Vitenskapskomiteen
for mat og miljø
Norwegian Scientific Committee
for Food and Environment

Protocol for an update of the scoping review of research on gastrointestinal effects of selected emulsifiers, stabilisers, and thickeners

Camilla Svendsen, Monica Andreassen, Ellen Bruzell, Eva Denison, Tove Gulbrandsen Devold, Berit Granum, Gro Haarklou Mathisen, Monica Hauger Carlsen, Trine Husøy

The Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food, and Cosmetics of the Norwegian Scientific Committee for Food and Environment

VKM Protocol 2024
Protocol for an update of the scoping review of research on gastrointestinal effects of selected emulsifiers, stabilisers, and thickeners

The Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food, and Cosmetics of the Norwegian Scientific Committee for Food and Environment
26.06.2024

ISBN: 978-82-8259-445-5
Norwegian Scientific Committee for Food and Environment (VKM)
Postboks 222 Skøyen
0213 Oslo
Norway

Phone: +47 21 62 28 00
Email: vkm@vkm.no

vkm.no

Cover photo: Colourbox

Suggested citation: VKM, Camilla Svendsen, Monica Andreassen, Ellen Bruzell, Eva Denison, Tove Gulbrandsen Devold, Berit Granum, Gro Haarklou Mathisen, Monica Hauger Carlsen, Trine Husøy (2024). Protocol for an update of the scoping review of research on gastrointestinal effects of selected emulsifiers, stabilisers, and thickeners. Scientific Opinion of the Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food, and Cosmetics. ISBN: 978-82-8259-445-5. Norwegian Scientific Committee for Food and Environment (VKM), Oslo, Norway.

Protocol for an update of the scoping review of research on gastrointestinal effects of selected emulsifiers, stabilisers, and thickeners

Preparation of the protocol

The Norwegian Scientific Committee for Food and Environment (Vitenskapskomiteen for mat og miljø, VKM) appointed a project group to draft the protocol. The project group consisted of VKM members and VKM staff. The Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food, and Cosmetics assessed and approved the final opinion.

Authors of the protocol

The authors have contributed to the opinion in a way that fulfils the authorship principles of VKM (VKM, 2019). The principles reflect the collaborative nature of the work, and the authors have contributed as members of the project group and/or the VKM Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food and Cosmetics.

Members of the project group (in alphabetical order after chair of the project group):

Camilla Svendsen – Chair of the project group and member of the Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food and Cosmetics. Affiliation: 1) VKM; 2) Norwegian Institute of Public Health

Monica Andreassen – Member of the Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food, and Cosmetics. Affiliation: 1) VKM; 2) Norwegian Institute of Public Health

Ellen Bruzell – Member of the Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food, and Cosmetics in VKM. Affiliation: 1) VKM; 2) Nordic Institute of Dental Materials

Tove Gulbrandsen Devold - Member of the Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food, and Cosmetics. Affiliation: 1) VKM; 2) Norwegian University of Life Sciences

Eva Denison – Member of the Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food, and Cosmetics. Affiliation: 1) VKM; 2) Retired, former Norwegian Institute of Public Health

Berit Granum – Member of the Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food, and Cosmetics. Affiliation: 1) VKM; 2) Norwegian Institute of Public Health

Trine Husøy – Chair of the Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food, and Cosmetics. Affiliation: 1) VKM; 2) Norwegian Institute of Public Health

Gro Haarklou Mathisen – Project lead, the VKM secretariat. Affiliation: VKM

Members of the VKM Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food and Cosmetics that contributed to the assessment and approval of the protocol (in alphabetical order before chair of the Panel)**:**

Monica Andreassen. Affiliation: 1) VKM; 2) Norwegian Institute of Public Health

Ellen Bruzell. Affiliation: 1) VKM; 2) Nordic Institute of Dental Materials

Monica Hauger Carlsen. Affiliation: 1) VKM; 2) University of Oslo

Eva Denison. Affiliation: 1) VKM; 2) Retired, former Norwegian Institute of Public Health

