TOX/2021/10

COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

Additional information requested by the Committee on allergenicity of chitin and chitosan based BBFCMs

Background

1. In September 2020, a discussion paper entitled "*Allergenicity of chitin and chitosan based BBFCMs* (TOX/2020/42)" was presented to the COT[1]. This paper described the commercial manufacture of chitin from the shells of crustaceans. Incomplete deproteinisation of chitin (up to 96 % weight (wt) using chemical methods) may lead to the presence of allergenic proteins, such as tropomyosin (Tm) in the final material. Tm is the main allergenic protein in sea food, which can cause allergic reactions in sensitised individuals. In addition, several studies were included which reported on the immunogenicity of small chitin and chitosan fragments, which may be recognised by the immune system as exogenous and cause an immune response. Furthermore, a case of immediate-type allergy for a chitosan-containing health food (Kato *et al.*, 2005) was provided to the Committee.

2. Members considered that the paper provided an overview of the potential hazards but needed to include additional information, such as clearly differentiating between fungal and shellfish sources of chitin, which pose different potential risks. It was considered that the risk of allergenicity from chitin- or chitosan-based BBFCMs on the basis of the potential presence of allergenic proteins appeared to be low. However, to confirm this, more information was needed. In particular, additional data characterising the protein content in chitosan and the final BBFCMs would be useful, together with data on migration from and consumption of BBFCMs. Information on the total amount of residual protein (expressed as mg/g BBFCM) would be helpful for estimating risks.

3. The Committee considered that the potential risks of dermal exposure to chitin and chitosan-based BBFCMs needed to be addressed. In this respect, liaison with MHRA for any relevant data on wound dressings or similar applications might be helpful. One Member noted that the ED01 value for crustacean-based proteins may provide an appropriate approach to assessing the risk of allergenicity. Furthermore, any data on human allergic reactions to chitin/chitosan in communities where eating edible insects is common would be helpful.

4. It was considered that the immunological properties of chitin and chitosan were of low concern in the context of BBCFMs. Chitin was well tolerated in supplements at higher exposures than would be expected from the use of BBFCMs. However, some adverse effects were associated with high intakes of

[1] https://cot.food.gov.uk/sites/default/files/2020-09/TOX-20-42%20Chitosan%20%26%20chitin%20BBFCMs.pdf

the raw materials in clinical studies, which were typically mild symptoms of gastrointestinal tract distress such as diarrhoea, bloating, or vomiting. It was agreed that these adverse effects were not of concern for BBFCMs as the processing produces a more inert final material. Furthermore, it was agreed that the phagocytosis of small fragments of chitin or chitosan appeared to be the same as that of similar-sized particles in general.

5. The Committee agreed that the limited information provided in the case report from Kato *et al.* (2005) did not suggest any additional concerns. It was considered that this reported case of immediate-type allergy is most likely due to residuals from the shellfish source from which the chitosan supplement was derived.

6. This paper presents additional information on the potential for allergenicity of BBFCMs that contain chitin and/or chitosan, based on the presence of shellfish protein. No measurements of the amount of shellfish protein in BBFCMs were found in the literature. Therefore, to assess the risk of allergenicity with respect to the ED01 of 26.2 mg for shrimp protein, a preliminary estimation of the % (wt) shellfish protein in BBFCMs was conducted for both edible BBCFCMs (films or coatings which can be consumed with the food), as well as inedible BBFCMs. No consumption or public usage data for chitin or chitosan based BBFCMs were identified in the literature or the National Diet and Nutrition Survey (NDNS) database.

Market uses of chitin and chitosan

7. Chitosan is widely used in as a food additive and functional ingredient in foods in Italy, Finland, Korea and Japan (Peter, 1997; Singla & Chawla, 2001). The Norwegian company “Norwegian Chitosan AS” trades chitosan (Kitoflokk™) for several applications, including food and beverages[2].

8. Chitin/chitosan derived from algae or fungi is devoid of Tm (Nwe & Stevens, 2002). However, commercialisation of non-animal chitosan is at its first steps, with few attempts to produce at large scale and a limited number of firms selling the products (EC, 2018). Most of the chitin/chitosan commercially available are derived from chemical isolation of shrimp or crab shell wastes (EC, 2018).

