European Food Safety Authority

Unit on BIOCONTAM

EFSA/CONTAM/2133
Parma, 14 February 2014

Trilateral meeting on perchlorate risk assessment

Trilateral meeting report of the meeting on 12 02 2014, Parma

(Agreed on 26 03 2014)

The below report reflects the common understanding of EFSA, ANSES and BfR of the meeting held on the 12 February 2014. This report is not, and cannot be regarded as, representing the position, the views or the policy of the European Food Safety Authority or of any national or EU Institution, agency or body.

Participants

The list of participants is enclosed (see Annex A)

1. Welcome and introduction to the meeting

The Chair, Diane Benford, welcomed the participants.

Apologies were received from Marco Binaglia.

EFSA gave a presentation highlighting the aim of the meeting, the legal framework and the points for discussion. The ANSES delegation asked EFSA some precisions about the requirements of Article 30. EFSA replied that the minutes of the meeting would be the document fulfilling these requirements, and that they will be published on EFSA's website.

2. Introduction of participants

The participants introduced themselves during a *tour de table*.

3. Adoption of the agenda

The agenda (see Annex B) was adopted without changes.

4. Presentation of the EFSA draft opinion on perchlorate

EFSA presented the draft statement on the risks to public health related to the presence of perchlorate in food, in particular fruits and vegetables (revision 10).

5. Presentation of the BfR perchlorate risk assessment

BfR gave a presentation on perchlorate and chlorate residues in food, addressing exposure pathways and residues in food, chronic and acute dietary exposure assessment and acute and chronic hazard characterisation.

6. Presentation of the ANSES perchlorate risk assessment

ANSES presented the following opinions:

- opinion on health risk related to the concentration of perchlorate in drinking water (July 2011),
- opinion on epidemiological data related to health effects associated with perchlorate exposure via drinking-water in sensitive populations (July 2012),
- opinion related to perchlorate in infant milk and drinking water in France (to be published first trimester 2014).

7. Discussion on the approaches for dietary exposure assessment to perchlorate

Potential sources of occurrence of perchlorate in food

In addition to the list of possible sources presented by EFSA, the ANSES delegation indicated that historical contamination due to the First World War in certain regions is possible (based on a study by the French national geological survey BRGM).

The BfR delegation indicated that illegal use of chlorine disinfectants in food production cannot be excluded. The CONTAM Panel delegation indicated that risk assessments of the CONTAM Panel do not cover illegal use, since otherwise the impression would be given that illegal use is approved.

The ANSES delegation asked EFSA if firework use was considered in the risk assessment. EFSA indicated that the industrial emissions due to the production of ammonium perchlorate used for the manufacturing of fireworks is considered in the opinion but not the perchlorate release during the use of firework, anyhow this would lead only to very local contaminations.

The BfR delegation indicated that there is a need for more information on sources of perchlorate.

The ANSES delegation mentioned that it would be helpful for the conclusion on sources of perchlorate contamination if more data on the occurrence of perchlorate in the environment would be available. BfR agreed and indicated that perchlorate is currently not included in water monitoring programmes in Germany.

Variability factors

The BfR delegation indicated that variability factors account for the residue distribution of single units in composite samples. Variability is not restricted to spray applications and surface distribution. It is observed also for exclusive root uptake and even post-harvest treatments such as dipping. Environment-based factors lead to variable root uptake within one growing site, which is relevant for both pesticides and other substances.

The CONTAM Panel delegation asked to put the variability by root uptake in perspective compared to the variability caused by spraying. The BfR delegation explained that the variability factors that are used for most fruit and vegetables are 3, 5 and 7 and depend on

the commodity. For blended and bulked commodities such as cereal grains or juices no variability factor needs to be taken into account. The factors are in the same range for different treatments. In studies measuring intra-field variability of spray applications, factors of up to 3 have been determined, however no such studies are available for pesticide applications directly on the soil.

The CONTAM Panel delegation underlined that a large dataset was used to calculate exposure and therefore the variability may be adequately covered by the data that are used for the dietary exposure assessment. The BfR delegation replied that the variability observed in the occurrence data is not representative of the unit to unit variability in composite samples; therefore variability factors are needed when composite samples are used and when consumers may be exposed to single commodities with higher residues.

Regarding the use of variability factors, the ANSES delegation indicated that since no acute dietary exposure assessment was carried out by ANSES so far, ANSES still needs to look into this issue.

The CONTAM Panel delegation indicated that variability factors have not been used by the CONTAM Panel for contaminants so far and indicated that the application of variability factors for contaminants that can occur as 'hot spots' and that can cause acute effects would need further consideration by the CONTAM Panel.

Approach for chronic dietary exposure assessment

Both the ANSES and BfR delegations agreed with the approach used by the CONTAM Panel for the chronic dietary exposure assessment.

