with this prolonged recovery, there were significant changes in the reticuloendothelial cells of the livers of the monkeys treated with the lower molecular weight carrageenan.

3. The 2016 TR states that "carrageenan can be avoided by sensitive individuals, as it is included in the label". This is incorrect. When carrageenan is a secondary ingredient, as in beer, condensed milk and cream, it is not listed on the label.
4. 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 are independent of the molecular weight, although more harmful effects are observed with lower molecular weight carrageenans.

5. The statement made by the NOSB subcommittee that “only some people are sensitive” is inaccurate. It might be true that only a subset of the population experience acute symptoms; however, the galactose-alpha-1,3-galactose bond is immunogenic to all humans and Old World apes. Humans do not make this bond, and exposure leads to activation of an immune response. Dr. Uri Galili has published frequently about this epitope.⁴⁸ The alpha-1,3-galactosyltransferase gene that makes the galactose-alpha-1,3-galactose bond was inactivated in ancestral primates, and anti-Gal antibodies react to this bond. This reaction leads to rejection of transplantation of organs from most mammals and is a universal human response.

The response to this epitope is different than allergic responses since the immunoglobulins stimulated include IgG, IgM, IgA, and IgE, not just IgE. Some variation in response may occur depending on ABO blood group. The natural IgG anti-Gal antibody is abundantly present in all humans, unless severely immunocompromised.

6. The statement made by the NOSB handling subcommittee that they are “troubled that the research showing inflammation and glucose intolerance is all from one research team and has not been replicated,” is simply not true.

There are a number of labs around the world that have studied the inflammatory effects of carrageenan. Thousands of references (roughly 10,000) in PubMed occur when “inflammation and carrageenan” is searched. In the European Commission review from 2003, hundreds of studies that discussed the effects of carrageenan on intestinal inflammation were reviewed. Many are referenced in this document (Appendix A). A few important references that are missing from the TR include:

- The clinical impact of carrageenan and diabetes, currently being studied by a German group (University of Tuebingen, Dr. Robert Wagner and Dr. Norbert Stefan).⁴⁹
- The effects of carrageenan on insulin resistance, currently being studied by T.W. Jung, S.Y. Lee, and H.C. Hong.⁵⁰
- The induction of diabetes by carrageenan in an animal model, studied by H.S. Baek and J.W. Yoon (1991).⁵¹

7. Several studies have shown the degradation of carrageenan in the digestive tract, including Uno et al. (2001)⁵² and Pittman, Golberg, and Coulston (1976).⁵³
8. Studies that look at the average molecular weight of carrageenan, many of which are discussed in the TR, are not useful because they obscure the presence of lower molecular weight forms.
9. Carrageenan is non-essential. Every organic product containing carrageenan has an organic alternative, being produced by one or more competitors, that does not contain the ingredient.
10. The amount of poligeenan detected is limited by poor detection capabilities.⁵⁴
11. The lack of more “dose-response” studies has been criticized in reports funded by industry, but dose-response studies have been performed. The amount of carrageenan exposure in experiments that demonstrate inflammation is often less than what is consumed in the typical diet, based on 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.
12. Industry has also tried to discount studies in established human colonic epithelial cell line NCM460, which, like most of the cell lines used in cell culture studies, is a transformed cell line, enabling survival in cell culture experiments. All of the studies had controls that were not exposed to carrageenan for comparison, and data were analyzed by appropriate statistics. 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.⁵⁵

It should be noted that the 2016 Technical Review on carrageenan was produced by the Organic Material Review Institute (OMRI). Its board and staff include individuals who have professional involvement in selling “approved” synthetic compounds to farming and manufacturing interests. Furthermore, the CEO of OMRI is the former chief executive of the nation’s largest certifier, CCOF, which compensates the NOSB handling subcommittee member who is acting as a lead on this material.

It should also be noted that the National Organic Program no longer publishes the names of the authors of the TRs. After identifying a number of past conflicts of interest, it is no longer possible for organic stakeholders or public interest organizations, or the NOSB for that matter, to scrutinize the qualifications or backgrounds of the scientists preparing these briefings for NOSB members.

Food Manufacturers' Responses to Scientific Data about Carrageenan

OVER THE PAST FIVE YEARS, a number of prominent companies have announced they have/will remove carrageenan from their product lines, including WhiteWave™, one of the largest marketers of organic/natural foods in the country. However, as of April 2016, WhiteWave's Horizon™ organic low-fat sour cream and cottage cheese still have carrageenan. They have removed it from many of their other products, including Tuberz yogurt for children, chocolate milk, and whipping cream. Many brands are now using the lack of carrageenan in their formulations as a marketing tool.

Other companies have stated they are actively working to remove carrageenan from all of their products, whereas some have ignored consumer's concerns. In some cases, when consumers inquire about carrageenan, companies ask their customers to be patient as they work to reformulate their products.

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®, and Good Karma®. So Delicious® (also owned by WhiteWave™) has removed it from their refrigerated coconut milk, but not their shelf-stable selections.

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

Organic Valley has failed to publicly acknowledge

the health risks of carrageenan and lobbied for its continued use in organic foods, but is, nonetheless, working to remove it. In November 2012, they reformulated their eggnog to be carrageenan-free. As of April, 2016, Organic Valley heavy whipping cream that is "ultra-pasteurized" contains carrageenan, whereas its heavy whipping cream that is labeled "pasteurized" (standard high temperature short time pasteurization — HTST) does not.

Unfortunately, other companies have not only resisted taking carrageenan out of their products, but are actively disseminating false information about it in their attempt to persuade their customers that carrageenan is safe. It is especially troublesome when this misinformation comes from organic brands.

Concerned consumers are encouraged to visit The Cornucopia Institute's webpage (cornucopia.org), and click on the "Reports" tab, where they will find resources on carrageenan, including a buyers guide to help families choose the safest possible products in terms of carrageenan content.

Industry Confirms, then Hides Poligeenan in Food-grade Carrageenan

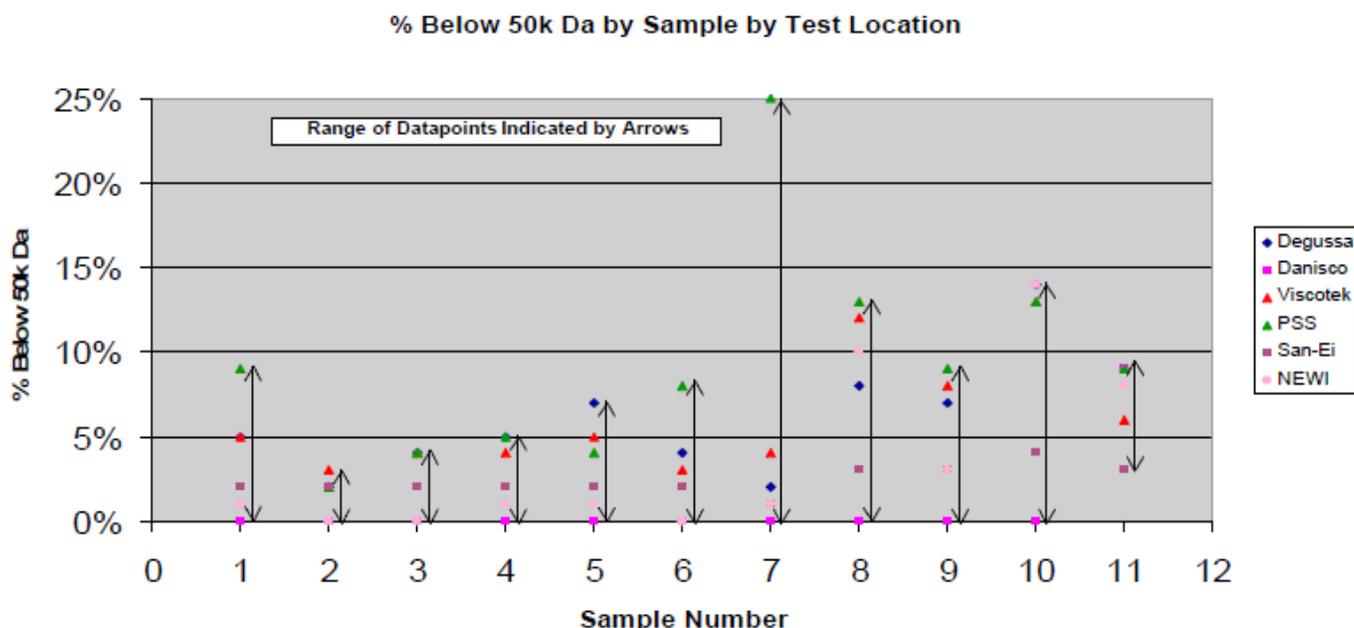
THE SPECIFICATION THAT CARRAGEENAN used in food must not contain more than 5% molar mass with molecular weight less than 50k Da was formally adopted by the European Commission (Directive 2004/45/EC on April 16, 2004) for implementation by Member States by April 1, 2005.

As a result of this directive, the Marinalg Working Group, composed of carrageenan producers, attempted to measure the poligeenan within food-grade carrageenan, but had difficulty replicating the results among labs. Results were posted online, but subsequently removed, since they proved that poligeenan was measured in food-grade carrageenan at quantities as high as 25%. Fortunately, Cornucopia has maintained these documents (Appendix B). Figure 1 from their report, showing the range in the percentage of low molecular weight carrageenan (less than 50k Da) is pictured below. At the time of this writing (April, 2016) the Marinalg Working Group still has not published a reliable method for molecular weight distribution measurement to meet the European Commission Directive.

The carrageenan industry has tried for decades to

retain the use of carrageenan in food products because of its 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 efforts by those with vested interests (such as tobacco and fracking). These cover-ups must not go unchallenged. The organic sector, especially, expects better.

Percent poligeenan found in twelve food-grade carrageenan samples (results were published by the carrageenan industry online, then subsequently removed). Results not only demonstrate that poligeenan is commonly found in food-grade carrageenan, but also that the industry is unable to accurately determine the amount of poligeenan that contaminates food-grade carrageenan.



Consumers: Taking Action

IN 2012, THE FDA DENIED a 2008 citizen petition to remove carrageenan from foods, indicating the agency is unlikely to act anytime soon in the interest of public health concerning carrageenan. It is, therefore, up to individuals to take action.

Protect your health: read labels carefully, check the ingredients list, and contact food companies to make sure that carrageenan is not already in the ingredients they use (and therefore not on the label).