Tove Gulbrandsen Devold. Affiliation: 1) VKM; 2) Norwegian University of Life Sciences

Berit Granum. Affiliation: 1) VKM; 2) Norwegian Institute of Public Health

Camilla Svendsen. Affiliation: 1) VKM; 2) Norwegian Institute of Public Health

Trine Husøy, Chair of the Panel. Affiliation: 1) VKM; 2) Norwegian Institute of Public Health

Competence of VKM experts

Persons working for VKM, either as appointed members of the Committee or as external experts, do this by virtue of their scientific expertise, not as representatives for their employers or third-party interests. The Civil Services Act instructions on legal competence apply for all work prepared by VKM.

Table of Contents

Abbreviations and/or glossary

Abbreviations

EST emulsifiers, stabilisers, and thickeners

EU European Union

GI gastrointestinal

IBS irritable bowel syndrome

PECO Population, Exposure, Comparator, Outcome

Glossary

Digestive system: The gastrointestinal tract and several accessory glands and organs that add secretions to these hollow organs. Included organs and glands are the following: mouth, oropharynx, esophagus, stomach, duodenum, small and large intestines, salivary glands, pancreas, liver, gallbladder, rectum, and anus (Boron and Boulpaep, 2016).

Emulsifiers, stabilisers, and thickeners: Food additives that affect the texture of food.

Emulsifier: Food additives which prevent liquids that normally do not mix, such as water and oil, from separating. Compounds used as emulsifiers are amphiphilic in nature. In food systems, emulsifiers are used to form stable lipid droplets in liquid systems, so called oil-in-water emulsions, such as mayonnaise, or to keep water droplets stable in oil-in-water emulsions, such as margarine.

Gastrointestinal tract: A tube specialised along its length for the sequential processing of food. It consists of a series of hollow organs stretching from the mouth to the anus, including mouth, oropharynx, esophagus, stomach, duodenum, small and large intestines, rectum, and anus (Berne and Levy, 2000; Vander et al., 1990).

Gastrointestinal tract effects: Include effects on digestion and absorption of food, gastrointestinal tract illness, effects on intestinal microbiota, effects on immune status, and gastrointestinal tract well-being (Bischoff, 2011).

Risk of bias: Systematic errors in the conduct of a study that can lead to misleading results and conclusions.

Scoping review: A type of knowledge synthesis that follows a systematic approach to map evidence on a topic and identifies main concepts, theories, sources, and knowledge gaps (Tricco et al., 2018).

Stabiliser: Food additives that maintain consistency, texture, and appearance by preventing separation such as creaming or settling of different ingredients in foods. In

emulsions, stabilisers prevent the dispersed lipid droplets from rising upward and forming a cream layer. In other food systems, stabilisers prevent settling of dispersed particles (e.g. settling of cocoa particles in chocolate milk). Stabilisers work similarly to thickeners by increasing the viscosity or gel-like properties of the product.

Thickener: Food additives that increase the viscosity or gel-like properties of the final product.

1 Introduction and aim

Emulsifiers, stabilisers, and thickeners (ESTs) are food additives that affect the consistency of food, and which are used in several food products on the Norwegian market. In 2023, the Norwegian Scientific Committee for Food and Environment (VKM) published a systematic scoping review on scientific literature investigating effects on the gastrointestinal (GI) tract after intake of either one of the following eight ESTs: agar (E 406), sodium alginate (E 401), carrageenan (E 407), processed Eucheuma seaweed (E 407a), sodium carboxymethyl cellulose (E 466), gellan gum (E 418), guar gum (E 412), and xanthan gum (E 415) (VKM et al., 2023a).

