CODEX ALIMENTARIUS COMMISSION

Food and Agriculture Organization of the United Nations

World Health Organization

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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON CONTAMINANTS IN FOODS

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PYRROLIZIDINE ALKALOIDS

INTRODUCTION

1. At the 15th session[1] of CCCF (CCCF15), CCCF agreed to re-convene the EWG, chaired by the EU, working in English, to prepare a discussion paper on pyrrolizidine alkaloids to look into the feasibility of possible follow-up actions for consideration by CCCF16.

2. The discussion paper has been prepared by the Chair of the EWG but has not been circulated to the EWG for comments.

3. The aim of this discussion paper in Appendix I is to present background information such as health risks, methods of analysis and sampling, prevention and control and knowledge gaps related to the presence of pyrrolizidine alkaloids in food and feed. The discussion paper contains also recommendations for CCCF to consider. A project document to update the Code of Practice for weed control, to prevent and reduce pyrrolizidine alkaloid contamination in food and feed (CAC/RCP 74-2014) based on the information provided in the discussion paper is also presented for consideration by CCCF (Appendix II). As the document has not been discussed in the EWG, the list of members to the EWG is provided for information only in Appendix III.

[1] REP22/CF15, para 224

APPENDIX I

DISCUSSION PAPER ON PYRROLIZIDINE ALKALOIDS

(For consideration by CCCF)

BACKGROUND

Pyrrolizidine alkaloids

1. Pyrrolizidine alkaloids (PAs) are toxins produced by an estimated 6000 plant species. More than 600 different PAs, mainly 1,2-unsaturated PAs, including their associated nitrogen oxides (*N*-oxides) are known, and new PAs continue to be identified in both new and previously studied plant species. The main plant sources are the families *Boraginaceae* (all genera), *Asteraceae* (tribes *Senecioneae* and *Eupatorieae*) and *Fabaceae* (genus *Crotalaria*). Different plant species in these families produce characteristic mixtures of 1,2-unsaturated PAs and their saturated analogues and varying amounts of their corresponding *N*-oxides. The PAs present in these plants are esters of pyrrolizidine diols. The pyrrolizidine moieties are referred to as necines, and the esterifying acids involved are necic acids. These PAs can be classified as open-chain monoesters, open-chain diesters and macrocyclic diesters.

2. Pyrrolizidines and PAs[2] are, by definition, fully saturated and have no double bonds. In this discussion paper, the term "PAs" used by itself refers to saturated and 1,2-unsaturated PAs and their associated *N*-oxides and the term "1,2-unsaturated PAs" refers to all 1,2-unsaturated PAs and their associated *N*-oxides. An overview of the structural formulae of the most relevant Pas in provided in figure 1 of the WHO Food Additives Series: 71 – S2[3]

3. PAs may be present in foods through three possible routes;

    a. as an inherent component of the food;

    b. through contamination of a food, with PA-containing plant material (e.g. contamination of food with PA-containing weeds); and

    c. transfer of PAs from plant material consumed by animals into foods of animal origin.

JECFA assessment

4. Pyrrolizidine alkaloids were assessed by the he of the Joint Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO) Expert Committee on Food Additives (JECFA), at its eightieth meeting which took, place in Rome, Italy, from 16 to 25 June 2015. Details of the assessment can be found in WHO Food Additives Series: 71-S2, Safety evaluation of certain food additives and contaminants, Supplement 2: Pyrrolizidine alkaloids[4].

5. JECFA noted that most studies of toxicity, and of occurrence of PAs in food, were focused on the 1,2-unsaturated PAs. The Committee concluded that while the saturated PAs could not elicit toxicity via the same mechanism as 1,2-unsaturated PAs, their toxicity in humans could not be excluded, but there were insufficient studies for evaluation. The Committee therefore decided to focus the evaluation on the 1,2-unsaturated PAs. Studies performed using extracts or material from PA-containing plants, which did not specify PA content did not allow the toxicity to be related to a dose of a specific PA, and were of limited relevance to the evaluation.