- As food manufacturers become aware that consumers want to avoid carrageenan, some are listing “Irish Moss” instead. “Irish Moss” is another name for carrageenan.
- Do not rely on internet data presented by companies that have an economic interest in carrageenan use. Some food manufacturers, aware that consumers are increasingly avoiding carrageenan, have removed carrageenan from the ingredients list on their websites. Check the label on the food itself, rather than exclusively relying on information supplied on websites.
- Carrageenan is not always on the ingredient label, even though it may be present as a “secondary” ingredient (an ingredient present in a listed ingredient). Carrageenan is often used to clarify beer and is not listed on the ingredients label. Cream and condensed milk are additional ingredients that may contain carrageenan without being listed on the ingredients label. If “cream” or “condensed milk” is listed, contact the company and ask them if carrageenan is in the cream or condensed milk.

Use Cornucopia’s shopping guide to find alternatives to foods that contain carrageenan (available online at www.cornucopia.org). Support the companies (generally, certified organic) that have made a commitment to the health and well-being of their customers.

- If your grocer does not yet stock carrageenan-free organic foods, ask them to carry the carrageenan-free alternatives.

Contact companies and ask them to remove carrageenan from your favorite products. Tell them you will no longer buy their products until carrageenan is removed.

- Consumer service phone numbers and email addresses can be found on the “About Us” or “Contact Us” page of most food manufacturers’ websites as well as on many labels.
- Some companies that have already committed to removing carrageenan will tell you, while others will staunchly defend the safety of carrageenan based on outdated science.

Share this information with others. Tell your friends and family about carrageenan, so that they can also protect their health. Also, tell your doctor if you have noticed improvements in your health after eliminating carrageenan from your diet.

In the absence of government regulatory action to protect citizens’ health, it is up to individual consumers to take action.

Remember: together, consumers have more power than all corporate lobbyists and inappropriately influenced government officials combined. “Pink slime” and hydrogenated oils (trans fats) have virtually disappeared from our food supply, not due to FDA action but, rather, due to consumer pressure.

Putting carrageenan in food is like putting poison ivy in skin lotion. The only difference is we cannot see the inflammation, lesions, ulcerations, and polyps in our intestines. Both are natural, and both are cause for concern.

Putting carrageenan in food is like putting poison ivy in skin lotion. The only difference is we cannot see the inflammation, lesions, ulcerations, and polyps in our intestines. Both are natural, and both are cause for concern.

Organic Dairy	
Buttermilk with Carrageenan (Organic buttermilk producers that used to add carrageenan have reformulated their products to be carrageenan-free)	Buttermilk without Carrageenan <ul style="list-style-type: none"> ✓ Clover Stonetta ✓ Friendship Brand ✓ Hawthorne Valley ✓ Kalona Supernatural ✓ Natural By Nature ✓ Organic Valley
Chocolate Milk With Carrageenan <ul style="list-style-type: none"> • Clover Stonetta • Horizon • Kalona Supernatural (Kalona had committed to removing carrageenan by the end of 2012. As of February 2013, they have not. Check ingredients list) • Natural By Nature • Organic Valley • Publix • Simply Smart 	Chocolate Milk without Carrageenan <ul style="list-style-type: none"> ✓ Castle Rock Organic Farms ✓ Crystal Ball Farms ✓ Equal Exchange Hot Chocolate (powdered) ✓ Strafford Organic Creamery ✓ Trickling Springs Creamery
Cottage Cheese with Carrageenan <ul style="list-style-type: none"> • 365 Whole Foods (lowfat and fat) 	Cottage Cheese without Carrageenan <ul style="list-style-type: none"> ✓ Kalona Supernatural (regular and

Cornucopia's Carrageenan Shopping Guide

Use Cornucopia's online shopping guide to help you avoid carrageenan in organic and non-organic products, including dairy, dairy alternatives, nutritional drinks, deli meats, dips, juice, prepared foods, desserts, and infant formula. Click the "Scorecards" tab at www.cornucopia.org.

If you notice improvements in your gastrointestinal health after removing carrageenan from your diet, please take a moment to fill out the online questionnaire (also available at www.cornucopia.org/carrageenan) to help medical researchers better understand the degree and severity of carrageenan-related gastrointestinal symptoms in the general public.

While the food industry and carrageenan manufacturers will likely continue for some time to dispute scientific findings pointing to harm, consumers

have the power to send a strong message to the food manufacturers who put their profit and convenience above our nation's health and well-being.

Appendix A: Scientific Findings 1969–2016

CARRAGEENAN HAS BEEN STUDIED for more than 40 years. The following studies are presented in chronological order. This is not a complete list of studies conducted using carrageenan, but is representative of studies by publicly funded scientists raising concern.

It is important to note that all studies cited here used food-grade, undegraded carrageenan. This is the type of carrageenan that manufacturers claim is safe. The findings summarized below reflect a very different conclusion.

The funding source is identified for studies that disclosed it.

1960s:

Watt J, Marcus R (1969) Ulcerative colitis in the guinea-pig caused by seaweed extract. *Journal of Pharmacy and Pharmacology* 21:187S-188S.

Summary of findings: This study was one of the first to show that food-grade carrageenan contributes to ulcerative colitis-like disease in laboratory animals (guinea pigs).

Author affiliations: University of Liverpool, United Kingdom

1970s:

Grasso P, Sharratt M, Carpanini FMB, Gangolli SD (1973) Studies on carrageenan and large-bowel ulceration in mammals. *Food and Cosmetics Toxicology* 11:555-564.

Summary of findings: The researchers administered both degraded and undegraded/food-grade carrageenan in the diet of several species of laboratory animals. Guinea pigs and rabbits experienced ulcerations in the large intestine, symptoms which were not detected in rats, squirrel monkeys, hamsters, and ferrets.

Author affiliations: The British Industrial Biological Research Association, a privately owned consulting firm.

Pittman K, Golberg L, and Coulston F (1976) Carra-

geenan: The effect of molecular weight and polymer type on its uptake, excretion and degradation in animals." *Food and Cosmetics Toxicology* 14 (2):85-93.

Summary of findings: Food-grade carrageenan was given to guinea pigs, monkeys, and rats through drinking water or in the diet. Fecal and liver samples were examined by gel electrophoresis and carrageenans present in the feces were reduced to 100kDa or less. Carrageenans were also found in the liver, demonstrating that high molecular weight carrageenans are degraded after passing through the digestive tract and can be absorbed.

Author affiliations: Institute of Comparative and Human Toxicology, Albany Medical College of Union University

Engster M and Abraham R (1976) Cecal response to different molecular weights and types of carrageenan in the guinea pig. *Toxicology and Applied Pharmacology* 38:265-282.

Summary of findings: In this short-term study, researchers administered different types of carrageenan in the diet and drinking water of guinea pigs for two weeks. They found ulceration of the intestines in guinea pigs given undegraded iota-carrageenan in the drinking water. No changes were observed in the other groups, and it is unclear what effects would have been seen if the experiment had been continued for longer than two weeks.

Funding: National Institute of Environmental Health Sciences, National Institutes of Health

Author affiliation: Albany Medical College

Watanabe K, Reddy BS, Wong CQ, Weisburger JH (1978) Effect of dietary undegraded carrageenan on colon carcinogenesis in F344 rats treated with azoxymethane or methyl nitrosourea. *Cancer Research* 38:4427-4430.

Summary of findings: This study found higher rates of tumors in rats fed undegraded carrageenan in the diet.

Funding: National Cancer Institute (National Institutes of Health)

Author affiliations: Naylor Dana Institute for Disease Prevention, American Health Foundation

1980s:

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.

Watt J and Marcus R (1981) Harmful effects of carrageenan fed to animals. *Cancer Detection and Prevention* 4(1-4): 129-34.

Review article: The authors reviewed the scientific literature and found "an increased number of reports ... describing harmful effects of degraded and undegraded carrageenan supplied to several animal species in their diet or drinking fluid."

"Harmful effects [of food-grade carrageenan] are almost certainly associated with its degradation during passage through the gastrointestinal tract. There is need for extreme caution in the use of carrageenan or carrageenan-like products as food additives in our 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*.

Arakawa S, Okumura 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 β -glucuronidase activities in feces and other tissues. *Journal of Nutritional Science and Vitaminology* 32:481-485.

Summary of findings: This study found higher rates of tumors in rats fed undegraded carrageenan in the diet.

Author affiliations: Nagoya City University, Japan

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 and Chemical Toxicology* 22:615-621.

Summary of findings: Researchers using undegraded carrageenan administered in the drinking water of rats showed that carrageenan penetrates the intestinal barrier.

Author affiliations: The British Industrial Biological Research Association, a privately-owned consulting firm.

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.

Funding: Food and Drug Administration

Author affiliations: Food and Drug Administration

1990s:

Weiner ML (1991) Toxicological properties of carrageenan. *Agents and Actions* 32(1-2): 46-51.

Summary of findings: Based on a review of animal feeding studies, carrageenan is safe.

Author affiliation: FMC Corporation (multibillion dollar chemical corporation and leading carrageenan manufacturer)

Wilcox DK, Higgins J, Bertram TA (1992) Colonic epithelial cell proliferation in a rat model of non-genotoxin-induced colonic neoplasia. *Laboratory Investigation* 67:405-411.

Summary of findings: This study shows an association between loss of epithelial cells (the cell membranes in the intestine) and the consumption of both undegraded and degraded carrageenan.

Funding: Proctor & Gamble Company

Author affiliations: Proctor & Gamble Company

Capron I, Yvon M, Muller G (1996) In-vitro gastric stability of carrageenan. *Food Hydrocolloids* 10(2):293-244.

Summary of findings: This study analyzed the rate of degradation in an artificial stomach which simulated realistic conditions for human digestion, wherein the pH gradually decreases from 5 to 1.5 over 3 hours prior to gastric emptying. The findings showed that, under the most unfavorable conditions of gastric digestion (slow emptying rate and rapid acidification), about 10% of the carrageenan had a molecular weight of less than 100 kDa.

Funding: Proctor & Gamble Company

Author affiliations: Proctor & Gamble Company

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.

Author affiliations: French National Institute of Agronomic Research, Toulouse, France

Tobacman JK (1997) Filament disassembly and loss of mammary myoepithelial cells after exposure to lambda-carrageenan. *Cancer Research* 57:2823-2826.

Summary of findings: Mammary myoepithelial cells exposed to lambda-carrageenan at rates as low as 0.00014% exhibited disruption of the internal cellular architecture and cell death. Destruction of these cells in tissue culture by a low concentration of a widely used food additive suggests a dietary mechanism for mammary carcinogenesis not considered previously.

Author affiliations: Department of Internal Medicine, College of Medicine, The University of Iowa

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: This study aimed to better understand the role of food-grade carrageenan in carcinogenesis. The experiments in this study were designed to test the hypothesis that carrageenan might function 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.