In the EU, there is a positive list (Regulation (EU) No 231/2012) for substances that can be used as food additives. This regulation also contains specifications for the food additives included in the positive list. These specifications must be met for the substance to be allowed to be added to food. The specifications include e.g. maximum concentrations of impurities or heavy metals, molecular weight limits, degree of substitution, and loss on drying. The specifications are crucial as deviations may alter the chemical properties and/or toxicological potential of the substance in question. In the previous (VKM et al., 2023b) and the current protocol, some of the specifications listed in Regulation No 231/2012 are included as eligibility criteria for the different ESTs (see Table 2.1-2).

Scientific publications studying effects in humans and mammalian animals as well as ex vivo studies were included in the scoping review (VKM et al., 2023a). GI tract effects reported were e.g. changes in microbiota composition and changes in the gastrointestinal epithelium. Fourteen studies fulfilled all eligibility criteria. However, 214 studies fulfilled all but the substance specific criteria given in Table 2.1-2.

1.1 Aim

The aim of the current systematic scoping review is to update the "Scoping review of research on gastrointestinal effects of selected emulsifiers, stabilisers, and thickeners" on GI tract effects caused by agar (E 406), sodium alginate (E 401), carrageenan (E 407), processed Eucheuma seaweed (E 407a), carboxymethyl cellulose (E 466), gellan gum (E 418, guar gum (E 412), and xanthan gum (E 415) (VKM et al., 2023a). The update will include i) a new literature search [1st March 2023 to search date] and ii) requests for additional information on the 214 studies that were excluded based on insufficient information on the tested EST. The latter point will be performed for studies excluded both in the previous and new literature search.

For the included studies, the following elements will be addressed:

• The extent and characteristics of the research literature on GI tract effects of the selected ESTs regarding

- populations

- data on exposures
- comparisons of exposure
- outcomes
- study designs

• Study hypotheses

• The extent to which the design and conduct of the studies are likely to have prevented bias (the degree of systematic errors).

2 Methods

We will adhere to the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist" (Tricco et al., 2018).

VKM will largely follow the protocol for the previous scoping review (VKM et al., 2023b). However, in the present update, VKM will inquire authors of studies with insufficient characteristics of the ESTs for additional information (section 2.4). We will contact the authors regarding both the studies identified in the previous scoping review and in the current update.

The software EPPI-Reviewer (Thomas et al., 2022) will be used for the study selection, data extraction, risk of bias evaluation, and the synthesis of findings.

2.1 Eligibility criteria

Studies addressing GI tract effects of agar (E 406), sodium alginate (E 401), gellan gum (E 418, guar gum (E 412), xanthan gum (E 415), carrageenan (E 407), Eucheuma seaweed (E 407a), and carboxymethyl cellulose (E 466) will be included in the scoping review. The eligibility criteria are given in Table 2.1-1 and Table 2.1-2.

Table 2.1-1. Eligibility criteria for studies on GI effects.

Population	Humans of all age groups, males, and females Mammals Ex vivo GI tract model systems (human faecal samples)
Exposure	• Oral intake of agar (E 406), sodium alginate (E 401), gellan gum (E 418, guar gum (E 412), xanthan gum (E 415), carrageenan (E 407), Eucheuma seaweed (E 407a), and carboxymethyl cellulose (E 466), tested separately • Dietary sources containing agar (E 406), sodium alginate (E 401), gellan gum (E 418, guar gum (E 412), xanthan gum (E 415), carrageenan (E 407), Eucheuma seaweed (E 407a), and carboxymethyl cellulose (E 466) • The substance tested must be approved for use as food additive in certain foods in Norway/EU (see Table 2.1-2).
Comparison	Placebo, no treatment, dose comparison
Outcomes	Any GI tract effects, including but not restricted to: *Human studies* • Diagnosed chronic diseases, such as colorectal cancer, food allergy, food intolerance (e.g., coeliac disease) and inflammatory bowel disease (IBD) i.e., Crohn's and ulcerative colitis • GI effects and symptoms, often reversible and without a defined diagnosis, such as nausea, vomiting, diarrhoea and abdominal pain. One or more of these symptoms also include irritable bowel syndrome (IBS). • (Non-symptomatic) GI alterations such as changes in the microbiota, mechanical barriers, immunity, or fecal biochemical composition