6. Exposure to 1,2-unsaturated PAs has been associated with a wide range of effects, with rats being the most sensitive species studied. In vitro studies on metabolic activation indicate that humans are also likely to be sensitive. Laboratory studies have identified the liver as the most sensitive organ in rats, following both short-term and long-term administration of a number of PAs. The 1,2-unsaturated PAs that have been tested form DNA adducts and are mutagenic. Based upon an understanding of their chemistry and metabolism, it is concluded that this property is common to all 1,2-unsaturated PAs, albeit with differing potencies, and that it is relevant to humans. PAs appear to be antimitotic in hepatocytes. A number of 1,2-unsaturated PAs have been shown to be carcinogenic in rodents, primarily causing haemangiosarcomas in the liver, i.e. originating in the endothelial cells rather than the hepatocytes. Carcinogenicity has not been investigated in case studies of human poisoning with PAs.

7. JECFA considered that derivation of a health-based guidance value for PAs was not appropriate in view of the genotoxic mode of action. From the carcinogenicity data in rats, a BMDL10 of 182 µg/kg bw per day for liver haemangiosarcoma in female rats from the USA National Toxicological Program (NTP) study on riddelliine, conducted in 2003, was calculated as the point of departure for use in a margin of exposure (MOE) approach.

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[2] The term "alkaloid" (alkali-like) refers to naturally occurring plant secondary chemicals with a basic nitrogen atom.

[3] WHO Food Additives Series: 71-S2, Safety evaluation of certain food additives and contaminants, Supplement 2: Pyrrolizidine alkaloids Available at https://apps.who.int/iris/rest/bitstreams/1318952/retrieve

[4] Available at: https://apps.who.int/iris/rest/bitstreams/1318952/retrieve.

8. JECFA considered whether it was possible to identify relative potency factors for different 1,2-unsaturated PAs. In addition to the carcinogenicity studies on lasiocarpine and riddelliine, carcinogenicity studies on other PAs were conducted with non-standard protocols, and these do not allow comparison of carcinogenic potency. Based on short-term toxicity and genotoxicity, it appears that the potency is broadly in the order: macrocyclic esters > diesters > monoesters, although there may also be differences depending on the type of necine base and the stereochemistry. The two PAs that have been tested for carcinogenicity, lasiocarpine and riddelliine, are among the more potent, and it is likely that many of the PAs present in food, such as lycopsamine, are less potent. Ingested PA N-oxides are efficiently reduced to PA free bases in the digestive tract, and to a lesser extent in the liver. JECFA concluded that the data were not sufficient to make assumptions about the potency of the N-oxides relative to the parent PA and adopted the conservative approach of assuming equal potency.

9. JECFA calculated MOEs between the BMDL of 182 µg/kg bw per day and mean and high-percentile (90th, 95th or 97.5th, depending on the study) chronic exposure estimates for children and adults from consumption of honey and tea, separately. As several national estimates of dietary exposure were available for each food, MOEs were calculated using a range from the lowest lower- bound mean or high-percentile dietary exposure to the highest upper-bound mean or high-percentile dietary exposures. This range takes into account the uncertainty in measurements of 1,2,-unsaturated PAs and their N-oxides and the variability in their concentrations and national estimates of food consumption.

10. For adult consumption of honey, mean and high-percentile chronic dietary exposures to 1,2-unsaturated PAs are in the range 0.00002 to 0.0039 µg/ kg bw per day and 0.005 to 0.026 µg/kg bw per day, respectively. These dietary exposures equate to MOEs in the range 46 000 to 9 million for mean exposures and 6900 to 36 000 for high-percentile exposures. For children consuming honey, the ranges of mean and high-percentile chronic dietary exposures to 1,2-unsaturated PAs are 0.00001 to 0.013 µg/kg bw per day and 0.006–0.082 µg/ kg bw per day, equating to MOEs in the range 14 000 to 18 million for mean exposure and 2200 to 30 000 for high-percentile exposure.

11. For adult consumption of tea, mean and high-percentile chronic dietary exposures to 1,2-unsaturated PAs are in the range 0.0013 to 0.13 µg/kg bw per day and 0.01 to 0.26 µg/kg bw per day, respectively. These dietary exposures equate to MOEs in the range 1400 to 140 000 for mean exposure and 700 to 18 000 for high-percentile exposure. For children consuming tea, the range of mean and high-percentile chronic dietary exposures to 1,2-unsaturated PAs are 0.005 to 0.018 µg/kg bw per day and 0.027–0.076 µg/kg bw per day, respectively. These dietary exposures equate to MOEs in the range 10 000 to 36 000 for mean exposure and 2400 to 6700 for high-percentile exposure. JECFA noted that estimates of dietary exposure to 1,2-unsaturated PAs and their N-oxides from tea consumption are likely to be overestimates, as concentration data from herbal teas have been combined with information on total tea consumption.

