EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Deputy Director General for the food chain

Brussels,
SANCO/E3/BD/bp D(2011)

Dear Ms Geslaine-Lanéelle,

Subject: Cumulative Risk Assessment under Regulation (EC) 396/2005

After receipt of your letter of 15 September 2010, containing 8 elaborate and complicated questions pertaining to the approach intended to be taken by the PPR Panel concerning Cumulative Risk Assessment (CRA) under Regulation (EC) No 396/2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin, the Commission has sought clarification from the Panel, discussed the matter twice at meetings of the Standing Committee on the Food Chain and Animal Health (SCFCAH) with the Member States and EFSA and finally consulted Member States by requesting written comments. In a meeting with Member States' experts on 18 May, a member of the Panel further clarified the questions and a discussion took place in which several Member States presented their position. Taking into account the clarifications, additional written comments[1], Member States' positions and internal consultation in the Commission services, I would like to provide you with responses to the questions, including some observations and comments.

First of all, I would like to express my disappointment at the delay of the whole process. In our letter of 11 July 2006 (D/530735), DG SANCO insisted on the urgency of developing the methodology by EFSA before the review exercise of the existing MRLs (under Article 12 of Regulation (EC) No 396/2005). This timeline (originally September 2009) was not achieved and the review of existing MRLs by EFSA, although also delayed considerably, is now being carried out without taking account of the synergistic and cumulative effects.

I acknowledge the complexity of the issue, which gradually became apparent in the course of the exercise and the fact that EFSA has already carried out much work to tackle the complex issue. EFSA's organisation of a workshop and the production of two reasoned opinions exploring the possibilities of existing methodologies are steps in the right direction.

In the first opinion[2], the Panel limited itself to the impact of dose addition, because response addition and interaction (synergistic effects), were according to the Panel not

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[1] Comments were received from Denmark, Germany, Ireland, France, The Netherlands, Latvia and UK. They are uploaded on circa, meeting section, SCFCAH pesticide residues.

[2] EFSA Journal 2008; 704: 1-84

relevant "for the risk assessment of pesticide residues at the levels occurring in food". From the explanation provided by the representative of the Panel, at the meeting of 18 May, I understand that this view has been abandoned in the light of recent evidence and scientific developments. If this is the case, I would like to know whether this means that the project has to be relaunched or whether the current state of development still stands.

Before I respond to the individual questions I would like to emphasize three points that are important for the Commission with regard to cumulative risk assessment:

(A) Any new methodology must be comprehensible for the general public. Risk communication is a task shared between the Commission, EFSA and Member States. The inclusion of the methodology in the routine risk assessment is strongly supported by the Commission, Council, the European Parliament and consumer and environmental organisations. Therefore, even though the issue is very complex, it has to be elaborated in such a way that the Risk Communicators will be able to explain the methodology to non-scientists.

(B) The new methodology must be comparable to the existing one. In other words, it must be made clear, whether and what the combined effects of several pesticides add to the single current pesticide approach. We should have a final answer to the question: "Did we overlook something when we analysed the risk of single pesticides only?"

(C) The final objective should be the availability of an electronic tool for risk assessment. Such a tool and the input data needed should be freely accessible to risk managers and the general public so that any decision on MRLs can be made transparent.

Finally, I would like to learn about the precise timeframe for the remainder of the project, in particular about when the method will be operational for EFSA and can be implemented in reasoned opinions for MRL setting.

I hope the answers contained in the annex to this letter are helpful for the further carrying out of this important project. I also hope that the results will be compatible with, and can be of use for other projects, such as the EU project concerning aggregate exposure via multiple exposure routes and multiple categories of chemicals.

Yours sincerely,

Ladislav Miko

Encl.: 1

Cc: Mr H. Fontier, Mr L.Mohimont (EFSA)

(SANCO)

Annex:
Responses to individual questions:

1. Adequacy of the Regulatory scenarios.

Further evolution of the thinking of the Panel on this subject was presented on 18 May. Taking this into account, my view is that the MRL-setting scenario is the most relevant, because in the legislation only in the MRL-setting context there is an explicit requirement for cumulative and synergistic effects to be taken into account. I agree that the third scenario does not differ from the first one because each MRL is linked to a GAP. The second, "actual exposure scenario" is also relevant, in particular for evaluating the actual consumer risk based on the results of the Annual EU report on pesticide residues. Concerning the further specification of scenario 1, at the meeting of 18 May, my view is that when adding the background exposure to the exposure resulting from the increased MRL, the contribution to the risk due to the increased MRL should be comparable to the risk currently calculated for MRL risk assessments. Currently this risk is calculated by a deterministic method; therefore it would be logical that the background is also calculated in this way. However, I am open to an alternative methodology, provided that this is illustrated with worked examples.

