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on Food Safety

SKLM

Opinion on the role of the concept of “history of safe use” in the safety assessment of novel foods and novel food ingredients

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The Council of the European Union has proposed a revision on the EU regulation on novel foods and novel food ingredients concerning safety assessment of traditional foods from non-EU countries and their introduction onto the EU market. The proposal stipulates that such foods may be placed on the EU market if their history of safe use in the country of origin is appropriately documented. The present statement of the SKLM gives an overview on current discussions on practical implementation of the "history of safe use" concept as well as examples of its application. The SKLM, in principle, agrees with these concepts, underscores, however, in connection with convincing evidence for a "history of safe use" the need for a range of additional information to achieve a comprehensive risk assessment. In the opinion of the SKLM such information must comprise compositional data as well as experience on adverse effects. A list of questions considered essential is presented.

1. Introduction

The proposed revision of the EU regulation on novel foods and novel food ingredients [1] foresees that traditional foods from third countries may be placed on the Community market under conditions that correspond to those for which the history of safe use has been demonstrated if they are included in the list of traditional foods from third countries. As regards the safety assessment and management of traditional foods from third countries, their history of safe food use in the third country of origin should be taken into account. The history of safe food use should not include non-food uses or uses not related to normal diets.

The following definitions have been provided in the proposal:

„Traditional food from a third country": means novel food derived from primary production with a history of food use in any third country, meaning that the food in question has been and continues to be part of the customary diet for at least 25 years in a large part of the population of the country.

"history of safe use in a third country": means that the safety of the food in question is confirmed with compositional data and from experience of use and continued use for at least 25 years in the customary diet of a large part of the population of a country.

If an applicant intends to place on the Community market a traditional food from a third country, the application shall include documented data demonstrating the history of safe food use in a third country.

The concept of using data available on the (safe) use of a food or food ingredient as one of the pieces of information to be considered in food safety assessments is not new *per se*. However, the foreseen implementation of the explicit term "history of safe use" in the regulatory framework and its consequences for type and extent of safety assessments requested for certain novel foods and novel food ingredients raises the question whether it is justified and feasible to translate this concept into science-based generic requirements.

The objectives of this statement are (i) to give an overview on areas building on the concept of "history of safe use" in the context of food safety assessments, (ii) to review activities to establish technical guidance for its practical application, and (iii) in the light of this

information to express the view of the SKLM on the role of the concept of “history of safe use” in the safety assessment of novel foods and novel food ingredients.

2. Examples from areas employing the concept of “history of safe use”

2.1 Introduction of a Qualified Presumption of Safety (QPS) approach for assessment of selected microorganisms referred to the European Food Safety Authority EFSA

A wide variety of microbial species are used in food and feed production. Some have a long history of apparent safe use, while others are less well understood and their use may represent a risk for consumers. Experience has shown that there is a need for a tool for setting priorities within the risk assessment of those microorganisms used in food/feed production referred to EFSA and consequently the subject of a formal assessment of safety. To meet this need a system was proposed for a pre-market assessment of selected groups of microorganisms leading to a “Qualified Presumption of Safety (QPS)” [2]. In essence this proposed that a safety assessment of a defined taxonomic group (e.g. genus or group of related species) could be based on four pillars (establishing identity, body of knowledge, possible pathogenicity and end use). If the taxonomic group did not raise safety concerns or, if safety concerns existed, but could be defined and excluded (the qualification) the grouping could be granted QPS status. Thereafter, any strain of microorganism the identity of which could be unambiguously established and assigned to a QPS group would be free from the need for further safety assessment other than satisfying any qualifications specified. Microorganisms not considered suitable for QPS would remain subject to a full safety assessment.

2.2 EFSA guidance document on safety assessment of botanicals and botanical preparations intended for use as ingredients in food supplements

A two-level tiered conceptual framework for safety assessment has been proposed, consisting of a safety assessment based on available knowledge and a subsequent level in which further testing and/or data are required [3]. Botanicals or botanical preparations for which an adequate body of knowledge exists can benefit from a “presumption of safety” without any need for further testing. Based on reasonable evidence, they can be assumed to be safe, sometimes under certain restrictions. The Scientific Committee of EFSA used as example the Qualified Presumption of Safety (QPS) approach developed for microorganisms in food and feed to propose criteria presuming a botanical or a botanical preparation to be safe.