Additional foods to be considered for the dietary exposure assessment

The ANSES delegation stressed the importance of including drinking water (including bottled water) in the exposure assessment, including the preparation of infant fomula.

The ANSES delegation indicated that the collection of occurrence data on perchlorate in food in France is ongoing.

The ANSES delegation indicated that ANSES has occurrence data on perchlorate in drinking water (including bottled water) and infant formula and is willing to submit the data to EFSA.

In addition to fruit and vegetables, drinking water, infant formula and milk were identified as the most important foods to be included in the risk assessment.

Data gaps

The ANSES delegation indicated that there is a need for data on the type of water that is used to prepare infant formula.

Chlorate

The BfR delegation indicated that both chlorate and perchlorate exhibit widely similar toxicological effects. Therefore, the risk assessment should follow the same lines. Co-occurrence between chlorate and perchlorate has been reported, but no clear link between the two substances was observed. Chlorate might result from pesticide use. The BfR delegation indicated that considering chlorate and perchlorate in the same assessment may be necessary to cover a possible cumulative risk and may lead to an easier conclusion on

the pathways. The European Commission representative indicated that perchlorate has never been authorised as a pesticide, while chlorate has been. He referred to chlorate occurrence data that he received and indicated that it is difficult to conclude that their occurrence is related. The BfR delegation indicated that most likely there is more than one exposure pathway. There might be different pathways for chlorate and perchlorate and some pathways might be relevant for both.

8. Discussion on the approaches for hazard characterisation of perchlorate

General

All delegations agreed that studies in animals are not suitable for human health risk assessment.

Acute toxicity

All delegations agreed that there are no reliable dose-response data to establish an acute reference dose, but that perchlorate has the potential to cause acute effects.

Chronic toxicity

The BfR delegation underlined the limitations of the study by Greer et al. (2002), namely the short exposure period, small number of individuals, and only healthy individuals with sufficient iodide intake were included. Vulnerable subpopulations (pregnant women, foetuses, neonates and young infants) as well as subpopulations with low iodide intake were not considered in this study. Based on the study by Steinmaus et al. from 2010 even with low levels of perchlorate exposure, increases in thyroid stimulating hormone (TSH) levels have been observed in neonates. However, it is unclear to what extent possible effects in neonates are fully covered by the uncertainty factor (UF) of 10. The BfR delegation indicated that for subjects with a sufficient iodide intake, the Provisional Maximum Tolerable Daily Intake (PMTDI) is sufficiently protective, however for neonates with low iodide intake, it is unclear what the correct UF should be. Most of the studies are inconclusive. The BfR is not in the position to evaluate all relevant studies on this topic and therefore does not propose an UF.

The ANSES delegation also stressed the limitation of the study by Greer et al. (2002) and referred to the short observation period, the small number of individuals, only adult healthy volunteers were included which is not representative for vulnerable groups (neonates, foetuses and pregnant women), dietary exposure intake (excluding water-related exposure) was not taken into account and the healthy volunteers selection was not clear. The ANSES delegation also underlined the importance of the iodine status, since in France the iodine status is not adequate for all populations especially among pregnant women. In addition, the uncertainty regarding the perchlorate exposure levels leading to adverse effects in fetus and neonates, the uncertainty regarding cumulative effects with other goitrogenic ions and the non-consistent conclusions drawn from epidemiological studies were taken into consideration. Based on the above mentioned arguments, ANSES followed a protective approach and used the no-observed-effect level (NOEL) of 0.007 mg/kg b.w. per day and an UF of 10.

All delegations agreed that the critical effect for chronic hazard characterisation was thyroid function. There was also agreement that inhibition of iodide uptake is not an adverse effect. All delegations agreed that no data on an adverse effect are available for the risk assessment and that therefore a non-adverse effect was selected as the basis for the risk

assessment. It was agreed that inhibition of iodide uptake could be a precursor effect of the actual adverse effect, namely the effect on the level of thyroid hormones. It was agreed that the study by Greer et al. (2002) is the most appropriate dataset for deriving the point of departure (POD).

The ANSES delegation proposed to link the discussion of the selection of the POD to the UF.

The CONTAM Panel delegation indicated that by using a non-adverse effect, a safety factor is already included in the selection of the POD. A benchmark response (BMR) of 50 % was selected, while even an inhibition of 75 % of the iodide uptake does not lead to changes in thyroid hormones in healthy adults. The ANSES delegation indicated the potential impact at a 50% inhibition of the iodine uptake in neonates is not clear.