Author affiliations: Michigan State University

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

Review study: This study examined existing research done to date (2001). The author concluded: "Because of the acknowledged carcinogenic properties of degraded carrageenan in animal models, and the cancer-promoting effects of undegraded carrageenan in experimental models, the widespread use of carrageenan in the Western diet should be reconsidered."

Funding: None

Author affiliation: University of Iowa College of Medicine

Cornucopia Note: The publication of this review, in the respected journal of the National Institutes of Health's National Institute for Environmental Health Sciences, marks a turning point.

It prompted independent researchers to more closely study the biological mechanisms that cause the observed negative health effects of consuming undegraded, food-grade carrageenan.

These studies, focusing exclusively on food-grade carrageenan, have advanced scientific understanding about the way in which carrageenan causes harm.

Hagiwara A, Miyashita K, Nakanishi T, Sano M, Tamano S, Asai I, Nakamura M, Imaida K, Ito N and Shirai T (2001) Lack of Tumor Promoting Effects of Carrageenan on 1,2-Dimethylhydrazine-induced Colorectal Carcinogenesis in Male F344 Rats. *Journal of Toxicologic Pathology* 14: 37.

Summary of findings: This study found no statisti-

Since 2000:

cally significant increases in malignant tumors in rats given food-grade carrageenan in the diet.

Author affiliations: Nagoya City University, Daiyukai Institute for Medical Science and San-Ei Gen FFI, Inc.

Cornucopia Note: This study has been widely cited by the carrageenan manufacturers and its trade lobby group Marinalg as “proof” that carrageenan is safe. One of the authors is a scientist with San-Ei Gen FFI, Inc, a Japanese carrageenan manufacturer.

The study has been criticized by publicly funded scientists, primarily because the study was terminated as higher rates of tumors in the carrageenan group were detected. The rats were killed after 90 days (a rat’s natural lifespan is 2 years). When the study was terminated, tumor rates were higher, but not yet high enough to be statistically significant.

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.

Summary of findings: The study measured the molecular weight of 29 samples of food-grade carrageenan and concluded that no sample had a significant level of degraded carrageenan. The detection limit was 5%.

Author affiliations: San-Ei Gen FFI, Inc, a Japanese food additive manufacturer. In addition to carrageenan, San-Ei Gen FFI manufactures flavors, colors, preservatives and the artificial sweetener sucralose.

Cohen SM and Ito N (2002) A critical review of the toxicological effects of carrageenan and processed eucheuma seaweed on the gastrointestinal tract. *Critical Reviews in Toxicology* 32(5): 413-44.

Summary of findings: The authors of this review criticized research studies pointing to gastrointestinal harm from consuming carrageenan. The authors conclude that “there is no credible evidence supporting a carcinogenic effect or a tumor-promoting effect on the colon in rodents.”

Cornucopia Note: The authors, with ties to the carrageenan industry, criticized the studies that have found higher rates of gastrointestinal disease in laboratory animals. The authors reviewed 23 studies, and found fault with every one.

Such studies, commissioning scientists to serve as apologists “debunking” science in defense of a

harmful substance, is a common tactic by corporate manufacturers whose product is scrutinized by publicly funded scientists (e.g. tobacco, aspartame).

Weiner M, Nuber D, Blakemore WR, Harriman JF and Cohen SM (2007) A 90-day dietary study on kappa-carrageenan with emphasis on the gastrointestinal tract. *Food and Chemical Toxicology* 45(1): 98-106.

Summary of findings: The study found no clinical signs in rats fed high doses of food-grade carrageenan with up to 12% degraded carrageenan, other than soft stool. The authors reported that the gastrointestinal tract “appeared normal,” even in the rats given high doses of carrageenan in the diet.

Author affiliations: FMC Corporation, a leading manufacturer of carrageenan. In addition to manufacturing carrageenan, FMC Corporation (a \$3.4 billion conglomerate) produces pesticides and industrial chemicals.⁵⁶

Borthakur A, Bhattacharyya S, Dudeja PK and Tobacman JK (2007) Carrageenan induces interleukin-8 production through distinct Bcl10 pathway in normal human colonic epithelial cells. *American Journal of Physiology, Gastrointestinal and Liver Physiology* 292(3): G829-38.

Summary of findings: Exposure of human colonic epithelial cells in tissue culture to small quantities of undegraded (food-grade) carrageenan produced inflammation by a second pathway of reactive oxygen species, as well as by the innate immune pathway.

Funding: Department of Veterans Affairs; National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health

Author affiliations: University of Illinois at Chicago and Jesse Brown Veterans Affairs Medical Center

Bhattacharyya S, Borthakur 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.

Funding: National Institutes of Health

Author affiliations: University of Illinois at Chicago

Bhattacharyya S, Dudeja PK and Tobacman JK (2008) Carrageenan-induced NFkappaB activa-

tion depends on distinct pathways mediated by reactive oxygen species and Hsp27 or by Bcl10. *Biochimica and Biophysica Acta* 1780(7-8): 973-82.

Summary of findings: Exposure to human colonic epithelial cells in tissue culture to small quantities of food-grade carrageenan produced inflammatory responses.

Funding: National Institutes of Health

Author affiliations: University of Illinois at Chicago
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.

Funding: National Institutes of Health

Author affiliations: University of Illinois at Chicago and Jesse Brown Veterans Affairs Medical Center

Bhattacharyya S, Gill R, Chen ML, Zhang F, Linhardt R, 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.

Funding: National Institutes of Health; Veterans Administration

Author affiliations: University of Illinois at Chicago; Jesse Brown Veterans Affairs Medical Center; Rensselaer Polytechnic Institute

Bhattacharyya S, Borthakur A, Tyagi S, Gill R, Chen ML, Dudeja PK, Tobacman JK (2010) B-cell CLL/lymphoma 10 (BCL10) is required for NF-kappaB production by both canonical and noncanonical pathways and for NF-kappaB-inducing kinase (NIK) phosphorylation. *Journal of Biological Chemistry*. 1;285(1):522-30.

Summary of findings: Carrageenan stimulates innate immune-mediated pathways of inflammation.

Funding: National Institutes of Health; Veterans

Administration

Author affiliations: University of Illinois at Chicago

Bhattacharyya S, Liu H, Zhang F, Jam M, Dudeja PK, Michel G, Linhardt R, and Tobacman JK (2010) Carrageenan-induced innate immune response is modified by enzymes that hydrolyze distinct galactosidic bonds. *Journal of Nutritional Biochemistry* 21(10): 906-13.

Summary of findings: This study examines the immune response by which food-grade carrageenan causes inflammation.

Funding: Veterans Administration

Author affiliations: University of Illinois at Chicago; Jesse Brown Veterans Affairs Medical Center; Rensselaer Polytechnic Institute; University Pierre and Marie Curie/Sorbonne University, Paris, France

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.

Funding: Veterans Administration

Author affiliations: University of Illinois at Chicago; Jesse Brown Veterans Affairs Medical Center

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

Summary of findings: Inflammation of the colon caused by exposure to low levels of food-grade carrageenan persists beyond the initial period of exposure.

Funding: National Institutes of Health

Author affiliations: University of Illinois at Chicago

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.

Funding: National Institute of General Medical Sciences, National Institutes of Health

Author affiliations: University of Illinois at Chicago; Jesse Brown Veterans Affairs Medical Center; Rensselaer Polytechnic Institute

Bhattacharyya S, O-Sullivan I, Katyal S, Unterman T and Tobacman JK (2012) Exposure to the common food additive carrageenan leads to glucose intolerance, insulin resistance and inhibition of insulin signalling in HepG2 cells and C57BL/6J mice. *Diabetologia* 55(1): 194-203.

Summary of findings: Carrageenan in the diet may contribute to diabetes. Carrageenan impairs glucose tolerance, increases insulin resistance, and inhibits insulin signalling in vivo in mouse liver and human HepG2 cells. These effects may result from carrageenan-induced inflammation.

Funding: National Institutes of Health; American Diabetes Association

Author affiliations: University of Illinois at Chicago

Further research continues. An ongoing study with ulcerative colitis patients aims to shed light on the effects of carrageenan in the diet on gastrointestinal disease. Other studies currently underway provide additional data to examine the link between food-grade carrageenan and diabetes.

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. This study showed that Sp1 activated Wnt9A transcription through changes in arylsulfatase B, chondroitin 4-sulfation, and galectin-3. In conclusion, a decline in arylsulfatase B leads to transcriptional effects mediated by Sp1 and galectin-3. The significance is that extracellular events can regulate transcription through changes in arylsulfatase B and chondroitin 4-sulfation.

Author affiliations: University of Illinois at Chicago; Jesse Brown Veterans Affairs Medical Center

Bhattacharyya S, Feferman L, Borthakur S and Tobacman JK (2014) Common Food Additive Carrageenan Stimulates Wnt/ β -Catenin Signaling in Colonic Epithelium by Inhibition of Nucleoredoxin

Reduction. *Nutrition and Cancer* 66(1): 117-127.

Summary of findings: Exposure to carrageenan may be a risk factor in development of colorectal cancer. The findings indicate that environmental exposure stimulates both Wnt signaling and suggest that carrageenan exposure in vivo may contribute to development of colonic neoplasia (uncontrolled growth of cells). Average daily intake of carrageenan in the U.S. in the 1970s was calculated to be 108 mg by the National Academy of Sciences, but recently the average daily carrageenan intake was reported to be ~250 mg/day. Increased attention to the effects of carrageenan on vital cell processes, including the Wnt/ β -catenin pathway, may lead to significant clinical benefit, as well as increased understanding of relationships between environmental exposures and human disease.

Funding: Veterans Affairs Merit Award

Author affiliations: University of Illinois at Chicago; Jesse Brown Veterans Affairs Medical Center

Bhattacharyya S, Feferman L, and Tobacman JK (2014) Regulation of Chondroitin-4-Sulfotransferase (CHST11) Expression by Opposing Effects of Arylsulfatase B, 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.

Funding: University of Illinois at Chicago

Author affiliations: Department of Medicine, University of Illinois at Chicago

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 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. ER stress plays a crucial role in selenoprotein P regulation. Salsalate relieves ER stress and is a new therapeutic strategy to treat insulin resistance.

Author affiliations: Division of Endocrinology and

Metabolism, Department of Internal Medicine, Korea University Guro Hospital

Bhattacharyya S, Feferman L, Unterman T, and Tobacman JK (2015) Exposure to common food additive carrageenan alone leads to fasting hyperglycemia and in combination with high fat diet exacerbates glucose intolerance and hyperlipidemia without effect on weight. *Journal of Diabetes Research* Volume 2015, Article ID 513429.