12. JECFA noted also that there is insufficient information to determine MOEs for other food types or for the total diet.

13. JECFA noted that a broad range of PAs has been reported in animal feed, but the data were not adequate to assess whether transfer to products of animal origin, such as milk, meat and eggs, could make a major contribution to dietary exposure.

14. The data were insufficient to identify a point of departure for use in calculating MOEs for acute exposure. However, the Committee noted that the estimates of mean and high-percentile acute exposure to 1,2-unsaturated PAs for children and adults were up to 0.784 µg/kg bw per day, which is 23-fold lower than the lowest reported exposure of 18 µg/kg bw per day associated with human disease following 6 weeks of exposure.

15. Based on limited occurrence data, JECFA noted that the calculated MOEs for honey (high consumers) and tea (mean and high consumers) indicated a potential concern. It should be noted that PAs measured in these commodities might not be representative for all food groups and all regions. However, it provided a conservative risk estimate as it was compared to the BMDL10 for the potent PA riddelliine, and most of the PAs commonly found in food are likely to be less potent than riddelliine.

16. JECFA considered it of concern that exposure to a single food product could result in such low MOEs. The Committee noted that exposure to PAs resulted from other food items as well, and animal products such as milk might contribute to the total exposure as a result of the presence of PAs in feed. A first indication of total exposure could be obtained from a small duplicate-diet study, from which an MOE of 140 000 could be derived, but it was unclear how representative these data were.

17. The comparison of estimates of acute dietary exposure to PAs from honey and tea with the lowest reported dose causing human disease did not indicate a concern. There was insufficient information to reach conclusions on food or beverages other than honey and tea.

Methods of analysis and sampling procedures

18. The specific analytical issues associated with the screening and quantification of PAs – saturated and unsaturated PAs and their N-oxides –in various foods and feeds , include:

    a. wide variations in PA concentrations in food and feed samples;

    b. variation in PA profiles between plants in various regions of the world;

    c. the stability of PAs during storage; and

    d. the issue of whether to quantify individual PAs or total necines.

19. PAs are extracted from plants and food samples with hot or cold methanol or ethanol, or dilute aqueous acid. The alcoholic or aqueous acid extracts are then applied to prepared strong cation exchange solid-phase extraction (SPE) cartridges, followed by washing of the cartridges with water and methanol to remove non-adsorbed impurities, and then elution of the PAs and N-oxide components using a small volume of ammoniated methanol. Subsequent evaporation and reconstitution of the residue in methanol or another suitable solvent produce samples ready for analysis of PAs.

20. Several screening methods are available, including thin-layer chromatography (TLC), electrophoresis, nuclear magnetic resonance (NMR) and immunological methods. TLC with colorimetric detection of 1,2-unsaturated PAs is inexpensive, but the results are qualitative rather than quantitative. NMR has been used to determine the total alkaloid content but it probably lacks the sensitivity required for food safety risk assessment purposes. Enzyme-linked immunosorbent assay (ELISA) -based screening methods for 1,2-unsaturated PAs and their N-oxides have been developed, but are currently limited by a lack of antibodies that specifically bind all of the 1,2-unsaturated PAs and their N-oxides with comparable affinity. At the same time, antibodies developed for specific 1,2-unsaturated PAs or their N-oxides seem to lack specificity for other 1,2-unsaturated PAs or their N-oxides. The development of sensitive ELISAs for quantifying necines could be useful in summation analysis methods for quantifying total 1,2-unsaturated PAs and their N-oxides based on hydrolysis. However, results from ELISA should always be confirmed using quantitative reference methods, such as gas chromatography – mass spectrometry (GC-MS) and/or high performance liquid chromatography – tandem mass spectrometry (HPLC-MS/MS) since immunological methods have limitations in selectivity and reproducibility.