	• Other effects Animal studies • Changes in the gut microbiota composition and/or the microbiota numbers • Enzymatic activity (microbial or colonic mucosa) • Faecal or caecal content, weight, colour, consistency, and/or viscosity • Gastric transit time and stool frequency • Inflammation (colon or markers measured in faeces) • Intestinal permeability (markers measured in serum) • Intestinal utilisation and fermentation of nutrients • Macroscopic changes • Microscopic changes • Mucosal weight and/or protein content • Presence of mucus or blood in the faeces • Tumour development • Weight and/or length of intestines
Study design	• Human controlled studies • Animal experimental studies • Ex vivo GI tract model studies • Systematic reviews
Publication year	From 1st of March 2023 to search date
Country	No restriction
Language	Danish, English, Norwegian and Swedish

A publication qualifies as a systematic review if 1) a specific research question and the specific criteria used for selecting studies are described, 2) the authors have performed a systematic literature search, and 3) it includes a quality assessment of the selected studies (Lasserson et al., 2022).

We will exclude systematic reviews that do not contain one or more of the specified study designs (see Table 2.1-1).

The protocol for the previous scoping review (VKM et al., 2023b) specified a sub-set of eligibility criteria (Table 2.1-2) that was developed for the exposure eligibility criterion "The substance tested must be approved for use as food additive in certain foods in Norway/EU". The sub-set of criteria are based on the regulatory specifications for food additives (Regulation (EU) No 231/2012) that require information for specific food additives about degree of substitution as well as description of hydrolysation and/or chemical degradation. All specifications depicted in the regulation are not included, but VKM included those that were considered to have the greatest impact on toxicological properties of the EST in the current work. If in the materials and methods section of an eligible study, the additive under investigation was referred to with E number, reviewers anticipated that the specifications for the food additive were in accordance

with the above-mentioned regulation. In this case, no further description was needed to fulfil the sub-set of eligibility criteria. This practice will also apply to the current scoping review.

Table 2.1-2. The sub-set of eligibility criteria for substances.

Food additive	**Information required to evaluate whether the investigated substances are approved for use as food additive in Norway/EU**						
Agar (E 406) Gellan gum (E 418) Sodium alginate (E 401) Xanthan gum (E 415) Guar gum (E 412) *	E number	OR	Either of the terms "food additives" or "food grade" are used in the description of the substance in the method section				
Sodium carboxymethyl cellulose (E 466)	E number	OR	Either of the terms "food additives" or "food grade" are used in the description of the substance in the method section	AND	Substitution is described Degree of substitution is ≥0.2 and ≤1.5 carboxymethyl groups (CH_2COOH) per anhydroglucose unit		
Carrageenan (E 407) Eucheuma seaweed (E407a)	E number	OR	Either of the terms "food additives" or "food grade" are used in the description of the substance in the method section	AND	The substance is not hydrolysed or chemically degraded	AND	MW is described and the MW fraction below 50 kDa is < 5%

*"Partially hydrolysed guar gum" is an acceptable term and is included.
Abbreviations: MW: molecular weight

2.2 Literature search

Research librarian Bente Foss developed and conducted the original search strategy in collaboration with the project group in February 2023. A research librarian will run the same search in MEDLINE (Ovid), Embase (Ovid), and Web of Science from March 2023 to search date. VKM will use the same search strategy as in the previous scoping review (VKM et al., 2023a).

2.3 Selection of sources of evidence

Reviewers will independently, in pairs, assess 1) titles and abstracts for relevance, and 2) full text articles against eligibility criteria (Table 2.1-1 and Table 2.1-2). Disagreements will be resolved by consensus or by consulting a third reviewer.

For included publications, the reference list will be screened for additional studies that fulfil the eligibility criteria.