Summary of findings: Mice exposed to 10mg/L food-grade lambda and kappa carrageenan in drinking water and fed an 8% fat diet for 1 year showed glucose intolerance after 6 days and earlier onset of fasting hyperglycemia, higher glucose levels, and exacerbated dyslipidemia compared with the control. This suggests that carrageenan exposure may exacerbate harmful effects of a high fat diet and contribute to development of diabetes.

Author affiliations: Department of Medicine, University of Illinois at Chicago

Bhattacharyya 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.

Summary of findings: Inflammation induced by exposure to the common food additive carrageenan leads to insulin resistance by increase in Ser(P)(307)-insulin receptor substrate 1 (IRS1) and subsequent decline in the insulin-stimulated increase in Ser(P)(473)-AKT. Studies were performed in human HepG2 cells and in C57BL/6J mice. and indicate that carrageenan inhibited insulin signaling by two mechanisms. These mechanisms provide internal feedback, mediated by Ser(P)(473)-AKT, Ser(P)(401)-GATA2, and nuclear GATA2, which modulates insulin responsiveness.

Author affiliations: University of Illinois at Chicago; Jesse Brown Veterans Affairs Medical Center

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: Antibodies to the oligosaccharide epitope galactose- α -1,3-galactose (alpha-gal) are of considerable interest because they are so prevalent, include all isotypes, and are specific to humans and Old World apes. Alpha-gal-mediated responses, including immediate and delayed anaphylaxis, appear to be increasing. In the recent review “The alpha-gal story: lessons learned from connecting the dots,” sources of exposure to the alpha-gal epitope were presented, with particular attention to cetuximab, mammalian meat products, and tick bites. This communication is intended to bring attention to including carrageenan, a very commonly used food additive, to the list of sources of exposure to the alpha-gal epitope.

Author affiliations: Department of Medicine, University of Illinois at Chicago

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. Certain food substitutions for dairy products may expose patients to additives like carrageenan, for which there is evidence of its contribution to gastrointestinal disturbances. Considering an etiology for gastrointestinal symptoms brought on by dietary additives in the diagnostic differential gives the practitioner avenues to pursue prior to ordering expensive testing and treatments.

Author affiliations: Louisiana State University School of Medicine

Appendix B: Marinalg Working Group on Molecular Weight Distribution Specification for Carrageenan

Technical Position on Measurements Related to Meeting the EC Molecular Weight Distribution Specification for Carrageenan and PES

The Marinalg Working Group on Molecular Weight Determination (William Blakemore FMC, Chairman; Dr. Harris Bixler, SIAP, Secretary; Arne Graff Anderson, CPKelco; Dr. Joop de Vries, Danisco; Dr. Patrick Boulenguer, Degussa) has been carrying out experiments since April, 2003 to measure the molecular weight distribution of commercial carrageenan and PES used in foods. It was on March 5, 2003 that the EC-SCF expressed an opinion proposing a new specification for these hydrocolloids to augment the 5 cps water viscosity “if feasible”.

The purpose of the new specification is to have better control over the amount of very low molecular

weight carrageenan and PES going into food products. Oligomers of carrageenan less than 10,000 daltons (Da) in molecular weight have a history of causing adverse toxicological effects when fed in large quantities to certain rodents; although there is no epidemiological evidence that the very small amounts of these oligomers that might be present in carrageenan or PES being used in foods have caused any harmful effects to humans.

Before the Marinalg Working Group of carrageenan producers had adequate time to determine the feasibility of measuring the new specification, it was formally adopted by the EC as Commission Directive 2004/45/EC on April 16, 2004 for implementation by Member States by April 1, 2005. This specification requires that carrageenan or PES used in food must not contain more than 5% molar mass with molecular weight less than 50,000 Da. To save space in this

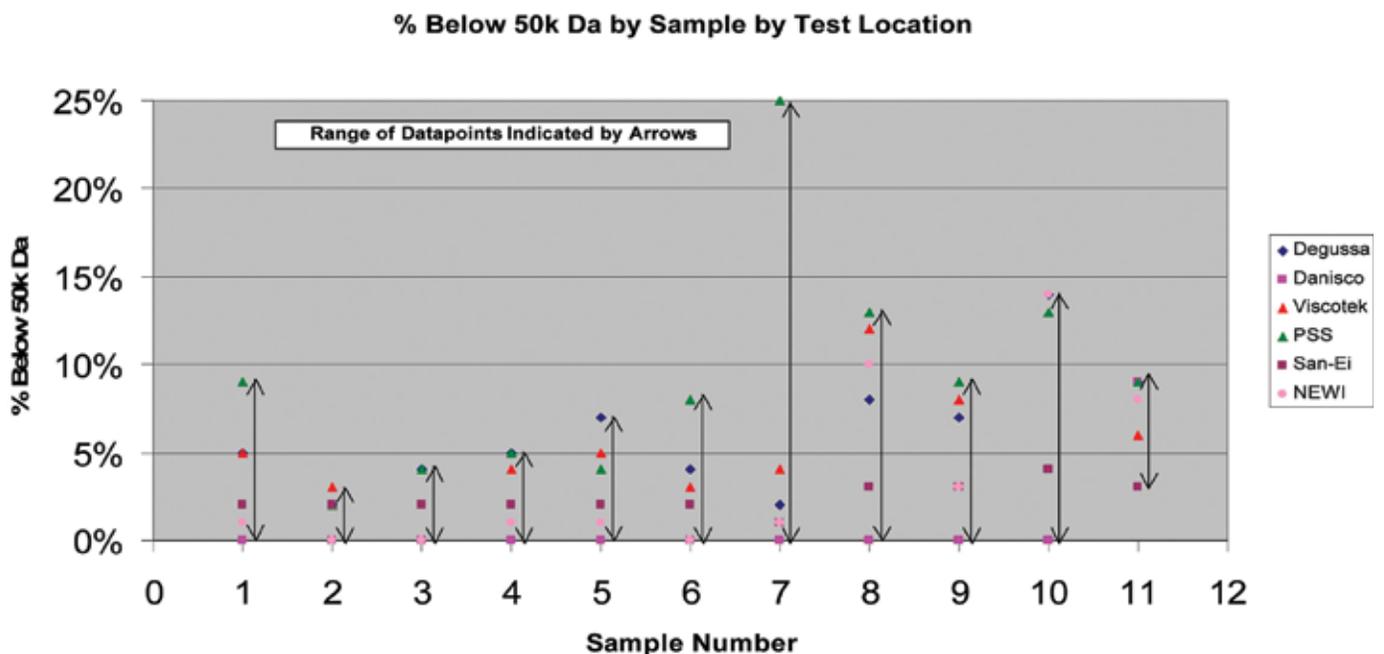


Figure 1

document, this low molecular weight tail will be abbreviated as the LMT.

At the time of writing (November, 2005) the Working Group has not found a method for molecular weight distribution measurement that is sufficiently accurate and reproducible to yield a validated and defensible method.

The methods studied have all been based on size exclusion chromatography (SEC) followed by concentration and molecular weight detection in the stream exiting the chromatography columns. SEC is used to spread out the carrageenan molecular size distribution in the flow stream exiting the columns. Note that this separation is by molecular size and not molecular weight, so physical models are used to convert molecular size data to molecular weights. The stream exiting the SEC columns flows through a series of detectors: refractive index for carrageenan concentration determination and light scattering and/or intrinsic viscosity for molecular weight determination. Some instruments include chemical detectors to be sure only carrageenan is being measured in the flow stream.

These are highly developed commercial research instruments of great technical sophistication. Nevertheless, none met the most important objective of the Working Group. Six laboratories participated in

this study, Degussa; Danisco; Viscotek, Ltd; Polymer Standards Services, GmbH; San-Ei Gen FFI, Ltd; North East Wales Institute/NEWI, all with state-of-the art equipment and with qualified scientists to run the experiments. Procedure details (sample preparation and concentration, eluent type and concentration, etc.) were recorded for each lab and approved by the Working Group. Eleven different commercial carrageenan and PES samples, representing different sulfated polygalactose types (nominally kappa, lambda and iota) made by five different producers, were tested by all laboratories under “Round Robin” conditions. Annex 1 (the Summary Sheet and the Sample Information Sheet) contains test results and physical characteristics of the Round Robin samples, respectively.

Despite all this technical discipline, inter-lab reproducibility of the LMT was shown to be poor (Fig. 1). (Readers desiring larger format figures for more careful study of results are referred to Annex II.). Detectors downstream of the SEC columns must be able to measure polymer concentration and molecular weight accurately in the range represented by the LMT. It appears that even under optimum SEC conditions, detector signal to noise ratio (S/N) in the LMT region is extremely low, especially for light scattering upon which molecular weight determination is based (Fig. 2). Several test locations have experienced drifting baselines, and variable recov-

Typical output from SEC/RI/MALLS - Degussa Data

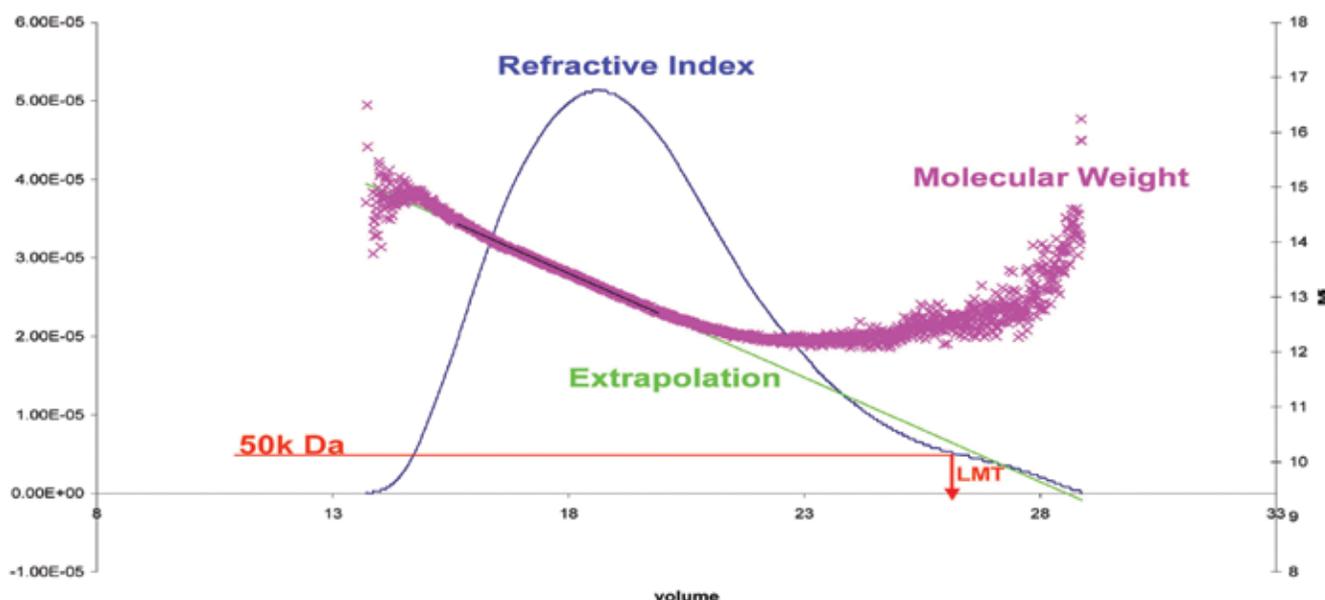


Figure 2

eries (measured concentration versus actual), both of which make data interpretation even more complex and unreliable. Initially the Working Group thought that the Viscotek triple detector method (refractive index, low angle light scattering and intrinsic viscosity) was giving promising results, and as a consequence published the method on the Marinalg website. However, further testing indicated that these same issues applied, but to a lesser degree.