9. The U.S. FDA has approved chitosan for medical uses such as use in wound dressings (e.g. the HemCon® Bandage[3] which is derived from shellfish) and drug encapsulation. Furthermore, a Norwegian company (Primex Ingredients ASA), which manufactures shrimp-derived chitosan, announced in 2001[4] that its purified chitosan product (ChitoClear®) for use in foods in general has self-affirmed GRAS (generally recognised as safe) status in the US market.

Case reports on dermal exposure to chitin or chitosan from medical applications

[2] http://www.chitosan.no/?page_id=1266

[3] https://www.tricolbiomedical.com/product/the-hemostatic-hemcon-bandage-pro/

[4] https://www.cfsanappsexternal.fda.gov/scripts/fdcc/?set=GRASNotices&id=73&sort=GRN_No&order=DESC&startrow=1&type=basic&search=chitosan

10. Despite the market uses of shellfish-derived chitosan alluding to its safety in humans, concerns have been expressed with regards to allergenicity. For example, in their review of the safety of chitosan, Ylitalo *et al.* (2002) noted that although "chitosan has caused no clinically significant adverse effects, and it has been freely available in health stores for decades…we cannot recommend chitosan products to subjects allergic to crustaceans".

11. Indeed, there are some case reports relating to hypersensitivity to some healthcare products which contain chitosan. In addition to the case of immediate-type allergy for a chitosan-containing health food that was reported by Kato *et al.* (2005), two additional cases were identified in the literature.

12. The first case relates to a moisturising cream containing chitosan gluconate (0.3 %; biological origin unstated), glucosamine, gluconic acid, pyrrolidone carboxylic acid, specific reconstituted sebum (3 %), preservatives, aromatic composition, and purified water. A 37-year-old female patient using this cream presented with papulovesicular eczema on the face and neck, with pronounced erythema of the eyelids. Patch tests showed a positive reaction to the chitosan gluconate. However, this patient developed neither urticaria nor any clinical symptoms of type 1 allergy after cutaneous contact with crustaceans or after eating them. Furthermore, patch tests with 10 % aq. shrimp and prawn integuments were negative. The study authors concluded that "dermatologists should think of it (chitosan) when seeking causes of skin allergies" (Cleenewerck *et al.*, 1994).

13. The second case relates to a cream also containing chitosan gluconate (concentration and biological origin unstated) and ethyl diglycol Carbitol. A 32-year-old female patient using this cream presented with hand dermatitis. Patch tests showed that the patient was sensitised to the chitosan gluconate and the ethyl diglycol Carbitol. Patch testing with these two ingredients was negative in 8 control patients (Pereira *et al.*, 1998). However, this short publication does not clarify whether the elicitation was from a previous or new allergy.

14. The FSA's FCM Policy team have presently identified four businesses that made direct queries to the FSA about the presence of chitosan in packaging and food films, and three businesses about chitosan-based drinking straws. Although no UK incidents have been raised formally, there is one report of a potential reaction to the use of a chitosan-based straw in a pub which was reported to a local authority. The local authority carried out an investigation with the supplier of the chitosan-based straws. Whilst there was some uncertainty, the circumstances in this situation made it difficult to rule out cross-contamination involving the meal that the individual also consumed on the premises. The individual who suffered the allergic reaction did have a seafood allergy but did not disclose this to the pub. Additional precautions were put in place concerning labelling, where pubs using chitosan-based straws are required to include clear labelling. Labelling regarding any potential risk to allergens comes under the general food contact materials legislation (specifically Article 15 of Commission Regulation (EC) No. 1935/2004, which states that with regards to necessary labelling "special instructions (are) to be observed for safe and appropriate use"). This information may need to be provided on the packaging, or as a standalone warning should they be sold loosely. The FSA FCM Policy requested the

Incidents team to relay this to the supplier in case they decided to stock the chitosan straws (or a similar product) in the future, though it transpired that the supplier no longer sold the chitosan-based straws.