2.4 Collection of missing data on ESTs

For the studies identified in the previous scoping review with insufficient information on the ESTs and for which the study fulfils all the other eligibility criteria, we will approach the corresponding authors of these studies with a request for clarification of the properties of the substance used in accordance with the criteria set forth in Table 2.1-2. If VKM does not receive a reply within 14 days, one reminder will be sent.

There are no restrictions on publication year.

A standard letter to authors can be found in Appendix 1.

Two reviewers will independently assess the following information in responses from authors: i) the credibility of the information provided (e.g. a simple statement or documentation in the form of a laboratory protocol or similar is provided), ii) whether the provided information is in accordance with the eligibility criteria outlined in Tables 2.1-1 and 2.1-2.

2.5 Data extraction

VKM will use the software EPPI-Reviewer 6.0 (Thomas et al., 2022) for the data extraction, and the data items listed below.

One reviewer will extract the data and a second reviewer will independently check the data extraction for accuracy and completeness. Disagreements will be resolved by consensus or by consulting a third reviewer.

Systematic reviews

We will extract the following data on study characteristics of each included systematic review:

- authors
- title
- journal
- year of publication
- funding
- reported conflict of interest
- main objective(s), including PECOs (population, exposure, comparator, outcome)
- number and study designs of included primary studies
- years of publication of the included studies (range)
- EST included in the review
- list of main outcomes/endpoints considered
- list of outcomes that relate to the systematic review questions
- the risk of bias tool used

We will extract the following data about the primary studies included in the systematic review:

- the country where the study was conducted
- the year/s the study was conducted
- any stated hypotheses regarding GI tract effects
- population, including number of participants
- exposure, including administration of the substance (in food or tested separately), dose, duration of exposure, and follow-up
- comparison, including placebo, no treatment, dose comparison
- outcomes measured as described in Table 2.1-1

Primary studies

We will extract the following study characteristics of each included primary study:

- authors
- title
- journal
- the country where the study was conducted
- year of publication
- funding
- reported conflict of interest
- main objective(s)
- any stated hypotheses regarding GI tract effects
- population, including number
- exposure, including administration of the substance (in food or tested separately), dose, duration of exposure, and follow-up

- comparison, including placebo, no treatment, dose comparison
- outcomes measured as described in Table 2.1-1

2.6 Risk of bias assessment

Risk of bias will be assessed to determine the extent to which the design and conduct of the studies are likely to have prevented bias (the degree of systematic errors) for:

- systematic reviews and human studies
- animal studies

The risk of bias assessment of systematic reviews will be performed using the ROBIS tool (Whiting et al., 2016) whereas the evaluation of primary studies will be performed according to the Handbook for Conducting a Literature-Based Health Assessment Using OHAT Approach for Systematic Review and Evidence Integration (OHAT handbook; (NTP, 2019)).

Reviewers will independently, in pairs, perform the risk of bias assessment. Disagreements will be resolved by consensus or by consulting a third reviewer.

2.7 Synthesis of findings

Data from included studies will be combined with data from the previous scoping review.

We will summarize the charted data to provide information on the body of research on GI tract effects of the selected EST as follows:

- Present the sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage (Page et al., 2021).
- Summarise characteristics of the studies, reporting populations, exposures, comparisons, and outcomes studied within each study design (i.e., human controlled studies, animal experimental studies, ex vivo GI tract model studies, systematic reviews).
- Present the hypotheses addressed according to health outcome.
- Present the overall risk of bias categorisation of included studies.

Text, figures, and tables will be used to present the results. In line with recommendations for scoping reviews we will not conduct any analysis or synthesis of the results identified or assess our confidence in the findings (Tricco et al., 2018). Using EPPI-reviewer (Thomas et al., 2022), we will arrange the studies into categories according to study design, the outcomes reported, type of exposure, and study population. At least two reviewers, independently of each other, will categorise the selected publications. Any disagreements will be resolved by discussion.

An overview of the categories used to present the results as evidence maps is given in Table 2.7-1. The categories will be piloted on a set of the included studies and improved when needed.

Table 2.7-1. Code book for EPPI-Reviewer for presenting the results as evidence maps.