Various physical models of molecular weight determination by light scattering (Zimm, Debye, Berry) are being used in SEC / light scattering software to extrapolate from a region of the distribution with good S/N into the region of poor S/N. For all of the carrageenan samples studied the S/N within the LMT was low and resulted in extrapolations having to be made from well outside the LMT range (Fig. 2, green line). This type of extrapolation is subject to enough error so as not to give defensible results for regulatory purposes. This can be seen in Fig. 2 where the LMT region is shown graphically. Clearly any shift in baseline or green line extrapolation will have a profound effect on the very small LMT region calculated for commercial carrageenan being used in foods. It is estimated that it is virtually impossible to determine the molecular weight of SEC-spread samples below about 10,000 Da by any of the light scattering techniques.

The Working Group’s experience with SEC/light scattering in no way detracts from its use as a valuable research tool. The technique is widely used for estimating polymer molecular structure in food and industrial applications. A higher level of accuracy, however, is required when it is to be used for specification and regulatory measurements. Even in the present study valuable information (from the Round Robin samples) was obtained. For instance, fairly good consistency was seen for inter-lab results obtained for the weight average molecular weight (Mw) (Fig. 3), except for one sample, a lambda type that is known to be a more rigid rod in solution than the kappa and iota types. Furthermore there was fairly good correlation for Mw versus water viscosity (Fig. 3), except for the one aberrant sample already noted. However, when looking at the LMT data, both these consistencies and correlations were generally poor (Fig. 4)

The Working Group has conferred with several world class scientists (Prof. Wayne Reed, Tulane University, Dr. Phillip Wyatt and his staff at Wyatt Technology, and the group consisting of Drs. Chi-San Wu, E. Malawer and L. Senak at ISP and Dr. Maguarite Rinaudo at CMRV) who have been involved in developing and using SEC/light scattering for a variety of research purposes. While some were confident that the Working Group’s goal could be reached, none had ever done so. Through this pro-

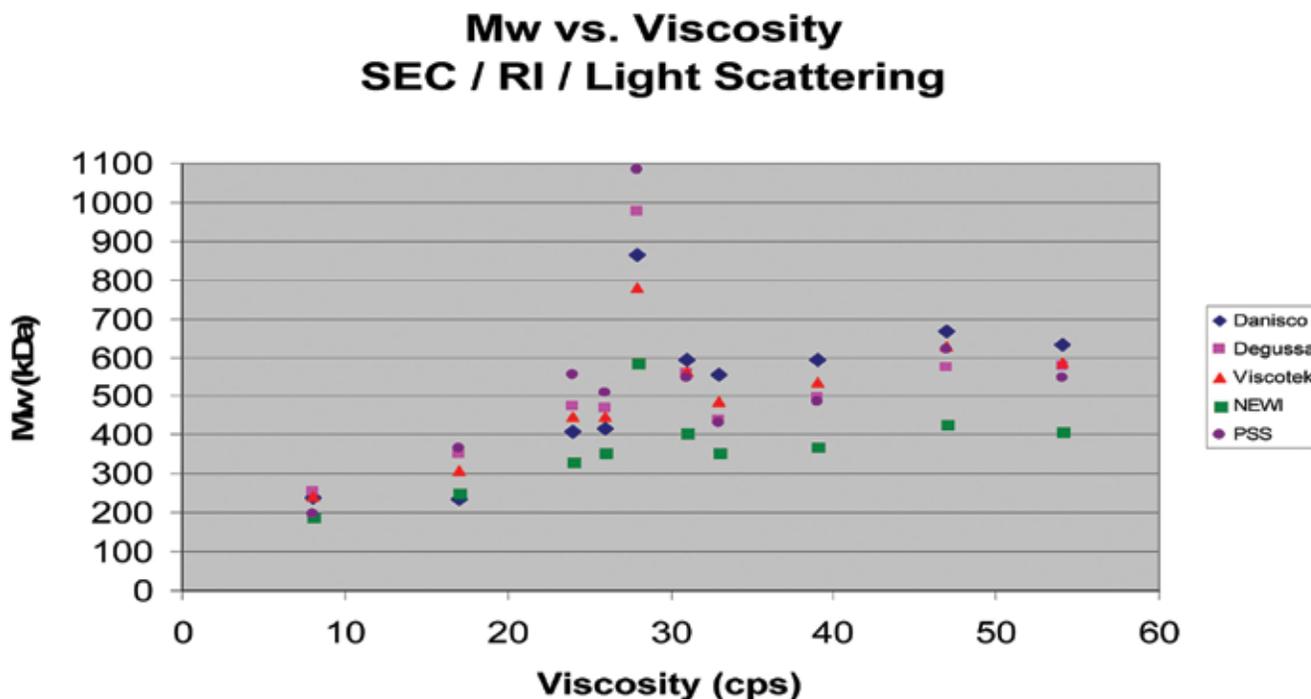


Figure 3

LMT vs. Viscosity SEC / RI / Light Scattering

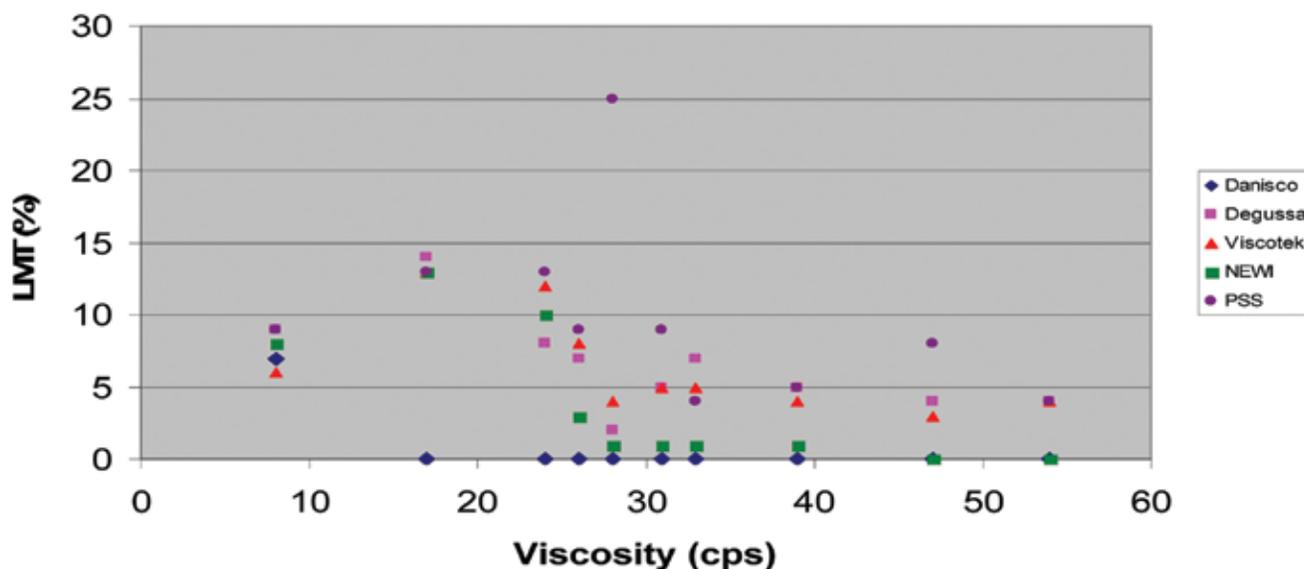


Figure 4

cess consensus was gradually reached that the current equipment employing light scattering and the attendant software will not measure the EC specification with sufficient accuracy to survive the necessary validation protocols.

While the work to date with light scattering has led to frustrating conclusions, it has pointed in a direction of potentially more promise which will be explored by the Working Group. Light scattering became dominant in the measurement of polymer molecular weight distributions because molecular weights exiting a SEC column over most of a samples' range (except the LMT) could be determined directly. Prior to this advancement, column calibration with molecular weight standards had to be used.

This technique involves preparing a calibration curve of exit time from the SEC column versus molecular weight for a set of standards of very narrow molecular weight distribution ($M_w/M_n < 1.2$) (polydispersity index or PDI). The molecular weight of the polymer standards is now usually determined by light scattering. No SEC is required when the molecular weights are being determined, and sample concentrations can be adjusted to optimize the S/N ratio. The polymer standards must encompass the molecular weight range of interest for samples being used in a SEC study. For water soluble hydrocolloids, the most widely used standards are eight

pullulans ranging in Mw from 5,300 to 760,000 Daltons that are commercially available from Shodex. This method has been tested on commercial carrageenans, and the results have been reported in the scientific literature by Japanese scientists (Uno, et al, Food Additives and Contaminants, 18, No. 9, pp763-772, 2001). No correction was applied in this work for the differences between pullulan and carrageenan sizes versus molecular weights, so validation of the LMTs reported by Uno remains in question.

Of course, having a set of carrageenan standards would be preferable and the Working Group is exploring the preparation of such a set. It should be noted, however, that producing carrageenan standards with PDI < 1.2 will be very difficult, and from past experience PDI values would be expected to be 1.6 at best and more likely closer to 2.0, probably outside the range of PDI needed for LMT accuracy.