15. The MHRA is aware of chitin and chitosan being used in medical devices, but is "not aware of a safety issue investigated by the MHRA related to this material that has come to light since receiving market authorisation" (FSA pers. comm.).

Edible packaging

16. The utilisation of chitosan in food packaging is either in the form of flexible films or coatings (Priyadarshi & Rhim, 2020). A "film" is preformed separately and wrapped onto a food surface later, whereas a "coating" is a thin layer formed directly onto the food's surface. Films may be edible or inedible, whereas coatings are almost always edible since they form a layer directly on the top surface of the food[5].

17. The widely used polymers for making edible films/coatings are polysaccharides (chitin/chitosan, cellulose, starch, pectin, seaweed extracts, gums, pullulan), proteins (gelatin, soy protein, zein, wheat gluten, myofibrillar protein, milk protein), and lipids (synthetic/natural waxes, vegetable/animal oils and fats, essential oils and extracts, resins). The properties of the film/coating, such as cohesion, adhesion and durability, depend on the composition of material, coating method and drying method (Jeevahan & Chandrasekaran, 2019).

18. Chitosan films can be divided into edible films or coatings (< 30 μm thickness), for application directly on food, and films (>30 μm thickness) and blends (Van den Broek et al., 2015). However, with the advancement of nanotechnology, new concepts such as nano-coatings, which consist of nanoscale layers (less than 100 nm) built-up onto surfaces, are being explored (Vasile, 2018; Müller *et al.*, 2017). In their review of "nanoedible films" for food packaging, Jeevahan & Chandrasekaran (2019) noted that production of edible films and coatings is still largely at the laboratory level and is not yet expanded to industrial level due to their high cost of production.

19. Flexible chitosan films are usually prepared by the solvent casting method in which chitosan is dissolved in suitable solvents, in most cases slightly acidified water, and is poured on a flat surface for allowing the solvent to evaporate (Kim *et al.*, 2006). Direct application of chitosan formulations onto food surfaces can be attained by spraying or dipping (Tharanathan, 2003). Recent reviews on food packaging applications of chitosan and chitin have been published (Priyadarshi & Rhim, 2020; Souza et al., 2020). Because chitosan films and coatings are created from diluted acid solutions, they can remain water sensitive, or even water soluble, which limits their range of applications.

20. The EU considers that an edible film is a special active part of the food and, seen from a legal point of view, it is to be regarded as a foodstuff, along

[5] Ibid.

with the food packed in the film, having to fulfil the general requirements for food (Fabec *et al.*, 2000). Subsequently, the presence of a known allergen on an edible film or coating on a food must be clearly stated in the label (Campos *et al.*, 2011). Due to hygienic reasons, it is anticipated that food products in edible films need to have an outer package, otherwise the film should not be eaten (Fabec *et al.*, 2000).

Allergenicity of shellfish proteins

21. It is estimated that about 1 % of the world population is allergic to shrimp, where serious adverse reactions can occur (Sicherer *et al.*, 2004; Castillo *et al.*, 1994). Rahman *et al.* (2010) analysed the allergenic proteins in Black Tiger shrimp using peptide mass finger printing and peptide fragment fingerprinting methods. Their study found the presence of Pen m 2 protein with arginine kinase activity, Tm, and myosin light chain (MLC) (Rahman *et al.*, 2010). Subsequently, Nguyen (2012) noted “a need to examine the presence of these proteins in chitin and chitosan” which “could cause allergic reactions”.

22. Tm is a muscle protein which, together with myosin and actin, is involved in muscle contraction. However, many isoforms of Tm exist and Tm is also present in non-muscle cell types (Reese *et al.*, 1999). Tm is a coiled-coil dimer that consists of two parallel alpha-helical Tm molecules wound around each other; this structure creates an average molecular weight of 34-38 kDa (Reese et al., 1999).

23. Tm is present in all species of vertebrates and invertebrates. However, only the Tm found in invertebrates such as crustaceans, arachnids, insects, and molluscs can cause allergic reactions (Lehrer *et al.*, 2003; Lopata *et al.*, 2010; Reese *et al.*, 1999). Tm is considered to be the major allergen in shellfish allergy (Faber *et al.*, 2016), and different IgE-binding B- and T-cell epitopes in Tm have been described (Subba *et al.*, 1998).