The following data have to be provided as a basis: (i) identity and nature of the source material, (ii) manufacturing process, (iii) chemical composition; (iv) specifications; (v) stability of the botanical or botanical preparation used as ingredient in food supplement; (vi) proposed uses and use levels. An additional requirement is that no significant increase of intake compared to historical levels is to be expected due to the intended levels of use in food supplements.

2.3 EFSA guidance document on the submission of a dossier on food enzymes for safety evaluation

Food enzymes shall be subject to safety evaluation by the EFSA [4] and EU-wide approval. Administrative and technical data shall be provided for all notified enzymes, the requirement for toxicological data may in some cases be reduced or completely waived; the justification for not supplying toxicological data may include:

- *A documented history on the safety of the source of the food enzyme, the composition and the properties of the food enzymes as well as its use in food, demonstrating no adverse affects on human health when consumed in a comparable way, supported by any existing toxicological studies. In such cases, a detailed rationale must be provided to EFSA for evaluation, e.g. edible parts of animals and (non GM) plants.*
- *Food enzymes produced by micro-organisms that have been given a status of Qualified Presumption of Safety (QPS), if it can be demonstrated that there are no concerns related to any residues, degradation products or substances originating from the total production process.*
- *If a food enzyme from a specific strain has been thoroughly tested and the manufacturing process does not differ significantly for other food enzymes from the same strain, the full testing battery may be waived for these food enzymes. This will be decided on a case-by-case basis.*

2.4 Opinion on an Application under the Novel Foods Regulation for Baobab Dried Fruit Pulp as a Food Ingredient

On 9 August 2006, the UK competent authority accepted an application for Baobab Fruit Pulp as a novel food ingredient [5]. The applicant had highlighted a number of publications indicating that the fruit pulp has a long and extensive history of consumption amongst indigenous Africans and that it could be consumed as such, in drinks or used as an ingredient in other foods. The applicant had also provided information on current use in Africa from two

questionnaires. The first was completed by nineteen Participants at the PhytoTrade Annual General Meeting in May 2006 and confirmed literature reports that the fruit pulp is widely consumed in the areas where it is available. The second questionnaire was completed by fifteen experts (nutritionists and botanists from Africa, the EU and the US with knowledge of African diets and food crops). These provided additional evidence that baobab pulp is a familiar food in various parts of Africa and that there are no known toxicity issues.

The applicant also presented a literature review indicating that the baobab fruit (*A. digitata*) is also consumed in India and other *Adansonia* species have a history of consumption in Australia. There are also references to limited sales in the European Union, for example in ethnic markets and in food supplements. The fruit pulp is sometimes used as a folk remedy and numerous medicinal uses have been reported in the literature.

The UK-Advisory Committee on Novel Foods and Processes (ACNFP) accepted that the information supplied indicated that the product has an extensive history of traditional consumption in a significant geographical area of Africa. The information supplied by the applicant was considered to offer sufficient reassurance that the consumption of the novel food ingredient does not give rise to concerns with respect to toxicology or allergenicity. ACNFP-members agreed that the absence of extensive toxicological analyses did not give cause for concern because baobab fruit was a staple part of the diet throughout Africa and a retrospective toxicological assessment would have limited value. In coming to this conclusion the ACNFP drew a distinction to other foods that previously had been subject to a novel food assessment and could be viewed to be regularly consumed outside the EU. In all previous cases there was either a specific safety concern (e.g. allergenicity or liver toxicity) or the food was of limited palatability and was consumed essentially as a natural remedy rather than as a staple part of the diet.

2.5 Scientific Opinion of the European Food Safety Authority (EFSA) on the safety of "chia seed (*Salvia hispanica* L.) and ground whole chia seeds" as food ingredient

"Chia" (*Salvia hispanica* L.) is a summer annual herbaceous plant belonging to the Labiatae family. The Panel on Dietetic Products, Nutrition and Allergies (NDA) of the EFSA was asked to deliver a scientific opinion on the safety of "chia seed (*Salvia hispanica* L.) and ground whole chia seeds" as food ingredient and to specify whether the authorisation of Chia as food ingredient for bread is likely to have an effect on public health [6].