21. Quantitative analysis of PAs is based on the determination of individual PAs, using LC-MS/MS, or a sum parameter method based on analysis of common necine groups, using GC-MS detection. In all cases, pre-concentration and sample clean-up prior to analysis are required. Some issues of concern are related to the instability of N-oxides during sample preparation and analysis. There are multiple variants of Liquid chromatography Tandem mass spectrometry (LC-MS/MS) methods. LC-MS/MS methods offer low detection limits of approximately 1 µg/kg or less and the ability to analyse PAs and PA-N-oxides simultaneously in one run as the main advantages. Challenges common to all analytical methods are the lack of high-quality standards, internal standards and certified reference materials.

22. A standardised method of analysis for the analysis of PAs in feed is available: EN 17683:2023 Animal feeding stuffs - Methods of sampling and analysis - Determination of pyrrolizidine alkaloids in animal feeding stuff by LC-MS/MS. For the analysis of pyrrolizidine alkaloids several described methods of analysis are available such as the method “Determination of pyrrolizidine alkaloids in plant-based food and feed materials, including (herbal) teas, herbal food supplements, fodder and feedstuffs by LC-MS/MS” developed by the EU Reference Laboratory for mycotoxins and plant toxins in food and feed (EURL-MP)[5] and the method “Determination of pyrrolizidine alkaloids (PA) in plant material by SPE-LC-MS/MS” developed by the Bundesinstitut für Risikobewerting from Germany[6].

23. PA contamination can be non-homogeneous owing to the uneven distribution of plant parts in a batch of feed or food. Similarly, teas, salads and pollen granules are also likely to be quite heterogeneous in regard to contamination. Distribution of PAs in dry teas can be very inhomogeneous owing to variation in distribution of the plant particles with inherent PA through the mix. Relatively more or larger-volume samples will probably be required for such foods than are needed for complex solids such as meat and especially liquid foods, such as milk, honey and mead, where more homogeneous contamination within a batch can be expected.

24. Proper sampling will, therefore, be critical. Sampling protocols will play a crucial role in the precision with which the levels of are measured in the wide range of foods that are currently known to be subject to contamination. It seems likely that significantly more practical experience will be required before optimum sampling protocols emerge that are suitable for different foods and foods at different stages of manufacture Existing sampling protocols for other natural toxins such as mycotoxins should be followed in sampling protocols for PAs in bulk commodities and in consumer products. Sampling protocols for PAs could initially be based on those specified for mycotoxins. Information on sampling

[5] Available at : https://www.wur.nl/nl/show/eurl-mp-method_002-pyrrolizidine-alkaloids-by-lc-msms-vs.htm
[6] Available at : https://www.bfr.bund.de/cm/349/determination-of-pyrrolizidine-alkaloids-pa-in-plant-material.pdf

for mycotoxins can be obtained from Codex Alimentarius standard CXS 193-1995[7], in which sampling protocols are compiled for several mycotoxins.

Effects of food and feed processing

25. PAs are expected to be stable during most processes applied for food and feed production. The removal of co-harvested seeds and weeds from the raw materials will reduce the content of 1,2-unsaturated PAs and their N-oxides significantly. The presence of PAs in foods and dietary supplements such as pollen and honey provides a confirmation of the stability of PAs during food processing. However, details on the rate of possible degradation during food processing are not available, with the exception of data on tea infusion. The 1,2-unsaturated PAs and their N-oxides are stable during tea infusion making.

26. Some information is available on the fate of 1,2-unsaturated PAs and their N-oxides during feed production The occurrence of PAs in animal feed shows that 1,2-unsaturated PAs and their N-oxides are fairly stable during feed production, although reliable data on the rate of degradation and the metabolites that are formed are lacking.

27. It is evident that more information is required on the effects of processing on PAs.

Prevention and control

28. Management practices currently focus on minimizing the occurrence of weeds containing 1,2-unsaturated PAs and their N-oxides in feed and food. Management practices to help prevent and reduce the levels of 1,2-unsaturated PAs and their N-oxides in food and feed are established in the Codex Alimentarius Code of practice for weed control to prevent and reduce pyrrolizidine alkaloid contamination in food and feed (CXC 74-2014[8]). Good agricultural practices, HACCP and good manufacturing practice strategies must be in place to prevent batches of food contaminated with PAs entering the food chain and mingling with uncontaminated products.