24. Tm is a heat-stable allergen (Daul *et al.*, 1994). It is also an “acidic” protein with an isoelectric point (pI) value of 4.5 (Reese *et al.*, 1999), and thus its conformational structure has some resistance to acidic conditions. Due to these characteristics, Tm can be present in processed foods (Hoffman *et al.*, 1981; Lopata and Lehrer, 2010; Nagpal *et al.*, 1989; Reese *et al.*, 1999).

25. The most widely accepted allergen reference doses for total shrimp protein, commonly measured using the Bradford assay, are ED01 (where <1% of the allergic population may be expected to react) at 26.2 mg of shrimp protein, and ED05 at 280 mg of shrimp protein (Remington *et al.*, 2020). These reference values are derived from human food challenge data, and represent acute intake levels that elicit reactions in IgE-mediated food allergies. An allergenic reference dose for Tm alone was not identified in the literature.

Nguyen (2012): studies on allergenic properties of chitin and chitosan (PhD thesis)

26. Nguyen (2012) collected polyclonal antibodies in rabbit sera after injecting rabbits with purified Tm antigens from four species of shrimp (Black Tiger, Banana, Vannamei, and School shrimp). The sera were then used to investigate the presence of Tm in protein extracts of shrimp, and also technical samples of chitin and chitosan using immunoblotting techniques.

27. Samples of technical chitin and chitosan (donated from Mahidol University, Thailand) were obtained from shrimp waste by decalcification (using HCl) and deproteination (using 1 N NaOH) and, in respect of chitosan, deacetylation (using 12.5 N NaOH at 70 °C). The degree of deacetylation (DD) of the chitin sample was reported to be between 5-15 %, and the DD of the chitosan sample about 85 %. The protein concentration in the extraction from chitin, measured using the Bradford assay, was 0.44 % (w/w)[6]. The protein concentration in the extraction from chitosan ranged from 0.05 to 1.0 % (w/w), though 9 of the 11 chitosan samples were < 0.4 %[7].

Measurement of Tm concentration in protein extracts of shrimp (Nguyen, 2012)

28. Raw shrimps from the local market were peeled to separate the shell (including shell, head - carapace and rostrum, and legs - pereopods and pleopods) from the tail meat. These specimens were used to prepare two different protein extracts: the “shell” protein extract and the “tail” protein extract[8].

29. Concentrations of Tm were measured in these protein extracts (raw and heat-treated). These measurements were achieved by using absorbance values of known concentrations from purified Tm to generate a standard curve against which absorbance values were compared. The percentage of Tm in total shrimp protein across all shell extracts was <0.5 %[9].

Detection of Tm in technical samples of chitin and chitosan (Nguyen, 2012)

30. The study could not isolate the residual proteins from the chitin and chitosan and thus measurements of Tm concentrations in chitin and chitosan samples were not reported. Nguyen (2012) noted that “many methods have been tried to isolate and identify the residual proteins in chitin and chitosan samples. However, they were not successful. There are many possibilities that make it hard to separate proteins from chitin and chitosan sample. Firstly, the residual proteins must be combined tightly in the structure of the chitin and chitosan powder, so they can survive after treatment with high acidic and alkaline solutions during their extraction. The second reason could be related to the solubility of chitin and chitosan. Chitin cannot dissolve in normal solution (Pillai *et al.*, 2009; Sannan *et al.*, 1975); if strong chemicals were used to dissolve chitin, harsh environment will break down the residual proteins. On the other hand, chitosan can dissolve in light acidic condition; however this solution is too viscous to run through the filter to separate proteins. Chitosan solutions are also very sticky that they cannot be separated by SDS-PAGE. Another reason could

[6] Ibid., p.100
[7] Ibid., p.104 (Table 5.6)
[8] Ibid., p.74 (Figure 4.1)
[9] Ibid., p. 86 (Figure 4.9C)

be because most of the proteins remaining in the chitin and chitosan were degraded and broken down into small fragments during extraction from the shrimp shell, so they cannot be separated by SDS-PAGE and Western blot".

