PAN Europe's position on the technical guidance on negligible exposure

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Technical guidance on points 3.6.3 to 3.6.5, and 3.8.2 of Annex II to Regulation (EC) No 1107/2009, in particular regarding the demonstration of negligible exposure to an active substance in a plant protection product under realistic conditions of use.

Background and objective

Points 3.6.3 to 3.6.5 of Annex II of Regulation (EC) No 1107/2009 provide that active substances, safeners or synergists, classified on the basis of Regulation (EC) No 1272/2008 as carcinogen category 1A or 1B or toxic for reproduction category 1A or 1B, or having endocrine disrupting properties which may cause adverse effects on humans, cannot be approved "*unless the exposure of humans to that active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible*".

In addition, point 3.8.2 of this same Annex stresses that active substances, safener or synergists, shall only be approved if they are not considered to have endocrine disrupting properties that may cause adverse effects on non-target organisms "*unless the exposure of non-target organisms to that active substance in a plant protection product under realistic proposed conditions of use is negligible*".

Therefore, the purpose of this guideline is to provide practical guidance in regulatory decision-making regarding this key concept of *"negligible exposure"* applied to some cut-off active substances, both in the context of human and environmental exposures.

1. Negligible exposure to humans (points 3.6.3 to 3.6.5)

a. Dietary exposure

Pursuant points 3.6.3 to 3.6.5 228 of Annex II to Regulation (EC) No 1107/2009, dietary exposure is negligible when "*residues of the active substance, safener or synergist concerned on food and feed **do not exceed the default value** set in accordance with Article 18(1)(b) of Regulation (EC) No 396/2005*".

Therefore, the provisions are clear. A dietary exposure can only be considered as negligible if the MRLs are not set at levels above the default value of 0.01 mg/kg or above the Level of Quantification following Article 18(1)(b).

b. Non dietary exposure

- **Conditions of use**

With respect to non-dietary human exposure, a definition of what is to be understood as negligible is also provided by points 3.6.3, 3.6.4 and 3.6.5 of Annex II. Those are "*conditions of use*" where "*the product is used in **closed systems** or in other conditions **excluding contact with humans**".*

Therefore, those conditions of use must be listed building on this clear condition of an absence of contacts with humans, starting with closed systems.

A closed system is one from which a substance cannot escape or be added. Building on this commonly agreed definition, systems such as greenhouses or walk-in tunnels cannot be considered as closed system (due to groundwater and surface water leakages)[1]. These are therefore not conditions of use that result in negligible exposure to a harmful substance.

To prevent human contacts, **other conditions of use than closed systems (if they technically exist) must also prevent any form of release of the substance**. For this purpose, all the different routes (air, water, soil) and pathways (inhalation, ingestion, dermal contact) of exposure for all exposed groups (operators, workers, bystanders and residents) must be considered.

When the proposed conditions of uses are failing to prevent such contacts in the applicant's dossier, it should be concluded that a negligible exposure cannot be demonstrated, without further assessment and in line with the cut off approach. Particularly, **risk mitigation measures (RMMs)**, whose aim is to *reduce* releases in order to *mitigate* exposure of humans, should not be further investigated. They do not and are not intended to completely eliminate human contact as required in points 3.6.3. to 3.6.5 of Regulation (EC) No 1107/2009. Therefore, they cannot ensure with certainty that the exposure to harmful substances will be negligible.

- **Reference values**

In line with the above statements, PAN Europe is firmly opposed to the use of toxicological reference values (eg. AOEL and/or MoE), which would not exclude human exposure but rather limit it to a threshold identified as 'safe'. This approach cannot be considered a suitable solution having regard to the definition of negligible exposure given in Annex II and to the hazard-based approach of Regulation 1107/2009.

This is particularly true for substances known or presumed to have non-threshold effects as carcinogenicity (3.6.3.), genotoxicity (3.6.4) or endocrine disruption (3.6.5). For those substances, no threshold is safe, particularly regarding the unborn children. For this precise reason, Regulation (EC) 1107/2009 provides that these substances must be banned on the sole basis of their hazardous intrinsic properties if human contact cannot be excluded and without further risk assessment. In this respect, the Regulation intendedly protects from non-threshold risks, which would not be addressed by implementing toxicological reference values. Their use would go against the cut-off approach and completely twist the purpose of the regulation, which is to remove the more harmful substances from the EU market rather than to try mitigating the related risks.

This objective was turned into a political commitment in the Farm to Fork Strategy, which calls for a 50% reduction in the use of the more harmful pesticides by 2030. Those latter are defined as those containing cut-off substances (as the one listed in points 3.6.3. to 3.6.5) and candidates for substitution (category under which these cut-off substances would theoretically be re-approved on the ground of a negligible exposure). In addition, the Chemical Strategy for Sustainability requires "*that consumers products (…) do not contain chemicals that cause cancers (…) affect the reproductive or the endocrine system*"[2].

Reference values and risk mitigation measures are risk-based tools of assessment which, even combined, cannot ensure with full certainty that conditions of uses of a substance exclude contact with humans. Additionally, looking into both implies going further in the risk assessment than what the hazard-based approach, applied to cut-off substances meeting points 3.6.3 to 3.6.5, requires from EFSA. For these reasons, and with regard to the new EU objectives to reduce significantly the use of the more harmful pesticides by 2030, reference values and risk mitigation measures should not be endorsed.

[1] EFSA Guidance Document on clustering and ranking of emissions of active substances of plant protection products and transformation products of these active substances from protected crops (greenhouses and crops grown under cover) to relevant environmental compartments.
[2] Chemicals Strategy for Sustainability. Towards a Toxic-Free Environment, page 10.

2. Negligible exposure to non-target organisms in the environment (point 3.8.2)

Unlike in points 3.6.3, 3.6.4 and 3.6.5 of Annex II, point 3.8.2 does not explicitly define what should be understood as a negligible exposure of non-target organisms to endocrine disrupting substances. However, Articles 4 (2b, 3e), 21 (1) and 44 (1) all stress the importance of protecting non-target species from the use of harmful active substances. Therefore, the statement that was developed above in the context of human exposure should also apply to non-target organisms in line with the One-Health principle. In substance, it means that an exposure should only be regarded as negligible if "*the product is used in **closed systems** or in other conditions **excluding contact with non-target organisms**".*

This integrated approach is most consistent with Regulation (EC) No 1107/2009, as well as the most scientifically relevant in the presence of non-threshold substances such as endocrine disruptors. Acting differently would introduce double standards between humans and non-target organisms and run the risk of a two-speed approach to the work on this technical guideline. This creates concern that environmental exposure could be ignored for substances of high concern, which would go against the EU commitment to perform a "*comprehensive environmental risk assessment by strengthening requirements across legislations*"[3].

Summary

The concept of negligible exposure must be understood according to Annex II of Regulation 1107/2209, which states that substances meeting the cut-off criteria can only remain on the market if the conditions of uses ensure no contacts with humans. To be consistent with the intent of Regulation 1107/2009, we recommend extending this definition to non-target organisms.

If it is not technically possible to completely exclude human contacts, with respect to the conditions of use, then the concept of negligible exposure cannot be used in regulatory decision-making. Reference values or risk mitigation measures are not intended to guarantee the absence of contact and will therefore never do so with certainty. They would rather run the risk to see the concept of negligible exposure being used to derogate[4] from the hazard-based approach of Regulation (EC) No 1107/2009.

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[3] Chemicals Strategy for Sustainability. Towards a Toxic-Free Environment, page 13.
[4] A cut-off substance can only be approved by derogation following Article 4.7 or Article 53 of Regulation (EC) No 1107/2009.