The ANSES delegation indicated that when a NOEL is selected, the sensitive population groups are taken into account. A lower 95 % confidence limit for a benchmark response of 50 % extra risk ($BMDL_{50}$) does not take the sensitive populations into account and therefore a higher UF is needed compared to the use of the NOEL as POD. The CONTAM Panel delegation asked ANSES if they could agree with the use of the $BMDL_{50}$ when increasing the UF. ANSES replied that adding an UF would be a way to take into account the sensitive population when using the $BMDL_{50}$ as POD as proposed by EFSA.

An UF to correct for the short term exposure was discussed. It was questioned whether the effect of perchlorate would be cumulative. If this would be the case, an UF for short term duration of the study is needed. The CONTAM Panel delegation also indicated that consideration should be given when applying a default factor of three for the extrapolation from subchronic to chronic studies, since the underpinning database of this factor is derived from animal studies.

The CONTAM Panel delegation also indicated that clinical data are not used in the risk assessment, but no adverse effects are observed on the thyroid hormones in subjects exposed for long periods to much higher doses than the PMTDI used by the CONTAM Panel. It was also indicated that a benchmark dose modelling was done for skin lesions observed in clinical studies and a higher dose than the selected POD was identified.

The ANSES delegation indicated that in neonates the storage of thyroid hormones is very limited.

The CONTAM Panel delegation indicated that the CONTAM Panel will reconsider the UF taking into account the short term duration of the study and whether the UF is sufficient for the vulnerable population groups.

Data gaps

The CONTAM Panel delegation indicated that more data on iodide uptake in neonates and changes in TSH and thyroid hormones are needed following exposure to perchlorate (including controls). This was supported by the other participants. The ANSES delegation indicated that there are currently 2 studies ongoing in France.

Uncertainty assessment

The ANSES delegation questioned why in the draft opinion the CONTAM Panel concluded that the uncertainty is moderate. The CONTAM Panel delegation explained how this conclusion was drawn and indicated that the CONTAM Panel will consider the raised points regarding the uncertainty when finalising the opinion.

9. Closure of the meeting

The Chair of the meeting thanked all participants for their contributions to the fruitful exchange of information and views during the meeting.

Annex A: list of participants distributed before the meeting

TRILATERAL MEETING ON PERCHLORATE RISK ASSESSMENT

12 February 2014

LIST OF PARTICIPANTS

Pierre-Marie Badot	Panel Chemical risk assessment in food (Chair)	**ANSES**
Katleen Baert	BIOCONTAM Unit	**EFSA**
Diane Benford	CONTAM Panel (Chair)	**EFSA**
Marco Binaglia[1]	BIOCONTAM Unit	**EFSA**
Thomas Cartier	Unit Risk Assesment in water	**ANSES**
Franck Foures	Risk Assessment Department - Food Safety (Deputy Director)	**ANSES**
Michel Joyeux	Working Group Risk assessment in water for human consumption (Chair)	**ANSES**
Helle Knutsen	CONTAM Panel	**EFSA**
Ernesto Liebana Criado	BIOCONTAM Unit (Acting Head of Unit)	**EFSA**
Karen Mackay	BIOCONTAM Unit	**EFSA**
Britta Michalski	Unit Residue assessment of pesticides and biocides (Head of Unit)	**BfR**
Jean-Nicolas Ormsby	Risk assessment Department - Environmental health (Deputy Director)	**ANSES**
Rudolf Pfeil	Unit Toxicology of pesticides and biocides (Head of Unit)	**BfR**
Ivonne Rietjens	CONTAM Panel	**EFSA**
Gilles Riviere	Unit Chemical risk assesment in food (Head of Unit)	**ANSES**
Frans Verstraete[2]	Unit Chemical contaminants, pesticides	**EC- DG SANCO**
Christiane Vlemickx	CONTAM Panel	**EFSA**

[1]Apologies were recieved

[2]Observer

Annex B: Agenda distributed before the meeting

Parma, 31 January 2014
EFSA/CONTAM/2121

TRILATERAL MEETING ON PERCHLORATE RISK ASSESSMENT

Meeting date: **12 February 2014**
Venue: **EFSA, Parma**
Meeting Room: **MTG Seat 00/M03**
Starting Hour: **09:00 hrs (CET)**
Finishing Hour: **16:00 hrs (CET)**

Draft Agenda

#	Items	Document Reference/ Comments
1.	Welcome and introduction to the meeting	Chair/EFSA
2.	Introduction of participants	All
3.	Adoption of the agenda	All
4.	Presentation the EFSA draft opinion on perchlorate	EFSA EFSA/CONTAM/2043
5.	Presentation of the BfR perchlorate risk assessment	BfR
6.	Presentation of the ANSES perchlorate risk assessment	ANSES
7.	Discussion on the approaches for dietary exposure assessment to perchlorate	All
8.	Discussion on the approaches for hazard characterisation of perchlorate	All
9.	Final remarks	All
10.	Closure of the meeting	All