29. Specific Codes of practice and/or guidelines and recommendations to reduce the presence of pyrrolizidine alkaloids have been developed such for tea, herbal infusions, food supplements and medicinal products of plant origin. Examples of these are "Code of Practice to prevent and reduce pyrrolizidine alkaloid contamination in raw materials for tea and herbal infusions[9]" developed by Tea and Herbal Infusions Europe, "Guidelines and recommendations to reduce the presence of pyrrolizidine alkaloids in food supplements[10]" developed by Food Supplements Europe, and "Guidelines for Good Agricultural and Wild Collection Practices for Medicinal and Aromatic Plants (GACP-MAP)[11]" developed by EUROPAM, the European Herb Growers Association and the "Code of practice to prevent and reduce pyrrolizidine alkaloid contaminations of medicinal products of plant origin[12]".

30. Given the relevance of the presence of pyrrolizidine alkaloids in tea, herbal infusions, honey, food supplements and herbs and spices it is appropriate to update the Codex Code of Practice for weed control to prevent and reduce pyrrolidine alkaloid contamination in food and feed (CXC 74-2014) as regards the good practices generally applicable to prevent and reduce pyrrolizidine alkaloids in food and feed supplemented with good practices for specific foods and feeds.

JECFA Recommendations

31. JECFA noted that several gaps still exist in the overall PAs database, from toxicological and epidemiological aspects, to methods of analysis and occurrence levels in different food products, among others. As the missing information has precluded a more definitive assessment, in order to fill these data gaps, JECFA recommended the following:

    a. To establish internationally agreed high-quality standards, and certified reference materials, that would allow accurate analytical determination and quantification of the different PAs;

    b. To further study the effects of processing on the occurrence of PAs, taking into account possible metabolites formed during processing;

    c. To generate occurrence data from areas other than the EU and on food products other than honey, particularly foods of animal origin, in order to improve dietary exposure estimates for PAs across the range of potentially PA-containing foods and from different geographical regions;

[7] https://www.fao.org/fao-who-codexalimentarius/codex-texts/list-standards/en
[8] Available at: https://www.fao.org/fao-who-codexalimentarius/codex-texts/codes-of-practice/en/
[9] Available at: https://thie-online.eu/files/thie/docs/2018-07-12_THIE_Code_of_Practice_PA_in_TEA-HFI_ISSUE_1.pdf
[10] Available at: https://foodsupplementseurope.org/wp-content/themes/fse-theme/documents/publications-and-guidelines/Pyrrolizidine_Guidelines-May2021.pdf
[11] Available at: https://www.europam.net/wp-content/uploads/2022/11/EUROPAM-GACP-2022.pdf
[12] Available at: https://media.journals.elsevier.com/content/files/cop-revision-20090245.pdf

d. To conduct additional toxicological investigations in order to establish:

   i. the relative potency of PAs, taking into account toxicokinetics and genotoxicity; and

   ii. a point of departure to be used in risk assessment of acute dietary exposure to PAs;

e. To carry out epidemiological studies on long-term follow-up of incidents of PA contamination, with the aim to assess the carcinogenic potential of PAs in humans;

f. To generate more information on:

   i. toxicity and occurrence of saturated PAs, as most available data are on the 1,2-unsaturated PAs, and also because the saturated PAs elicit toxicity by a different mode of action;

   ii. transfer from feed to food, to estimate whether PA concentrations in food resulting from PAs in feed could be of concern for human health.

Call for data

32. Taking into account the recommendations from JECFA, it is appropriate to issue a call for data on the presence of pyrrolizidine alkaloids in food and feed. In order to obtain occurrence data that are comparable and reliable, it is important to define the methods of analysis to be used for analysing pyrrolizidine alkaloids and/or to define specific analytical performance criteria with which methods of analysis have to comply with to ensure that data are obtained with methods of analysis with e.g. sufficient sensitivity and precision. Furthermore, it is important to determine if PAs are to be quantified individually or if they can be determined as sum of alkaloids. In case of analysing individual PAs, it is relevant to determine which PAs at least should be analysed. Before launching the call for data, it is appropriate to define the minimum requirements for submission of data to the GEMS/Food database.

