European Federation of Associations of Health Product Manufacturers

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Subject: EHPM position on maximum levels of Pyrrolizidine Alkaloids(PA) in food supplements

Background and feedback on the EFSA opinion

EHPM considers it fundamental to guarantee the consumers' safety and in case of concerns take the relevant measures. Our Association is aware of the potential risk posed by pyrrolizidine alkaloids (PAs) and supports appropriate actions to ensure the safety of the consumers.

Those actions should be proportionate, taking into account the potential risk for the consumers and at the same time the impact on the sector. Limits should be established based on the knowledge we currently have. Further studies and more data should help better addressing the issue, avoiding unfair and unnecessary constraints for the whole chain, from growers to food supplements manufacturers.

The EFSA scientific opinion on PAs relied on studies criticized by the EFSA Panel itself because of several uncertainties. Those uncertainties refer to important factors, as, for instance, the overall exposure of the European population. According to the EFSA Panel, the dietary exposure to PAs may overestimate the exposure level. This point is especially relevant when addressing the issue of PAs in food supplements. Food supplements consumption is not generally chronic, the exposure is rather acute. As EFSA itself affirmed, food supplements do not represent the main source of PAs in the diet. Therefore, limits on those products should consider those elements.

Furthermore, as recognized by the EFSA Panel too[1], the carcinogenic effect of many PAs present in food is expected to be lower than the potency of the two PAs in the long term studies available, lasiocarpine and riddelliine. Therefore, **an approach that would consider the carcinogenicity of those two PAs only, known to be more toxic, is in our view limited**. Uncertainties on this point are acknowledged by the Panel and described in the opinion. Also, it should be noted that recent studies show that **PAs have different level of safety risk for the consumers**[2,3] linked to their structural differences. These studies suggest applying relative potency factors for the different PAs, thus taking into account the different toxicities in the risk assessment.

[1] 1 EFSA CONTAM Panel (EFSA Panel on Contaminants in the Food Chain), Knutsen HK, Alexander J, Barreg□ard L, Bignami M, Br€uschweiler B, Ceccatelli S, Cottrill B, Dinovi M, Edler L, Grasl-Kraupp B, Hogstrand C, Hoogenboom LR, Nebbia CS, Oswald IP, Petersen A, Rose M, Roudot A-C, Schwerdtle T, Vleminckx C, Vollmer G, Wallace H, RuizGomesJA and Binaglia M, 2017. Statement on the risks for human health related to the presence of pyrrolizidine alkaloids in honey, tea, herbal infusions and food supplements. EFSA Journal 2017;15(7):4908, 34 pp.

[2] Merz KH and Schrenk D. Interim relative potency factors for the toxicological risk assessment of pyrrolizidine alkaloids in food and herbal medicines. Toxicol Lett. 2016 Nov 30;263:44-57.

The lack of toxicological data of the most common PAs in food, with particular reference to the toxicokinetics, metabolic activation and carcinogenic potency of those, represent a significant uncertainty of the risk assessment. **As emerged for the EFSA opinion, more studies and relevant data are needed to properly evaluate the safety of PAs in food.**

Maximum levels of PAs in food supplements

Based on that, and on the necessity to adopt measures for the protection of the consumers, the EHPM believes that limits on the finished products might represent a balanced measure guaranteeing at the same time the protection of the consumer and limiting the impact on the sector. Considering the need of more studies on PAs and the lack of data, and in line with the evaluation criteria proposed by the Commission, we believe:

- **1000 mcg/kg for the finished products would be appropriate**. **The limit of 1000 mcg/kg for the finished product should be considered provisional and valid for a transition period of 3 years.** This period will serve to acquire new data that will allow to appropriately re-evaluate the proposed limit.

It is more appropriate to monitor and have common defined limits on the finished product, rather that working on the individual plants or opting for other approaches at this stage. For instance, the reference to the daily intake would not be applicable and not in line with the relevant regulations.

- The **use of maximum levels expressed per mcg/kg are commonly indicated in the EU legislation in several regulations, such as the Regulation EC 1881/2006 setting maximum levels for certain contaminants in foodstuffs, that covers food supplements too for example by the amending Regulation EC 629/2008 and Regulation EU 212/2014.**

The maximum content of heavy metals in food supplements and other foodstuffs, for instance, is set per mcg/kg, e.g. Lead 1000 mcg/kg. The same applies to the maximum content of citrinin, of concern for nephrotoxicity, which is set per 2000 mcg/kg in food supplements.

Implementation and adaptation timeline

Therefore, to address the issue, we need to work throughout the value chain. It is necessary to consider the difficulties the introduction of a sudden change might have. New production standards need time to be fully implemented. It will be important to identify the origin of the contamination and take relevant measures. **Plants may have different PAs content and that is influenced by many factors, natural occurrence of PAs in the plants, systematic and occasional contamination by weeds, characteristics of the soil, etc.** Agricultural practices request time to be adjusted. Additionally, the content on PAs could be influenced by processing methods as well.

Companies, especially SMEs, need to adapt to the limits and need time to implement ad hoc controls and procedures to make sure those limits are respected.

[3] Chen L. et al. Risk assessment for pyrrolizidine alkaloids detected in (herbal) teas and plant food supplements. Regulatory Toxicology and Pharmacology. Volume 86, June 2017, Pages 292-302

- **A 3 years implementation time is therefore required to guarantee the transition to the new standards.**

Different actors are involved, from growers, to extract producers, to the product manufacturers. It will be important then to ensure all key stakeholders are involved and properly informed about the new limits. Moreover, during those 3 years, other studies can be conducted and more information collected.

EHPM believes that consumers' safety is fundamental for our sector, and companies are ready to respond appropriately, provided that those measures are proportionate and allow operators to continue working.

Yours Sincerely, 22 May 2019

Michel Horn
EHPM Chair