31. Overall, the studies demonstrated the presence of Tm protein in the chitin and chitosan samples, where the antibodies were able to interact with Tm. Subsequently, Nguyen (2012) noted that "special care should be taken when using chitin and chitosan in food or medical preparations. Warning statements should state clearly the presence of Tm in products derived from chitin or chitosan, especially when the consumers are sensitised to crustaceans".

Estimation of shellfish protein in chitin and chitosan based BBFCMs

32. The estimations of shellfish protein in chitin- and chitosan-based BBFCMs, as shown in Tables 1-2, use the following information as assumptions:

- The protein content of commercial chitin being ≤ 3-4 % (w/w), a percentage range also noted by Changrkrachang (1996) (as cited in Nguyen, 2012). Thus, a conservative percentage of 4 % protein content in commercial chitin is used.
- The protein concentration in the extraction from technical chitosan ranged from 0.05 to 1.0 % (w/w) (Nguyen, 2012). Thus, a percentage of 1 % protein content in chitosan is used.

33. Table 1 shows some non-edible BBFCMs and the % of chitin nano-whiskers and/or chitosan in their compositions. The % (wt) of shellfish protein in the overall BBFCM is estimated using the information in Paragraph 32. This estimation assumes that the concentration of shellfish protein in chitin or chitosan is unaffected by the processing which generates the final BBFCM. The amount of BBFCM that would contain shellfish protein equivalent to the ED01 is estimated for each BBFCM.

Table 1: Estimated concentrations of shellfish protein in some **non-edible** BBFCMs, based on chitin nano-whisker and/or chitosan content.

Material type	% Concentration of chitin and/or chitosan in BBFCM	Matrix material/ solvent	Literature reference	Estimated % (wt) shellfish protein in BBFCM*	Estimated amount of BBFCM that would contain shellfish protein equivalent to the ED01 (nearest gram)**
Chitosan film	5 % (w/v) chitosan	carboxy-methyl cellulose	Hu *et al.* (2016)	0.05	52 grams
Film with chitosan and chitin nano-whiskers	2 % (w/v) chitosan and 1 % (wt) chitin nano-whiskers	chitosan	Ma *et al.* (2014)	0.06	44 grams
Film with chitin nano-whiskers	Up to 5 % (wt) chitin nano-whiskers	maize starch	Qin *et al.* (2016)	0.2	13 grams
Film with chitin nano-whiskers	Up to 10 % chitin nano-whiskers	gelatin	Sahraee *et al.* (2017)	0.4	7 grams

Film with chitosan and chitin nano-whiskers	2 % (w/v) chitosan and up to 29.6 % (wt) chitin nano-whiskers	chitosan	Sriupayo *et al.* (2005)	1.2	2 grams

*Assumes %(wt) of shellfish protein in chitin nano-whiskers and chitosan is 4 % and 1 %, respectively. E.g. if 5 % BBFCM is chitin nano-whiskers, and 4 % of chitin nano-whiskers is protein, then % wt of BBFCM composed of shellfish protein is 5 % x 4 % = 0.2 %.
** Uses the ED01 of 26.2 mg for shrimp protein, where <1 % of the allergic population may be expected to react (Remington *et al.*, 2020). E.g. if 0.2 % (wt) of BBFCM is shrimp protein, then 26.2 mg ÷ 0.2 % = 13.1 g of BBFCM which contains shellfish protein equivalent to the ED01.

34. Chitin is present in some BBFCMs as nanofibers (Ifuku & Saimoto, 2012) or “nano-whiskers” (Zeng et al., 2012). Chitin nano-whiskers are the crystalline part of fibers, often termed nanocrystals that are devoid of amorphous regions. They are shorter and have more defined dimensions. The dimensions of chitin nano-whiskers, when extracted from shrimp shells using hydrochloric acid hydrolysis, are 110-975 nm (length) and 5-74 nm (width) across reviewed studies (Mincea et al., 2012). Incorporation of chitin nano-whiskers into starch-based films has been shown to improve the film’s mechanical and barrier properties (Qin et al., 2016), and may be regarded as a “passive” material. Chitosan, on the other hand, is an “active” agent as it has antimicrobial and antioxidant properties (Vasile, 2018); and inhibits fungal growth including Fusarium spp. and thus reduces mycotoxin production (Zachetti et al., 2019).