The applicant claimed that *Salvia hispanica* L. is commonly consumed in several countries, including the USA, Canada and Australia. According to the applicant, these countries would

now have a “history of safe use” regarding *Salvia hispanica* L., and “the data from these countries would be typical of a modern society”. The applicant provided a worldwide overview on the consumption of chia seeds or oil and claimed that a ”history of safe use” is based on the absence of records of adverse affects, including allergenicity, anti-nutritional or toxic effects for Chia seeds in the listed countries.

The information on toxicology and safety of Chia seeds provided from animal and controlled human studies was limited. However, the NDA-Panel considered that the experience gained from previous and current use of Chia seeds for food purposes in non-EU countries can be regarded as supportive evidence to allow a positive conclusion on the safety of Chia seeds and ground whole Chia seeds under the proposed conditions of use.

3. Activities to establish technical guidance for the practical application and use of the concept of “history of safe use”

3.1 Risk assessment and risk management of novel plant foods – concepts and principles elaborated by the Nordic Working Group on Food Toxicology and Risk Evaluation (NNT)

The Nordic Working group on Food Toxicology and Risk Evaluation (NNT) has developed a proposal for a set of definitions and criteria for determining if a plant is traditional or novel and proposed an approach for the safety assessment of such foods with no or limited documented history of safe consumption [7]. The Nordic Working Group recommends to introduce:

- *The use of a two-step procedure, first to establish the novelty and secondly to define and to commit resources for the safety assessment.*
- *The use of a worldwide net of global, regional, local and ethnobotanical positive lists for food plants to guide the decision on novelty at the fist step and to enable the safety assessment in the second step.*

To support and ease the availability of a high quality “history of use” data set, the NNT particularly recommends the worldwide development of individual positive lists of foods plants recognizing the plants as sources of foods at the global, regional or local level or known as ethnobotanical foods in different places. This would create a complete worldwide inventory of the use of plant foods.

3.2 ILSI Europe

The ILSI Europe Novel Foods Task Force has published a paper aiming to assist food safety professionals in the safety evaluation and regulation of novel foods by describing the practical application and use of the concept of "history of safe use" [8]. The paper emphasizes that although "history of safe use" of traditional foods forms the benchmark for the comparative safety assessment of novel foods, the concept is hard to define, since it relates to an existing body of information which describes the safety profile of a food, rather than a precise checklist of criteria. The term should be regarded as working concept used to assist the safety assessment of a food product. Important factors in establishing a history of safe use include: the period over which traditional food has been consumed; the way in which it has been prepared and used and at what intake levels; its composition and the results of animal studies and observations from human exposure.

For the different parts of the term "history of safe use" the following key issues were discussed:

History: Correct identification; biology (origin, genetic diversity); length of use; geographic/demographic distribution of use; details of use; evidence of adverse effects; reliability of data

Safe: Composition (especially toxic, allergenic, metabolic, nutritional and anti-nutritional components as well as health compromising compounds); *in silico* tests (e.g. structural homology to known allergens or toxins); *in vitro* tests (e.g. serum screening, digestibility tests); animal studies (toxicology and nutrition studies); experience from human exposure; clinical studies; epidemiological evidence

Use: Type/purpose, e.g. as food, ingredient, supplement or pharmaceutical; preparation and processing; known precautions; pattern of consumption (occasional, regular or co-administration); intake (level, populations exposed, mean/extremes).

3.3 UNCTAD/BioTrade Initiave

In a paper published among others by UNCTAD and BioTrade Initiative issues concerning the proposed amendments to the Novel Foods Regulation with particular reference to traditional foods from developing countries have been discussed [9]. The paper recommends a two-step procedure: Step 1: Identity and Traditional Food Status; Step 2: History of Safe Food Use Assessment

For Step 1 the importance of several key terms has been discussed.