The difficulties in obtaining the Standards has lead the Working Group to explore the application of a technology referred to as "universal calibration", a physical model for converting a pullulan calibration curve to a carrageenan calibration curve (Grubisic, Z. et al, Polymer Letters, 5, pp753-759, 1967). The model takes into consideration size and shape differences for the two polymers when their molecular weights are the same. Initial work applying this technique to the Uno data shows some promise, but

% Below 50k Da vs Viscosity
Commercial Carrageenan and PES Samples - Viscotek Data

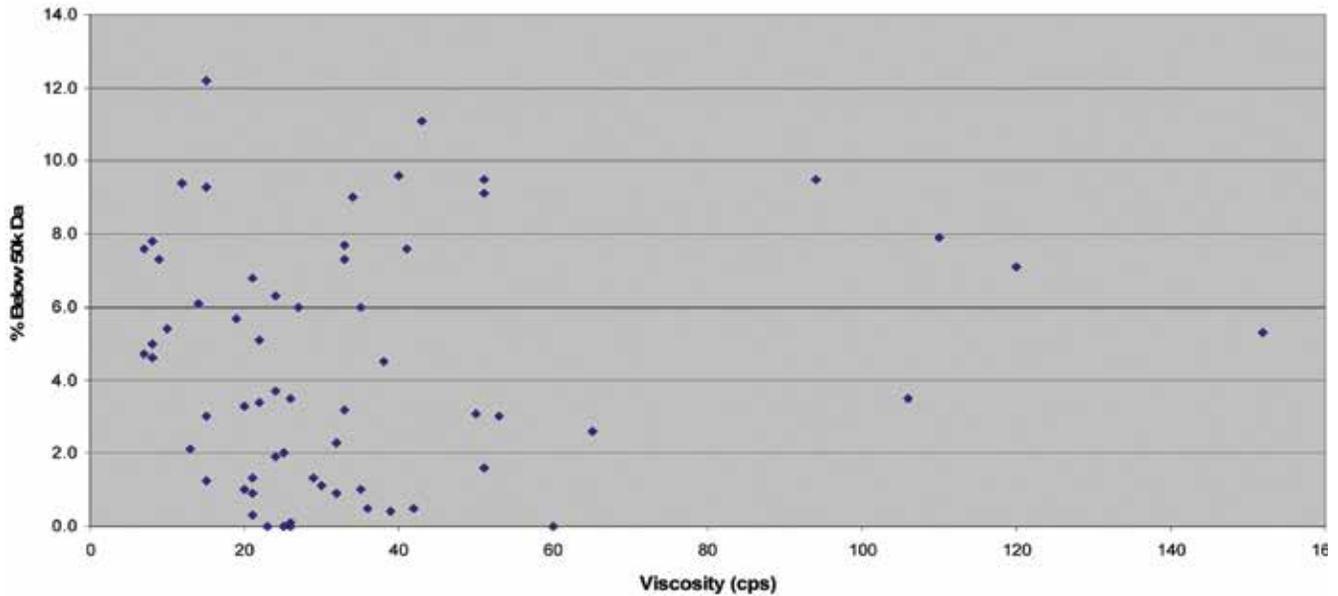


Figure 5

it is too early to draw any conclusions.

A related technology referred to as "polydisperse or broad standard calibration" is also under investigation (Malawer, E.G. and A.J. Montana, *Journal of Polymer Science: Polymer Physics Edition*, 18, pp2303-2305, 1980). For this purpose, a very broad molecular weight distribution carrageenan is prepared as a standard that has relatively high concentrations of carrageenan in the low and high molecular weight tails and spans the range of Mw of interest. Again, physical modeling and computer analysis is employed to convert SEC exit time to a carrageenan molecular weight.

There is no assurance until experiments can be run to know whether to poor accuracy of LMT calculation from light scattering can be improved upon by use of either universal or polydisperse calibration.

The Working Group also went back to the JECFA and FCC water viscosity method of specifying a pseudo molecular weight limit on carrageenan and PES to see if it could be improved upon to identify commercial products with a satisfactory LMT. Fig. 5 shows that products of nearly identical water viscosity can have very different LMTs, at least to the qualitative degree to which light scattering LMT measurements can be relied upon. Note however, that although there is no correlation between the

LMT and viscosity, the correlation between molecular weight (Mw) remains fairly good as described earlier (Fig. 3).

It is clear at this point in time that successfully measuring the EC specification is not currently feasible. The Marinalg Working Group will continue to explore methods, but cannot guarantee success.

Of greater significance to human safety are the results of a recent 90-day rat feeding study that was performed with a carrageenan very close to the 5 cps water viscosity limit (8cps). The study showed no adverse toxicological effects in the test animals. A poster presentation of this work, delivered at the Society of Toxicology 2004 annual meeting, is contained on the Marinalg Website, and a complete article that is to appear in 2006 in a peer reviewed journal is pending.

This very important feeding study is more thoroughly summarized in an introduction and synopsis to this technical position paper. It was prepared by members of Marinalg's Technical and Regulatory Committee and appears as a position paper on the Marinalg website. It should satisfy even the most concerned reader that failing to measure the new EC specification results in no increased risk to human health.

Sample ID	Round Robin	Testing Org.	Testing Method	Mw	Mass Rec. (%)	% <50K
9939-03	#2	NEWI	RI-MALLS; 0.2u filter	406 000	86%	1%
		NEWI	RI-MALLS; 0.45u filter	395 000	89%	1%
Avg Water Vis.	31 cps	San-Ei	RI-Pullulan Stds-ICP	1 259 000	NA	2%
		San-Ei	RI-Pullulan Stds	1 201 000	NA	2%
		Viscotek	RI-Vis-LALLS (04)	578 000	103%	0%
		Viscotek	RI-Vis-LALLS (05)	563 000	99%	5%
		Degussa	RI-MALLS (04)	662 000	NA	2%
		Degussa	RI-MALLS (05)	561 200	NA	5%
		PSS/PSS	RI-MALLS	549 000	72%	9%
		PSS/Mod	RI-MALLS	459 000	NA	NA
		Danisco I	RI-MALLS	613 000	NA	0%
		Danisco II	RI-MALLS	595 000	79%	0%
7834-03	#2	NEWI	RI-MALLS; 0.2u filter	548 000	85%	0%
		NEWI	RI-MALLS; 0.45u filter	553 000	87%	0%
Avg Water Vis.	703 cps	San-Ei	RI-Pullulan Stds-ICP	504 000	NA	2%
		San-Ei	RI-Pullulan Stds	470 000	NA	2%
		Viscotek	RI-Vis-LALLS (04)	810 000	95%	0%
		Viscotek	RI-Vis-LALLS (05)	899 000	96%	3%
		Degussa	RI-MALLS (04)	1 497 000	NA	0%
		Degussa	RI-MALLS (05)	933 400	NA	2%
		PSS/PSS	RI-MALLS	911 000	75%	2%
		PSS/Mod	RI-MALLS	749 000	NA	1%
		Danisco I	RI-MALLS	2 022 000	NA	0%
		Danisco II	RI-MALLS	1 870 000	21%	0%
MW_KAPPA	#2	NEWI	RI-MALLS; 0.2u filter	408 000	91%	0%
		NEWI	RI-MALLS; 0.45u filter	401 000	95%	0%
Avg Water Vis.	54 cps	San-Ei	RI-Pullulan Stds-ICP	1 293 000	NA	2%
		San-Ei	RI-Pullulan Stds	1 449 000	NA	1%
		Viscotek	RI-Vis-LALLS (04)	642 000	91%	0%
		Viscotek	RI-Vis-LALLS (05)	586 000	111%	4%
		Degussa	RI-MALLS (04)	615 000	NA	1%
		Degussa	RI-MALLS (05)	580 000	NA	4%
		PSS/PSS	RI-MALLS	548 000	79%	4%
		PSS/Mod	RI-MALLS	511 000	NA	1%
		Danisco I	RI-MALLS	650 000	NA	0%
		Danisco II	RI-MALLS	634 000	86%	0%
MW-IOTA	#2	NEWI	RI-MALLS; 0.2u filter	372 000	89%	1%
		NEWI	RI-MALLS; 0.45u filter	388 000	91%	0%
Avg Water Vis.	39 cps	San-Ei	RI-Pullulan Stds-ICP	1 189 000	NA	2%
		San-Ei	RI-Pullulan Stds	1 232 000	NA	1%
		Viscotek	RI-Vis-LALLS (04)	618 000	97%	1%
		Viscotek	RI-Vis-LALLS (05)	536 000	103%	4%
		Degussa	RI-MALLS (04)	532 000	NA	1%

Sample ID	Round Robin	Testing Org.	Testing Method	Mw	Mass Rec. (%)	% <50K
		Degussa	RI-MALLS (05)	496 900	NA	5%
		PSS/PSS	RI-MALLS	485 000	66%	5%
		PSS/Mod	RI-MALLS	471 000	NA	1%
		Danisco I	RI-MALLS	605 000	NA	0%
		Danisco II	RI-MALLS	593 000	10%	0%
TS-C6336	#2	NEWI	RI-MALLS; 0.2u filter	355 000	76%	0%
		NEWI	RI-MALLS; 0.45u filter	352 000	76%	1%
Avg Water Vis.	33 cps	San-Ei	RI-Pullulan Stds-ICP	1 025 000	NA	2%
		San-Ei	RI-Pullulan Stds	1 096 000	NA	1%
		Viscotek	RI-Vis-LALLS (04)	580 000	93%	1%
		Viscotek	RI-Vis-LALLS (05)	486 000	102%	5%
		Degussa	RI-MALLS (04)	506 000	NA	2%
		Degussa	RI-MALLS (05)	438 900	NA	7%
		PSS/PSS	RI-MALLS	433 000	72%	4%
		PSS/Mod	RI-MALLS	409 000	NA	2%
		Danisco I	RI-MALLS	546 000	NA	0%
		Danisco II	RI-MALLS	557 000	66%	0%
13754(Rad)	#2	NEWI	RI-MALLS; 0.2u filter	428 000	86%	0%
		NEWI	RI-MALLS; 0.45u filter	429 000	87%	0%
Avg Water Vis.	47 cps	San-Ei	RI-Pullulan Stds-ICP	1 020 000	NA	2%
		San-Ei	RI-Pullulan Stds	1 020 000	NA	2%
		Viscotek	RI-Vis-LALLS (04)	687 000	97%	3%
		Viscotek	RI-Vis-LALLS (05)	629 000	100%	3%
		Degussa	RI-MALLS (04)	635 000	NA	1%
		Degussa	RI-MALLS (05)	576 100	NA	4%
		PSS/PSS	RI-MALLS	621 000	72%	8%
		PSS/Mod	RI-MALLS	409 000	NA	1%
		Danisco I	RI-MALLS	657 000	NA	0%
		Danisco II	RI-MALLS	669 000	64%	0%
13754(Chon)	#2	NEWI	RI-MALLS; 0.2u filter	586 000	69%	1%
		NEWI	RI-MALLS; 0.45u filter	767 000	70%	0%
Avg Water Vis.	28 cps	San-Ei	RI-Pullulan Stds-ICP	1 623 000	NA	1%
		San-Ei	RI-Pullulan Stds	1 651 000	NA	1%
		Viscotek	RI-Vis-LALLS (04)	1 100 000	85%	0%
		Viscotek	RI-Vis-LALLS (05)	778 000	107%	4%
		Degussa	RI-MALLS (04)	1 078 000	NA	1%
		Degussa	RI-MALLS (05)	974 600	NA	2%
		PSS/PSS	RI-MALLS	1 084 000	50%	25%
		PSS/Mod	RI-MALLS	NA	NA	NA
		Danisco I	RI-MALLS	872 000	NA	0%
		Danisco II	RI-MALLS	865 000	50%	0%
20ND	#2	NEWI	RI-MALLS; 0.2u filter	333 000	75%	11%
		NEWI	RI-MALLS; 0.45u filter	351 000	75%	9%