Level 1	Level 2
Population	Human
	Animal
	Baboon
	Dog
	Guinea pig
	Hamster
	Mouse
	Pig
	Rabbit
	Rat
Substance	Sodium alginate (E 401)
	Agar (E 406)
	Carrageenan (E 407)
	Eucheuma seaweed (E407a)
	Guar gum (E 412)
	Xanthan gum (E 415)
	Gellan gum (E 418)
	Sodium carboxymethyl cellulose (E 466)
Outcome	Changes in gut microbiota composition and/or number
	Enzymatic activity (microbial or colonic mucosa)
	Faecal or caecal content weight, colour consistency, and/or viscosity
	Gastric transit time and stool frequency
	Inflammation (colon or markers measured in faeces)
	Intestinal permeability (markers measured in serum)
	Intestinal utilisation and fermentation of nutrients
	Macroscopic changes (stomach, small intestine and/or colon)
	Microscopic changes (stomach, small intestine and/or large intestine)
	Mucosal weight and/or protein content (colon)
	Presence of mucus or blood in faeces
	Tumour development (small intestine and/or colon)
	Weight and/or length (stomach, small intestine and/or large intestine)
	Tier 1

Risk of bias	Tier 2
	Tier 3

References

Berne R., Levy M. (2000) Principles of Pshyiology, 3rd. edition.

Bischoff S.C. (2011) 'Gut health': a new objective in medicine? BMC Medicine 9:24. DOI: 10.1186/1741-7015-9-24.

Boron W.F., Boulpaep E.L. (2016) Medical Physiology. 3. edition ed. Elsevier - Health Sciences Division, https://evolve.elsevier.com/cs/product/9781455743773?role=student.

Lasserson T., Thomas J., Higgins J. (2022) Chapter 1: Starting a review. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.3 (updated February 2022). Cochrane, 2022. Available from www.training.cochrane.org/handbook.

NTP. (2019) Handbook for Conducting a Literature-Based Health Assessment Using OHAT Approach for Systematic Review and Evidence Integration, Office of Health Assessment and Translation (OHAT), Division of the National Toxicology Program, National Institute of Environmental Health Sciences, https://ntp.niehs.nih.gov/ntp/ohat/pubs/handbookmarch2019_508.pdf.

Page M.J., Moher D., Bossuyt P.M., Boutron I., Hoffmann T.C., Mulrow C.D., Shamseer L., Tetzlaff J.M., Akl E.A., Brennan S.E., Chou R., Glanville J., Grimshaw J.M., Hróbjartsson A., Lalu M.M., Li T., Loder E.W., Mayo-Wilson E., McDonald S., McGuinness L.A., Stewart L.A., Thomas J., Tricco A.C., Welch V.A., Whiting P., McKenzie J.E. (2021) PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. Bmj 372:n160. DOI: 10.1136/bmj.n160.

Regulation (EU) No 231/2012. Commission Regulation (EU) No 231/2012 of 9 March 2012 laying down specifications for food additives listed in Annexes II and III to Regulation (EC) No 1333/2008 of the European Parliament and of the Council. European Union, https://op.europa.eu/en/publication-detail/-/publication/a42dd9b2-b63f-438b-a790-1fa5995b7d41.

Thomas J., Graziosi S., Brunton J., Ghouze Z., O'Driscoll P., Bond M., A. K. (2022) EPPI-Reviewer: advanced software for systematic reviews, maps and evidence synthesis, version 4.13.0.2, EPPI-Centre, UCL Social Research Institute, University College London., https://eppi.ioe.ac.uk/cms/Default.aspx?tabid=2914.

Tricco A.C., Lillie E., Zarin W., O'Brien K.K., Colquhoun H., Levac D., Moher D., Peters M.D.J., Horsley T., Weeks L., Hempel S., Akl E.A., Chang C., McGowan J., Stewart L., Hartling L., Aldcroft A., Wilson M.G., Garritty C., Lewin S., Godfrey C.M., Macdonald M.T., Langlois E.V., Soares-Weiser K., Moriarty J., Clifford T., Tunçalp Ö., Straus S.E. (2018) PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Intern Med 169:467-473. DOI: 10.7326/m18-0850.