"normal diet": Implies a regularity of consumption of a diet that has (in some way) been defined as a standard for a typical member of a population

*"customary diet":R*efers to the diet that itself forms part of the custom and tradition of a society, without inferring any degree of regularity of consumption

"*large part of the population of the country":*

- "large": statistical validity or nutritional and/or toxicological significance of the numbers involved are essential
- "population of a country: from tens of thousands to hundreds of millions
- "population": in many countries not a homogenous group, but may comprise several ethnic and/or religious sub-populations, each with their own differing long-standing dietary habits and preferences; these ethnic/religious groups may comprise, numerically, only a small proportion of the overall population and live in a small area ("region") of a given country, yet still represent a discrete and identifiable "population"; equally, these ethnic/religious populations may be more thinly spread within a given country but be represented more widely over several countries (i.e. wider, geographical region that shares a common cultural history)
- the concept of "a (single) country" does not address the politically-driven changes to country boundaries that have occurred in some regions (e.g. Africa) well within the timescales of the use of traditional foods

For Step 2 the following information requirements were discussed:

Specification of the Novel Foods and Processing Operations

- Specification should include maximum limits for undesirable substances.
- All operations from harvest or collection resulting in the final specification
- Plant parts that are used
- Special cultivation or harvesting practices
- Traditional practices to ensure that known toxic components do not enter the food chain at this stage
- Specific processing operations carried out to ensure that toxic components or other anti-nutritional factors harmful to human health are consistently less than maximum safe permitted levels
- Specific handling and/or storage requirements

Proposed Use in European Diet and Downstream Processing

- Detailed description how the Novel Food or Novel Food ingredient will be used, should be used or is anticipated to be used after export to the EU
- Specific storage and/or handling requirements at industrial and/or domestic level
- Further processing at industrial or domestic level necessary before consumption
- Detailed explanation why this further processing is necessary (to improve palatability/nutritional value and/or to reduce toxicants to safe levels)
- Differences between the processing operations carried out for the traditional food in the third country and the processing operations carried out in the EU

Human Exposure to the Novel Foods and Estimated Levels and Patterns of Exposure in the EU

- Average and maximum per capita consumption data in the third country
- consumption patterns and consumption data among population groups
  (sources: • scientific and non-scientific publications
  • third country food data base
  • data from other countries
  • appropriate competent authority in third country
  • other recognised authority)
- Estimated average per capita exposure to European consumers
- Data to demonstrate whether exposure to European consumers is estimated to be less than or greater than the maximum exposure to consumers in a third country
- Consideration of population groups.

3.4 EFSA Scientific Colloquium

On 19-20 November 2009 EFSA organised a Scientific Colloquium with international experts to discuss scientific information needed for applications on novel foods and novel food ingredients submitted for authorisation in the European Union [10]. One of the discussion groups addressed the theme “History of (safe) use and traditional foods from non EU-countries”.

The group concluded that from a scientific point of view, it may be challenging to translate the assessment of traditional foods from non-EU countries on the basis of a history of safe use, as foreseen in the proposed revision of the Novel Foods Regulation, into general requirements, valid for widely diverging types of foods.

Foods consumed for more than 25 years in a given country could include primary products, whole foods derived from these primary products, food ingredients, and even food supplements. Products used as food supplements are generally not considered as part of the customary diet, and extracts from primary products should not be assessed as traditional foods. Furthermore, the application of production techniques not used traditionally would contradict the basic concept of a separate procedure for traditional foods. Therefore, for example, products obtained by application of novel breeding techniques should not be considered as traditional foods. Similarly, marketing products to other target groups or consuming products at a different stage of their development conflicts with accepting the established history of consumption as evidence for safety.

Compositional data should be used to characterise the traditional food and serve as a baseline for comparison for actual products to be marketed. Both nutrients and other known substances have to be considered. The experience gained in gathering and reporting general food composition data, both within the world and in other countries should be exploited. These databases could be used to model the general requirements for characterising the traditional food by using analytical data, including macronutrients and the most relevant micronutrients. It can be envisaged that more detailed data will be relevant for specific product types, such as the fatty acid profile for oils. In these cases, useful information form other sources, such as CODEX standards, may be available.