2. Basis for and establishment of CAGs (Common or Cumulative Assessment Groups) at EU level.

The Commission is in favour of the tiered procedure proposed by the Panel. In the case of absence of information it is certainly not justified to assume that chemicals have no common mechanism of action, especially not when these are chemically related substances. Incidentally, chemically unrelated substances can also have a common mechanism or could have an effect of dose addition on certain endpoints even without a common mechanism (see the Kortenkamp State of the Art Report on Mixture Toxicity[3]). I would appreciate it if you could explain how the Panel will address this.

3. Tiered approach for exposure assessment.

The Commission agrees that for assessment of the actual exposure, probabilistic risk assessment is the most suitable way of estimating probabilities of co-occurring exposure events. Such an assessment would count as the highest tier; however, the Panel is not clear about how the lower tiers are defined.

4. Tiered approach for hazard assessment.

The Commission is in favour of a tiered approach if this saves time and resources. The question is whether Tier 2 is indeed saving time and resources as the starting point of deriving an Acute Reference Dose (ARfD) and Acceptable Daily Intake (ADI) would be the same No Observed Adverse Effect Levels (NOAEL) which are later used in Tier 3. Therefore, I believe that one should aim to move from Tier 1 immediately to Tier 3 and derive the Relative Potency Factor (RPF). The decision to use Benchmark Dose (BMD) or NOAEL has no specific relevance to the discussion on CRA. The decision to move from NOAEL to BMD might be taken in a more general toxicological context; it would

[3] http://ec.europa.eu/environment/chemicals/pdf/report_Mixture%20toxicity.pdf

not be appropriate to proceed with the introduction of this new approach only for the cumulative risk.

5. Risk characterisation

The Commission does not object to the methodology proposed, but it is not made clear why a tiered approach is needed. If the reason is to reduce the workload and speed up the process, the Commission is in favour of the proposed approach.

6. Acute risk and MRL setting scenario: definition of the background exposure for the deterministic assessments.

It is difficult to understand the meaning of background exposure in the context of the MRL-setting scenario. One option could be to focus on the combination of a rare (but not unrealistic) event with a co-occurring event of average frequency. The approach in the triazole opinion[4] using average chronic exposure is not a very bad one, but if one wants to stay in the context of acute exposure, it would be sensible to assume a certain percentile event as the background exposure. Some worked examples should be done with several percentiles, e.g. 5, 10, 25 and 50. This is, of course a rather theoretical approach, and it should be investigated what the real co-occurrence of such rare and average exposure events is in order to validate the method. Concerning the overall level of protection, you indicate that this level is high when using deterministic risk assessment. I have often heard this criticism, but I have never seen this quantified and compared with probabilistic methods. I would encourage you to make such comparison by defining an event used for the deterministic model and estimating the probability of occurrence of such an event on population level over a medium term time period.

7. Monitoring data, handling of non-detect sample

It is in the short term not realistic to use data from Regulation (EC) No 1185/2009 to estimate the contribution of the non-detect samples. It is also questionable whether this would be relevant because residues would, to a large extent, also be present due to uses in third countries for which we are not likely to get the statistics. It might be better to adopt a simplified approach and show the results under certain assumptions e.g. for 50% of the lowest limit of analytical quantification (LOQ) and no residues in case of non-detects, or indicate separately the contribution by the non-detects in the model (cf. PRIMO-model). It should be borne in mind that neither in the current risk assessment is a precise estimation of the contribution by non-detects possible.

8. Residues in drinking water and residues of substances used as veterinary drugs.

Monitoring data on drinking water, veterinary drugs and biocides residues may be limited at EU level, but at national level they should be available. Using the available data it should be possible to correct for the underestimation of these residues. It is important to address this because otherwise it would be too easy to criticise us for only presenting part of the picture.

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[4] EFSA Journal 2009; 7 (9); 1167 [187 pp.].