RECOMMENDATIONS

33. It is recommended to CCCF to:

a. Agree to elaborate a document defining the minimum requirements to which occurrence data have to comply with for submission to the GEMS/Food database for consideration by CCCF17 in view of issuing a call for data on the presence of pyrrolizidine alkaloids in food and feed.

b. To consider if new work should be proposed on an update of the Codex Alimentarius Code of practice for weed control to prevent and reduce pyrrolizidine alkaloid contamination in food and feed (CXC 74-2014) or if the EWG should revise the discussion paper for consideration by CCCF17.

c. To review the proposal for new work in Appendix II in case there is agreement to proceed with new work on the update of the CoP;

d. To establish an the EWG to prepare document defining the minimum requirements to which occurrence data have to comply with for submission to the GEMS/Food database and to work on an update of the Codex Alimentarius Code of practice for weed control to prevent and reduce pyrrolizidine alkaloid contamination in food and feed (CXC 74-2014) or to revise the discussion paper for consideration by CCCF17.

APPENDIX II

PROPOSAL FOR A NEW WORK ON AN

UPDATE OF THE CODEX ALIMENTARIUS CODE OF PRACTICE FOR WEED CONTROL TO PREVENT AND REDUCE PYRROLIZIDINE ALKALOID CONTAMINATION IN FOOD AND FEED (CXS 74-2014)

PROJECT DOCUMENT

(For consideration by CCCF)

1) Purpose and scope of the project

The purpose of the proposed new work is to update the Codex Alimentarius Code of Practice for weed control to prevent and reduce pyrrolidine alkaloid contamination in food and feed (CXC 74-2014) as regards the good practices generally applicable to prevent and reduce pyrrolizidine alkaloids in food and feed and to supplement the Code with good practices for specific foods and feeds, such as tea, herbal infusions, food supplements, herbs and spices. .

2) Relevance and timeliness

Pyrrolizidine alkaloids were assessed by the Joint Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO) Expert Committee on Food Additives (JECFA), at its eightieth meeting which took, place in Rome, Italy, from 16 to 25 June 2015. Details of the assessment can be found in WHO Food Additives Series: 71-S2, Safety evaluation of certain food additives and contaminants, Supplement 2: Pyrrolizidine alkaloids Available at https://apps.who.int/iris/rest/bitstreams/1318952/retrieve . JECFA concluded that the presence of pyrrolizidine alkaloids in certain foods are of concern.

3) Main aspects to be covered

This work will address all relevant measures for prevention or reduction of pyrrolizidine alkaloids at the different steps in the food and feed chain: production, harvest, storage, processing and distribution

4) Assessment against the criteria for establishment of work priorities

(a) **Consumer protection from the point of view of health and fraudulent practices**. To protect consumer health, exposure to pyrrolizidine alkaloids should be prevented or reduced. An update of the existing Code of Practice providing recommendations to governments, feed and food business operators will help prevent contaminated food from entering the market.

(b) Diversification of national legislations and apparent resultant or potential impediments to international trade. Currently, best practices and legislations. An update of the existing Code of Practice is needed to ensure that the most recent information on recommended practices for preventing and reducing pyrrolizidine alkaloids is available to all member countries. It also will provide the means to enable exporters to ensure reduced levels of pyrrolizidine alkaloids and to assist in compliance with any MLs that may be established in the future.

(c) Scope of work and establishment of priorities between the various sections of the work.

The update of the existing Code of Practice will address all relevant all relevant measures for prevention or reduction of pyrrolizidine alkaloids at the different steps in the food and feed chain: production, harvest, storage, processing and distribution.

(d) **Work already undertaken by other international organizations in this field.**

Codes of practice and/or guidelines and recommendations to reduce the presence of pyrrolizidine alkaloids have been developed by sector organisations for specific foods (such as tea and herbal infusions, food supplements and herbs.

5) Relevance to Codex Strategic Goals

(a) **Goal 1 Address current, emerging and critical issues in a timely manner.** Updating the Code of Practice for prevention or reduction of pyrrolizidine alkaloids in food and feed will address the current need for guidance to ensure the health of consumers.

(b) Goal 2 Develop standards based on science and Codex risk-analysis principles. This work will apply risk analysis principles in the update of the Code of Practice by using scientific data and recommendations from FAO/WHO and other recognized expert bodies to support a reduction in exposure of consumers to pyrrolizidine alkaloids.

(c) **Goal 3 Increase impact through the recognition and use of Codex standards.** The proposed update of the Code of Practice ensures that information on recommended practices to prevent and reduce the presence of pyrrolizidine alkaloids consist of current best practices and are available to all member countries, especially those with fewer resources to devote to this topic.