35. Regarding chitin nano-whiskers, and nanoparticles more generally, migration studies are scarce. This is due to the difficulties in characterising nanoparticles in composites, and the lack of methods for qualitative and quantitative analysis (Han et al., 2011). Indeed, the use of nanoparticles in the development of food packaging materials is still a novel field (Huang et al., 2015). Food matrices are complex, and one single technique is not enough to provide all information, thus extra fractionation procedures and combined detection methodologies are often needed.

36. In Directive 90/128/EEC, the European Commission published overall migration limits (OMLs) and specific migration limits (SMLs) which apply to plastic food contact materials (EC, 1990). This Directive has been superseded by Regulation 10/2011 (EC, 2011), in which the majority of migratory limit values remain unchanged. Whilst there are no specific migration limits for BBFCMs, industry can refer to legislation that may be pertinent (the same holds true for other materials lacking specific legislation).

37. Table 2 shows some edible BBFCMs and the % of chitosan in their composition. The emerging chitosan-based films/coatings for fruits, vegetables, fish, and meat products have been reviewed (Wang et al., 2018; Kumar et al., 2020) and the concentrations of chitosan across the different films/coatings are generally ≤ 2.0 % (w/v). The % (wt) of shellfish protein in the overall BBFCM is estimated by assuming a 1 % protein content in chitosan, and assuming that the concentration of shellfish protein in chitosan is unaffected by the processing which generates the final BBFCM. The estimated consumption of edible film required reach the ED01 in terms of shellfish protein content is estimated for each BBFCM. No films with chitin or chitin nano-whiskers that were identified in the literature were described as “edible”.

Table 2: Estimated concentrations of shellfish protein in some **edible** BBFCMs, based on chitosan content.

Material type	% Concentration of chitosan in BBFCM	Matrix material/ solvent	Literature reference	Estimated % (wt) shellfish protein in BBFCM*	Estimated consumption of BBFCM to reach ED01 (nearest gram)**
Edible chitosan film	1 % (w/v) chitosan	gelatin	Guo *et al.* (2019)	0.01	262 grams
Edible chitosan coating	1 % (w/v) chitosan	glycerol	Han *et al.* (2005)	0.01	262 grams
Edible chitosan coating	1 % (w/v) chitosan	acetic acid	Vargas *et al.* (2006)	0.01	262 grams
Edible chitosan coating	1 % (w/v) chitosan	acetic acid	Huang *et al.* (2019)	0.01	262 grams
Edible chitosan film	2 % (w/v) chitosan	glycerol	Riaz *et al.* (2018)	0.02	131 grams
Edible chitosan coating	Up to 2 % chitosan	acetic acid	Chien *et al.* (2007)	0.02	131 grams
Edible chitosan coating	2 % (w/v) chitosan	acetic acid	Moreira *et al.* (2011)	0.02	131 grams

*Assumes %(wt) of shellfish protein in chitosan is 1 %. E.g. if 1 % BBFCM is chitosan, and 1 % of chitosan is shellfish protein, then % wt of BBFCM composed of shellfish protein is 1 % x 1 % = 0.01 %.
**Uses the ED01 of 26.2 mg for shrimp protein, where <1 % of the allergic population may be expected to react (Remington *et al.*, 2020). E.g. if 0.01 % (wt) of BBFCM is shrimp protein, then 26.2 mg ÷ 0.01 % = 262 g of BBFCM consumed to reach ED01.

38. It may be possible that the digestion of chitosan liberates Tm which is not otherwise be as freely available. In their review of the safety of chitosan, Ylitalo *et al.* (2002) noted that chitosan is not specifically hydrolysed by digestive enzymes, but limited digestion of chitosan may occur due to bacterial flora and the unspecific activities of some digestive enzymes such as amylase and lipase. In addition, several mammalian chitinases and chitinase-like genes have been identified in humans (Boot *et al.*, 2001). Boot *et al.* (2005) discussed the possibility that gastrointestinal chitinases might have a dual function, in immune defence and in food digestion.

