

# Determination of pyrrolizidine alkaloids according to Commission Regulation 2020/2040

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Pyrrolizidine alkaloids are known to be highly toxic to humans, these are nitrogen containing compounds biosynthesised as secondary metabolites by different plant species. These substances were studied and the information on the tested includes hepatotoxicity, genotoxicity and carcinogenicity.

For this reason, in 2017 EFSA was asked by the European Commission to define the risks for human health for a dietary exposure to pyrrolizidine alkaloids in honey, tea, herbal infusions and food supplements<sup>1</sup>.

Neutron set up and validated an analytical method to monitor the 28 Pyrrolizidine alkaloids (PAs) listed in the EFSA publication 2016<sup>2</sup> and in the EMA document “Public statement on contamination of herbal medicinal products/traditional herbal medicinal products with pyrrolizidine alkaloids - Transitional recommendations for risk management and quality control (2016)<sup>3</sup>”.

In December 2020 the European Commission published the **Commission Regulation (EC) 2020/2040 of 11 December 2020** amending Regulation (EC) No 1881/2006 as regards maximum levels of pyrrolizidine alkaloids in certain foodstuffs<sup>4</sup>.

For details please see Annex to Regulation (EC) No 2040/2020 at the following link:  
<https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32020R2040&from=EN>.

This Regulation sets the maximum level referred to the lowerbound sum of the following 21 pyrrolizidine alkaloids (**Figure 1**):

Intermedine/Lycopsamine, Intermedine-N-oxide/Lycopsamine-N-oxide
Senecionine/Senecivernine, senecionine-N-oxide/Senecivernine-N-oxide
Seneciphylline, Seneciphylline-N-oxide
Retrorsine, Retrorsine-N-oxide
Echimidine, Echimidine-N-oxide
Lasiocarpine, Lasiocarpine-N-oxide
Senkirkine
Europine, Europine-N-oxide
Heliotrine and Heliotrine-N-oxide

**Figure 1:** 21 PAs reported in Commission Regulation (EC) 2020/2040<sup>4</sup>.

The above 21 pyrrolizidine alkaloids could co-elute with the following additional 14 pyrrolizidine alkaloids (**Figure 2**):

Indicine, echinatine, Rinderine (possible co-elution with lycopsamine/intermedine)
Indicine-N-oxide, Echinatine-N-oxide, Rinderine-N-oxide (possible co-elution with lycopsamine-N-oxide/intermedine-N-oxide)
Integerrimine (possible co-elution with senecivernine/senecionine)
Integerrimine-N-oxide (possible co-elution with senecivernine-N-oxide/senecionine-N-oxide)
Heliosupine (possible co-elution with echimidine)
Heliosupine-N-oxide (possible co-elution with echimidine-N-oxide)
Spartioidine (possible co-elution with seneciphylline)
Spartioidine-N-oxide (possible co-elution with seneciphylline-N-oxide)
Usaramine (possible co-elution with retrorsine)
Usaramine N-oxide (possible co-elution with retrorsine N-oxide)

**Figure 2:** 14 possible co-elution PAs reported in Commission Regulation (EC) 2020/2040<sup>4</sup>.

Pyrrolizidine alkaloids, which can be individually and separately identified with the used method of analysis, shall be quantified and included in the sum<sup>4</sup>.

In order to guarantee a quality control of these substances, Neutron has developed and validated an analytical method.

## Neutron proposal

Neutron performs the analysis of pyrrolizidine alkaloids by LC-MS/MS technique, permitting to detect the residues, carrying out co-elutions tests, with a limit of quantification of 0,001 mg/kg for most matrices (PYRROL-NEW group request, see **Annex 1**).

This method is in compliance with Commission Regulation (EC) 2020/2040 of 11 December 2020, that shall apply from 1 July 2022.

<b>Analytes</b>	
Echimidine	Lasiocarpine
Echimidine-N-oxide	Lasiocarpine-N-oxide
Echinatine-N-oxide/Indicine-N-oxide/ Intermedine-N-oxide/Lycopsamine-N-oxide/ Rinderine-N-oxide	Monocrotaline
Echinatine/Indicine/Intermedine/Lycopsamine/ Rinderine	Monocrotaline-N-oxide
Erucifoline	Retrorsine
Erucifoline-N-oxide	Retrorsine-N-oxide
Europine	Riddelliine
Europine-N-oxide	Senecionine
Heliosupine	Senecionine-N-oxide
Heliosupine N-Oxide	Seneciphylline-N-oxide/Spartioidine-N-oxide
Heliotrine	Seneciphylline/Spartioidine
Heliotrine-N-oxide	Senecivernine
Integerrimine	Senkirkine
Integerrimine N-Oxide/Senecivernine-N-oxide	Trichodesmine
Jacobine	Usaramine
Jacobine-N-oxide	Usaramine N-Oxide
Pyrrolizidine alkaloids, sum (Reg UE 2020/2040)	

**Annex 1:** PYRROL-NEW group, according with Commission Regulation (EC) 2020/2040<sup>4</sup>.

### References:

1. Risks for human health related to the presence of pyrrolizidine alkaloids in honey, tea, herbal infusions and food supplements, EFSA Panel on Contaminants in the Food Chain (CONTAM), *EFSA Journal* **2017**; 15(7):4908.
2. Dietary exposure assessment to pyrrolizidine alkaloids in the European population, European Food Safety Authority (EFSA), *EFSA Journal* **2016**; 14(8):4572.
3. Public statement on contamination of herbal medicinal products/traditional herbal medicinal products with pyrrolizidine alkaloids Transitional recommendations for risk management and quality control, Committee on Herbal Medicinal Products (HMPC), EMA (2016).
4. Commission Regulation (EC) 2020/2040 of 11 December 2020 amending Regulation (EC) No 1881/2006 as regards maximum levels of pyrrolizidine alkaloids in certain foodstuffs.