In principle, the requirements regarding batch testing, methods, validations, certifications and documentation should be similar to those used for testing other foods. Reliable data should be produced, by using up to date analytical methods and recognized international standards. The analyses should be performed by qualified laboratories. In order to apply the concept of traditional foods in a meaningful way, the identity of the traditional food should be determined beyond doubt. Together with the compositional data, this will ensure that the historical data on previous consumption is relevant for the actual product. If the traditional food is well defined, this may help to substantiate the safety of an essentially identical product with a different geographical origin.

Data on known anti-nutrients and inherent toxicants should be provided on a case-by-case basis. Any data from literature on adverse effects, related to the traditional food, should be discussed by the applicant. This should also include any reports on possible allergenicity of the product. Data on previous use in other countries than the country of origin may also be useful.

It is important to establish that the previous consumption was not just anecdotal, and therefore reference is made to the number of consumers in the country of origin. Nevertheless, it is impossible to determine from a scientific point of view if a certain number of consumers would be sufficient to demonstrate the history of consumption. Furthermore, the definition refers to *a large part of the population of a country*, but a regional product in a large country could be consumed by more people than a product that is consumed by everyone in a very small country. It therefore seems to be more useful to compare the historical use to the intended level of use and the intended target groups. The consequences of any differences therein should be considered.

In principle, the product should be identical to the traditional food, for which historical data are available. However, it is to be expected that changes or improvements in production methods will be applied in the course of time. Nevertheless, the concept of a traditional food could still be applied if the product matches approved standards of identity, including compositional data.

The presence of non-nutritive dietary constituents such as secondary plant metabolites, anti-nutritional factors and contaminants can only be considered on a case-by-case basis. Several sources of information may be available, such as scientific literature on the species itself and related species, and expert judgement by botanical specialists. The conditions of use of the traditional food may be important, since these can reflect traditional risk management solutions.

4. Views of the SKLM

The foregoing chapters present an overview on ongoing activities and concepts referring to "history of safe use" in the context of food safety assessment. The SKLM supports the concepts of the various international organizations outlined above (3.1-3.4) to establish technical guidance for their practical application and use. Yet, the SKLM considers it a major scientific challenge to use demonstration of a "history of safe use" as the sole criterion for decision making, as foreseen in the proposed revision of the EU regulation on novel foods and novel food ingredients. Information on the "history of safe use" of novel foods and novel food ingredients constitutes an intrinsic, valuable element of their safety assessment. It is underlined, however, that this should be just one of the elements of the safety assessment procedure of a novel food and novel food ingredient and ideally should be accompanied by

other type of information providing plausible evidence for safety. The totality of information should be embedded into a broader decision approach. The SKLM underlines that such an approach requires that the evidence provided has to meet particularly stringent and high quality requirements (see 4.1).

Taking into account the broad spectrum of potential novel foods and novel food ingredients expected to be imported from third countries, the SKLM considers it difficult to provide generic requirements and to request a precise and comprehensive checklist of criteria. However, at the least, the demonstration of a "history of safe use" of a novel food or novel food ingredient is to be based on two essential types of information: (i) compositional data/specification and (ii) experience of use/intake/potential adverse effects. Within that context, questions considered essential are listed below (4.1).

4.1 Essential questions to provide convincing evidence for "history of safe use"

Compositional data / Specification

- Are compositional data provided proving accordance with specifications, based on appropriate parameters determined by accredited laboratories using validated methods?
- Do the compositional data/specifications cover environmental variability?
- Are essential nutrients/anti-nutrients/toxicants/allergens known for the organism or its family covered and are they adequately taken into consideration?
- For processed novel foods: What is the relation between the novel food and the primary product, taking into account food production, processing, including fermentation, and storage?
- Altogether, do the compositional data convincingly demonstrate the identity of the novel food and the traditional food in the third country?

Intake

- Is the intended use comparable to the traditional use (e.g. types of preparation, anticipated use/intake levels, target groups)?
- Is the introduction of the novel food anticipated to result in a substantial change of the dietary behaviour/pattern of the target group?

Potential adverse effects

- How strong is the evidence for the absence of adverse effects for the traditional food?
- Are potential differences in human metabolism of the novel food between traditional population and target groups adequately addressed?
- Are potential interactions with other diet ingredients taken into account?

If this set of information is not provided, a comprehensive safety evaluation as requested for other novel foods and novel food ingredients has to be performed.

5. References

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