Allergic reactions to chitin/chitosan in communities where entomophagy is common

39. Adverse reactions after eating insects are scarce and only two population studies were identified in the literature which report on the prevalence of food allergy to insects. A review of insect (food) allergy and allergens conducted by

Gier & Verhoeckx (2018) showed that various insect allergens have been identified, including Tm.

40. Taylor & Wang (2018) investigated the prevalence of allergic reactions caused by consuming edible insects. The investigation was conducted in the North Eastern (or the Isan region) of Thailand, in an area where insect consumption (or entomophagy) is a common practice. Information concerning insect consumption and allergic reactions were gathered from multiple sources in four locations: Nongki, Nang Rong, Nong Bun Mak, and Nakhon Ratchasima. The survey included questions about eating habits in relation to insects, other known food allergies, and presented a list of symptoms the participants may have experienced. The prevalence of allergic reactions caused by consuming edible insects was much higher than expected across the 2,500 respondents. In the Isan region, approximately 7.4 % of people experienced an adverse reaction indicative of an edible-insect allergy, and 14.7 % of people experienced multiple adverse reactions “indicative” of an edible-insect allergy. Furthermore, approximately 46.2 % of people that already suffer from a known food-based allergy also experienced symptoms indicative of an allergic reaction after insect consumption. According to the study authors, “the most common symptoms appear to be gastrointestinal (diarrhoea and vomiting)”. The study authors concluded that “the allergy aspect of entomophagy is a serious issue and has the potential to adversely affect the future of entomophagy, especially in introducing the concept to western cultures”.

41. Barennes *et al.* (2015) assessed the prevalence of food allergy to insects amongst insect-eaters. In this survey, 8 teams (which included medical physicians) collected data to address socioeconomic characteristics of the consumers, types of insects consumed, frequency of consumption and reports of side effects. This study was conducted in Laos, and included 1,059 subjects that had previously eaten insects, 81 of whom (7.6 %) reported “allergy problems after eating insects”. Of these 81 subjects, 38 reported that allergy problems were “mostly with grasshoppers or stink bugs”. None of the subjects reported severe anaphylaxis. In this survey, it was not possible to know how much the consumption of edible insects represents the daily diet of the population, or provide detail on the way insects were harvested. It does not mention any clinical confirmation of allergy problems.

Summary and conclusions

42. This discussion paper focuses on the potential for allergenicity of BBFCMs that contain chitin and/or chitosan, based on the presence of shellfish protein.

43. No measurements of the amount of shellfish protein in BBFCMs were found in the literature. Therefore, to assess the risk of allergenicity with respect to the ED01 of 26.2 mg for shrimp protein, a preliminary estimation of the % (wt) shellfish protein in BBFCMs was conducted. This estimation uses the highest reported level of 1) the measured amount of shrimp protein in crustacean-derived chitin and chitosan, and 2) the stated amounts of chitin and/or chitosan in the compositions of some BBFCMs. Thus this estimate is likely to overestimate potential exposure.

44. For non-edible BBFCM films containing chitosan and/or chitin nano-whiskers, it was estimated that the amount of BBFCM that would contain shellfish protein equivalent to the ED01 was 2-52 grams across the studies reviewed (Table 1).

45. For edible BBFCM films and coatings containing chitosan, it was estimated that the consumption of BBFCM to reach ED01 was 131-262 grams across the studies reviewed (Table 2).

Questions on which the views of the Committee are sought:

I. Does the Committee agree with the approach taken for estimation of shrimp protein in BBFCMs that contain crustacean-derived chitin and/or chitosan?

II. Do Members consider that this would represent a worst case estimate?

III. Given the ED01 of 26.2 mg for shrimp protein is for acute intake levels, do the following estimates pose a public health concern:
- consumption of edible BBFCMs required to reach the ED01?
- amount of BBFCM that contains shellfish protein equivalent to the ED01?

IV. Is any further information requested from the Secretariat?

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