Vander A., Sherman J., Luciano D. (1990) Human Physiology 5th edition.

VKM. (2019) Criteria for authorship and scientific responsibility in VKM's statements (in Norwegian), Norwegian Scientific Committee for Food and Environment, https://vkm.no/download/18.48566e5316b6a4910fc2dbd6/1561035075341/VKMs%20forfatterskapskriterier_revidert%20versjon%2020.06.2019.pdf.

VKM, Denison E., Andreassen M., Bruzell E., Carlsen M.H., Devold T.D., Granum B., Mathisen G.H., Svendsen C., Rasinger J.D., Husøy T. (2023a) Scoping review of research on gastrointestinal effects of selected emulsifiers, stabilisers, and thickeners. The Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact at the Norwegian Scientific Committee for Food and Environment (VKM), Oslo, Norway. VKM Report 2023:24, ISBN: 978-82-8259-435-6, ISSN: 2535-4019.

VKM, Denison E., Andreassen M., Bruzell E., Carlsen M.H., Devold T.G., El Yamani N., Granum B., Mathisen G.H., Svendsen C., Rasinger J.D., Husøy T. (2023b) Protocol for a scoping review of research on gastrointestinal effects of selected emulsifiers, stabilisers, and thickeners, Norwegian Scientific Committee for Food and Environment, https://vkm.no/download/18.5348de361864a581c39b3273/1677057768892/Protocol%20for%20a%20scoping%20review%20of%20research%20on%20gastrointestinal%20effects%20of%20selected%20emulsifiers,%20stabilisers,%20and%20thickeners_22.02.2023_final.pdf.

Whiting P., Savović J., Higgins J.P., Caldwell D.M., Reeves B.C., Shea B., Davies P., Kleijnen J., Churchill R. (2016) ROBIS: A new tool to assess risk of bias in systematic reviews was developed. J Clin Epidemiol 69:225-34. DOI: 10.1016/j.jclinepi.2015.06.005.

Appendix 1: Letter to author

Oslo, xx.xx.2024

Dear Dr. [Name of corresponding author]

We are contacting you to enquire about specific chemical properties of [Name of substance] which was investigated in your study [Name of study] published in [Journal, date].

The Norwegian Scientific Committee for Food and Environment (VKM) has recently carried out a systematic scoping review to map the scientific literature investigating effects on the gastrointestinal tract after intake of emulsifiers, stabilisers, and thickeners (Scoping review of research on gastrointestinal effects of selected emulsifiers, stabilisers, and thickeners). Your study was one retrieved in the literature search; however, it could not be included in the scoping review because it had insufficient description of chemical properties.

We are currently updating the scoping review, and would appreciate to receive the following documentation which will enable us to determine whether we can include your study in the update (*select the information for the relevant substance*):

- Carrageenan (E 407); processed Eucheuma seaweed (E 407a):
    - Was the substance hydrolysed or chemically degraded? If yes, how was this documented?
    - Was the molecular weight fraction less than 50 kDa no more than 5%? If yes, how was this documented?
- Sodium carboxymethyl cellulose (E 466):
    - Was substitution described and degree of substitution not less than 0.2 and not more than 1.5 carboxymethyl groups ($-CH_2COOH$) per anhydroglucose unit? If yes, how was this documented?
- Alginate (E 401); agar (E 406); guar gum (E 412); xanthan gum (E 415); gellan gum (E 418)
    - Was the substance food grade? If yes, please describe how this was documented. We would also appreciate a copy of the documentation.

Your response will be of high value to ensure that all relevant data are included in the updated scoping review. Please contact us if you have any questions.

Kind regards,

Gro Haarklou Mathisen,

on behalf of the project team.