(d) **Goal 4 Facilitate the participation of all Codex Members throughout the standard setting process.** Updating the Code of Practice through the Codex Step process will make information on recommended practices to prevent and reduce presence of pyrrolizidine alkaloids in food and feed available to all Codex members.

(e) Goal 5 Enhance work management systems and practices that support the efficient and effective achievement of all strategic plan goals. An update of the Code of Practice will help ensure development and implementation of effective and efficient work management systems and practices by providing basic guidance for countries and producers to keep foods and feeds, highly contaminated with pyrrolizidine alkaloids out of the marketplace.

6) Information on the relationship between the proposal and other existing Codex documents

This proposal concerns an update of the existing Codex Alimentarius Code of Practice for weed control to prevent and reduce pyrrolidine alkaloid contamination in food and feed (CXC 74-2014) e is no known related Codex document.

7) Identification of any requirement for any availability of expert scientific advice

Pyrrolizidine alkaloids were assessed by the Joint Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO) Expert Committee on Food Additives (JECFA), at its eightieth meeting which took, place in Rome, Italy, from 16 to 25 June 2015.

8) Identification of any need for technical input to the standard from external bodies

Currently, there is no identified need for additional technical input from external bodies.

9) Timeline for completion of the new work

Work will commence following recommendation by CCCF and approval by CAC in 2023. Completion of work is expected by 2027 or earlier.

APPENDIX III

List of Members of the Electronic Working group

Chair

Frans Verstraete	European Commission	EU

Member Nations and Member Organisations

Matthew Joseph O'Mullane	Food Standards Australia New Zealand	Australia
Christine Vinkx	FPS Health, Food Chain Safety and Environment	Belgium
Larissa Bertollo Gomes Porto	ANVISA	Brazil
Carla Hilts	Health Canada	Canada
Elizabeth Eliott	Health Canada	Canda
Yi Shao	China National Center of Food Safety Risk Assessment (CFSA)	China
Yongning Wu	National Center of Food Safety Risk Assessment (CFSA)	China
Dawei Chen	China	China
Shuang Zhou	National Center of Food Safety Risk Assessment (CFSA)	China
Yeni Restiani	Indonesian Food and Drug Authority	Indonesia
Tetsuo Urushiyama	Ministry of Agriculture, Forestry and Fisheries	Japan
Yoshiyuki Takagishi	Ministry of Agriculture, Forestry and Fisheries	Japan
Tomoaki Miura	Ministry of Agriculture, Forestry and Fisheries	Japan
Kei Iwata	Ministry of Agriculture, Forestry and Fisheries	Japan
Tania Daniela Fosado Soriano	Secretaría de Economía	Mexico
Weiluan Chen	RIVM	Netherlands
Nikki Emmerik	Ministry of Health	Netherlands
Jeane Nicolas	Ministry for Primary Industries, New Zealand Food	New Zealand
Fiapaipai Ruth Auapaau	Ministry for Primary Industries	New Zealand
Ewelina Kowalczyk	National Veterinary Research Institute	Poland
Republic of Korea/ Codex Secretariat	Ministry of Agriculture, Food and Rural Affairs	Republic of Korea
Yeon Ju Kim	Ministry of Food and Drug Safety	Republic of Korea
Mohamed A Bineid	Saudi Food and Drug Authority	Saudi Arabia
Leau Yu Lee	Singapore Food Agency	Singapore
Juliet Masuku	Department of Health	South Africa
Nurun Nahar	Swedish Food Agency	Sweden
Bengi Akbulut Pınar	Ministry of Agriculture and Forestry	Turkey
Sinan Arslan	Ministry of Agriculture and Forestry	Turkey
Craig Jones	Food Standards Agency	United Kingdom

Anthony Adeuya	US Food and Drug Administration	USA
Lauren Posnick Robin	US Food and Drug Administration	USA
Quynh-Anh Nguyen	FDA/CFSAN	USA

Non-Governmental Organisations

Shannen Kelly	International Organisation of Spice Trade Association	USA
Farshad La-Rostami	THIE | Tea & Herbal Infusions Europe	Germany
Maximilian Wittig	THIE | Tea & Herbal Infusions Europe	Germany