Sample ID	Round Robin	Testing Org.	Testing Method	Mw	Mass Rec. (%)	% <50K
Avg Water Vis.	24 cps	San-Ei	RI-Pullulan Stds-ICP	993 000	NA	3%
		San-Ei	RI-Pullulan Stds	973 000	NA	3%
		Viscotek	RI-Vis-LALLS (04)	527 000	91%	0%
		Viscotek	RI-Vis-LALLS (05)	448 000	108%	12%
		Degussa	RI-MALLS (04)	482 000	NA	7%
		Degussa	RI-MALLS (05)	474 500	NA	8%
		PSS/PSS	RI-MALLS	554 000	55%	13%
		PSS/Mod	RI-MALLS	NA	NA	NA
		Danisco I	RI-MALLS	448 000	NA	1%
		Danisco II	RI-MALLS	411 000	59%	0%
70CI	#2	NEWI	RI-MALLS; 0.2u filter	357 000	69%	3%
		NEWI	RI-MALLS; 0.45u filter	364 000	70%	3%
Avg Water Vis.	26 cps	San-Ei	RI-Pullulan Stds-ICP	1 034 000	NA	3%
		San-Ei	RI-Pullulan Stds	1 080 000	NA	2%
		Viscotek	RI-Vis-LALLS (04)	469 000	98%	4%
		Viscotek	RI-Vis-LALLS (05)	449 000	111%	8%
		Degussa	RI-MALLS (04)	487 000	NA	6%
		Degussa	RI-MALLS (05)	469 800	NA	7%
		PSS/PSS	RI-MALLS	511 000	58%	9%
		PSS/Mod	RI-MALLS	NA	NA	NA
		Danisco I	RI-MALLS	496 000	NA	1%
		Danisco II	RI-MALLS	418 000	61%	0%
01T1	#2	NEWI	RI-MALLS; 0.2u filter	252 000	65%	13%
		NEWI	RI-MALLS; 0.45u filter	245 000	71%	14%
Avg Water Vis.	17 cps	San-Ei	RI-Pullulan Stds-ICP	751 000	NA	4%
		San-Ei	RI-Pullulan Stds	747 000	NA	4%
		Viscotek	RI-Vis-LALLS (04)	436 000	90%	1%
		Viscotek	RI-Vis-LALLS (05)	308 000	111%	13%
		Degussa	RI-MALLS (04)	482 000	NA	17%
		Degussa	RI-MALLS (05)	351 200	NA	14%
		PSS/PSS	RI-MALLS	366 000	52%	13%
		PSS/Mod	RI-MALLS	NA	NA	NA
		Danisco I	RI-MALLS	319 000	NA	4%
		Danisco II	RI-MALLS	235 000	16%	0%
6371-03	#2	NEWI	RI-MALLS; 0.2u filter	189 000	88%	7%
		NEWI	RI-MALLS; 0.45u filter	188 000	89%	8%
Avg Water Vis.	8 cps	San-Ei	RI-Pullulan Stds-ICP	559 000	NA	3%
		San-Ei	RI-Pullulan Stds	632 000	NA	2%
		Viscotek	RI-Vis-LALLS (04)	257 000	96%	5%
		Viscotek	RI-Vis-LALLS (05)	243 000	109%	6%
		Degussa	RI-MALLS	253 000	NA	9%
		PSS/PSS	RI-MALLS	195 000	78%	9%
		PSS/Mod	RI-MALLS	190 000	80%	12%
		Danisco III	RI-MALLS 0.1M LiNO3	256 000	NA	5%

Sample ID	Round Robin	Testing Org.	Testing Method	Mw	Mass Rec. (%)	% <50K
		Danisco IV	RI-MALLS 0.05M LiNO3	238 000	NA	9%
2217-01	#1	NEWI	RI-MALLS; 0.2u filter	213 000	86%	8%
		NEWI	RI-MALLS; 0.45u filter	217 000	91%	6%
Avg Water Vis.	12 cps	San-Ei	RI-Pullulan Stds-ICP	686 000	NA	2%
		San-Ei	RI-Pullulan Stds	652 000	NA	1%
		Viscotek	RI-Vis-LALLS (04)	273 000	NA	2%
		Viscotek	RI-Vis-LALLS (05)	NA	NA	NA
		Degussa	RI-MALLS	253 000	NA	10%
		PSS/PSS	RI-MALLS	274 000	NA	8%
		PSS/Mod	RI-MALLS	NA	NA	NA
6370-03	#1	NEWI	RI-MALLS; 0.2u filter	188 000	86%	8%
		NEWI	RI-MALLS; 0.45u filter	188 000	89%	8%
Avg Water Vis.	9 cps	San-Ei	RI-Pullulan Stds-ICP	658 000	NA	2%
		San-Ei	RI-Pullulan Stds	630 000	NA	2%
		Viscotek	RI-Vis-LALLS (04)	228 000	NA	5%
		Viscotek	RI-Vis-LALLS (05)	NA	NA	NA
		Degussa	RI-MALLS	202 000	NA	10%
		PSS/PSS	RI-MALLS	215 000	NA	8%
		PSS/Mod	RI-MALLS	NA	NA	NA

Sample Information

				SPI WATER VISCOSITY 1.5%; 75C				
RR#2 Sample ID	Carrageenan Type	Producer	Approx. Gum Content (%)	SIAP 5/04 (cps)	SIAP 7/05 (cps)	FMC 6/04 (cps)	FMC 7/05 (cps)	AVERAGE (cps)
9939-03	Kappa IPA	FMC	75%	28	24	36	34	31
7834-03	Radula IPA	FMC	82%	690	650	745	728	703
MW-kappa	Kappa GP	CPK	79%	48	44	60	64	54
MW-iota	Iota IPA	CPK	79%	36	35	42	44	39
TS-C6336	Radula GP	Danisco	77%	32	28	35	37	33
13754(Rad)	Radula IPA	Degussa	78%	44	42	53	49	47
13754(Chon)	Chondrus IPA	Degussa	62%	26	23	33	30	28
20ND	PES Kappa	Shemberg	67%	24	20	26	27	24
70C1	PES Kappa	Shemberg	66%	28	23	26	28	26
01T1	PES Iota	Shemberg	66%	19	15	15	20	17
6371-03	Kappa IPA	FMC	85%	NA	7	8	8	8
RR#1 Sample ID								
2217-01	Kappa IPA	FMC	84%			12	12	12
6370-03	Kappa IPA	FMC	85%			9	9	9

Endnotes

- 1 Pubmed search “carrageenan induced inflammation” 3,855 results, March 23, 2016.
- 2 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.
- 3 Bhattacharyya S, O-Sullivan I, Katyal S, Unterman T and Tobacman JK (2012) Exposure to the common food additive carrageenan leads to glucose intolerance, insulin resistance and inhibition of insulin signaling in HepG2 cells and C57BL/6J mice. *Diabetologia* 55(1): 194-203.
- 4 Watt J and Marcus R (1981) Harmful effects of carrageenan fed to animals. *Cancer Detection and Prevention* 4(1-4): 129-134.
- 5 Watt J and Marcus R (1981) Harmful effects of carrageenan fed to animals. *Cancer Detection and Prevention* 4(1-4): 129-134.
- 6 Tobacman JK (2001) Review of Harmful Gastrointestinal Effects of Carrageenan in Animal Experiments. *Environmental Health Perspectives* 109(10): 983-994.
- 7 Wilcox DK, Higgins J, Bertram TA (1992) Colonic epithelial cell proliferation in a rat model of nongenotoxin-induced colonic neoplasia. *Laboratory Investigation* 67:405–411.

See also: Hagiwara A, Miyashita K, Nakanishi T, Sano M, Tamano S, Asai I, Nakamura M, Imaida K, Ito N and Shirai T (2001) Lack of Tumor Promoting Effects of Carrageenan on 1,2-Dimethylhydrazine-induced Colorectal Carcinogenesis in Male F344 Rats. *Journal of Toxicologic Pathology* Vol. 14; 37.
- 8 Carthew P (2001) Safety of carrageenan in foods. *Environmental Health Perspectives* 110(4): A176-177.
- 9 See Appendix A “Scientific Findings” for citations.
- 10 IARC Working Group on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Carrageenan. *IARC Monogr Eval Carcinog Risk Hum* 31:79–94. 1983.
- 11 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 Chem Toxicol* 22:615–621.
- 12 Thomson AW and Fowler EF (1981) Carrageenan: a review of its effect on the immune system. *Agents and Actions* 1:265–273.
- 13 Salyers AA, West SHE, Vercelotti JR, Wilkins TD (1977) Fermentation of mucins and plant polysaccharids by anaerobic bacteria from the human colon. *Applied Environmental Microbiology* 334:529–533.
- 14 Di Rosa M. (1972) Review: Biological properties of carrageenan. *Journal of Pharmacy and Pharmacology* 24:89–102. 1972
- 15 International Agency for Research on Cancer. World Health Organization. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. 1998. Available online: <http://monographs.iarc.fr/ENG/Monographs/vol31/volume31.pdf>. Last accessed on March 23, 2016.
- 16 Marinalg (seaweed-based hydrocolloid industry trade lobby group, representing carrageenan manufacturers) test results show contamination of food-grade carrageenan with degraded carrageenan, classified as a “possible human carcinogen.” Was available online at <http://www.marinalg.org/wp-content/uploads/2012/09/Final-Full-Report.pdf>. Last accessed on January 30, 2013. No longer available online.
- 17 Tobacman JK (2001) Review of Harmful Gastrointestinal Effects of Carrageenan in Animal Experiments. *Environmental Health Perspectives* 109(10): 983-994.
- 18 Bhattacharyya S, Dudeja PK and Tobacman JK (2008) Carrageenan-induced NFκB activation depends on distinct pathways mediated by reactive oxygen species and Hsp27 or by Bcl10. *Biochimica and Biophysica Acta* 1780(7-8): 973-82.

See also: Bhattacharyya S, Liu H, Zhang F, Jam M, Dudeja PK, Michel G, Linhardt RJ, and Tobacman JK (2010) Carrageenan-induced innate immune response is modified by enzymes that hydrolyze distinct galactosidic bonds. *Journal of Nutritional Biochemistry* 21(10): 906-13.

See also: Borthakur A, Bhattacharyya S, Anbazhagan AN, Kumar A, Dudeja PK and Tobacman JK (2012) Prolongation of carrageenan-induced inflammation in human colonic epithelial cells by activation of an NFκB-BCL10 loop. *Biochimica and Biophysica Acta* 1822(8): 1300-7.
- 19 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.
- 20 Status report on the work of Marinalg International to measure the molecular weight distribution of carrageenan and PES in order to meet the EU specification: less than 5% below 50,000 Daltons. Marinalg. Was available online at: http://www.marinalg.org/PDF/_FULL_Molecular_weight_distribution_of_carrageenan_and_PES.pdf. Taken off-line. Last accessed April 4, 2012.
- 21 In an earlier version of the Working Group’s report, Marinalg admitted: “At the time of writing (November, 2005) the Working Group has not found a method for molecular weight distribution measurement that is sufficiently accurate and reproducible to yield a validated and defensible method.” The file is no longer available on the Marinalg International website, but a PDF of the report is available upon request from The Cornucopia Institute.
- 22 Singh SK, Shen BC, Chou ST and Fan LT (1994) Acid hydrolysis of k-carrageenan in batch reactor: stochastic simula-

- tion of change of molecular weight distribution over time. *Biotechnology Progress* 10: 389-397.
- 23 Ekström, L.G. (1985) Molecular-weight-distribution and the behaviour of kappa-carrageenan on hydrolysis. Part II. *Carbohydrate Research* 135: 283-289.
 - 24 Ekström L.G. and Kuivinen J (1983) Molecular weight distribution and hydrolysis behaviour of carrageenans. *Carbohydrate Research* 116: 89-94.
 - 25 Capron I, Yvon M and Muller G (1996) In-vitro gastric stability of carrageenan. *Food Hydrocolloids* 10(2): 239-244.
 - 26 Tobacman JK, Hanauer S, Goldstein J, Halline A, Shumard T, Bhattacharyya S, Katyal S, West R, Gilet F and Dodda A. Effect of carrageenan-free diet on activity of ulcerative colitis. Abstract available online: <http://www.cdfa.org/science-and-professionals/broad/about/annual-meetings/abstracts-for-2011.html#Tobacman>. Last accessed on March 23, 2016.
 - 27 <https://clinicaltrials.gov/ct2/show/NCT02629705>. Last accessed on March 23, 2016.
 - 28 American Diabetes Association grant to Dr. Joanne Tobacman. Available online: <http://www.diabetes.org/in-my-community/local-offices/chicago-illinois/research.html>. Last accessed on March 23, 2016.
 - 29 Coleman MR and Coleman MT (2015) "Dairy-free" dietary substitute, abdominal pain, and weight loss. *Clinical Medical Reviews and Case Reports* 2:8.
 - 30 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 selenoprotein P in HepG2 hepatocytes. *Molecular and Cellular Endocrinology* 382(1):66-73.
 - 31 Baek HS and Yoon Jw (1991) Direct involvement of macrophages in destruction of beta-cells leading to development of diabetes in virus-infected mice. *Diabetes* 40(12):1586-97.
 - 32 Sarett HJ (1981) Safety of carrageenan used in foods. *The Lancet* 317(8212): 151-152.
 - 33 Carthew P (2002) Safety of carrageenan in foods. *Environmental Health Perspectives* 110(4): A176-177. Available online: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1240816/pdf/ehp0110-a0176a.pdf>. Last accessed on March 23, 2016.
 - 34 http://www.unilever.com/images/IntroductiontoUnilever_tcm13-283368.pdf.
 - 35 Weiner M, Nuber D, Blakemore WR, Harriman JF and Cohen SM (2007) A 90-day dietary study on kappa-carrageenan with emphasis on the gastrointestinal tract. *Food and Chemical Toxicology* 45(1): 98-106.
 - 36 Hagiwara A, Miyashita K, Nakanishi T, Sano M, Tamano S, Asai I, Nakamura M, Imaida K, Ito N and Shirai T (2001) Lack of Tumor Promoting Effects of Carrageenan on 1,2-Dimethylhydrazine-induced Colorectal Carcinogenesis in Male F344 Rats. *Journal of Toxicologic Pathology* Vol. 14; 37.
 - 37 Kanneganti M, Mino-Kenudson M and Mizoguchi E (2011) Animal models of colitis-induced carcinogenesis. *Journal of Biomedical Biotechnology*. Available online: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3025384/>. Last accessed on March 23, 2016.
 - 38 Marinalg. Safety of carrageenan and processed eucheama seaweed. Available online: <http://www.marinalg.org/wp-content/uploads/2012/09/Safety-of-carrageenan-and-processed-eucheama-seaweed.pdf>. Last accessed March 24, 2016.
 - 39 Joint Expert Committee on Food Additives. United Nations World Health Organization and Food and Agriculture Organization (2007) Compendium of Food Additive Specifications. 68th meeting. Available online: <ftp://ftp.fao.org/docrep/fao/010/a1447e/a1447e.pdf>. Last accessed March 23, 2016.
 - 40 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.
 - 41 Examples include Organic Valley eggnog and Tofu Shop chocolate soymilk.
 - 42 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
 - 43 Organic Foods Production Act of 1990, Sec. 2118(c)(1)(A)(i) - "the National List may provide for the use of substances only if ... the use of such substances would not be harmful to human health or the environment."
 - 44 Code of Federal Regulations. 7 CFR 205.600(b)(6)
 - 45 Carrageenan TAP review. 1995. Performed by Richard Theuer, Steven Harper and Steve Taylor. Available from the National Organic Program, United States Department of Agriculture.
 - 46 Weiner ML et al (2015) An infant formula toxicity and toxicokinetic feeding study on carrageenan in preweaning piglets with special attention to the immune system and gastrointestinal tract. *Food and Chemical Toxicology* 77:120-131.
 - 47 Benitz KF, Golberg L, and Coulston F. (1973) Intestinal effects of carrageenans in the Rhesus monkey (*Macaca mulatta*). *Food and Cosmetics Toxicology* 11:565-575.
 - 48 Galili U (2015) Significance of the evolutionary α 1,3-galactosyltransferase (GGTA1) gene inactivation in preventing extinction of apes and old world monkeys. *Journal of Molecular Evolution* 80(1):1-9.
 - 49 <https://clinicaltrials.gov/ct2/show/NCT02629705>. Last accessed on March 23, 2016.
 - 50 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 selenoprotein P in HepG2 hepatocytes. *Molecular and Cellular Endocrinology* 382(1):66-73.
 - 51 Baek HS and Yoon Jw (1991) Direct involvement of macrophages in destruction of beta-cells leading to development of diabetes in virus-infected mice. *Diabetes* 40(12):1586-97.
 - 52 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.
 - 53 Pittman KA, Goldberg L, and Coulston F (1976) Carrageenan: the effect of molecular weight and polymer type on

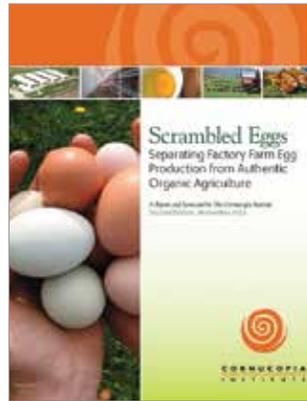
its uptake, excretion and degradation in animals. *Food and Cosmetics Toxicology* 14(2):85-93.

- 54 Marinalg International (2006) Technical Position on Measurements Related to Meeting the EC Molecular Weight distribution Specification for Carrageenan and PES. (Appendix B). Formally available online, but later removed by the company.
- 55 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.
- 56 FMC Corporation investor relations page. Available online at <http://phx.corporate-ir.net/phoenix.zhtml?c=117919&p=irol-homeProfile&t=&id=&>. Last accessed on March 23, 2016.

Also published by The Cornucopia Institute:



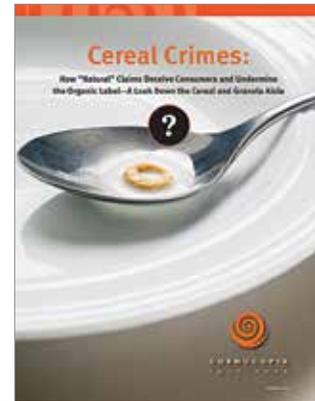
Protecting Children's Health: Choosing Organic Food to Avoid GMOs and Agricultural Chemicals



Scrambled Eggs: Separating Factory Farm Egg Production from Authentic Organic Agriculture, 2nd edition.



Culture Wars: How the Food Giants Turned Yogurt, a Health Food, into Junk Food



Cereal Crimes: How "Natural" Claims Deceive Consumers and Undermine the Organic Label—A Look Down the Cereal and Granola Aisle



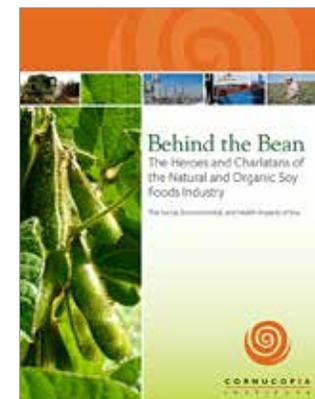
Decoding Pet Food: Adulteration, Toxic Ingredients, and the Best Choices for Your Companion Animals



Maintaining the Integrity of Organic Milk: Showcasing ethical family farm producers, exposing the corporate takeover — factory farm production



Replacing Mother—Imitating Human Breast Milk in the Laboratory. Novel oils in infant formula and organic foods: Safe and valuable functional food or risky marketing gimmick?



Behind the Bean. The Heroes and Charlatans of the Natural and Organic Soy Foods Industry



CORNUCOPIA
INSTITUTE

THE CORNUCOPIA INSTITUTE is engaged in research and educational activities supporting the ecological principles and economic wisdom underlying sustainable and organic agriculture. Through research and investigations on agricultural and food issues, The Cornucopia Institute provides needed information to family farmers, consumers, stakeholders involved in the good food movement, and the media.

P.O. Box 126 Cornucopia, Wisconsin 54827

TEL: 608-625-2000 FAX: 866-861-2214 www.cornucopia.org