Minutes of the third EFSA/ECHA/JRC drafting group meeting on development of Guidance for Endocrine Disruption hazard identification

Held on 20-24 March 2017, Parma

(Agreed on 29 May 2017)

Participants

- **European Chemicals Agency (ECHA)**
  Lepper P.; Andersson N.; Pellizzato F.
- **DG SANTE, European Commission (EC)**
  Fabrizi, L. (Observer)
- **Joint Research Centre (JRC)**
  Munn, S.; Kienzler, A.; Van der Linden, S., Lostia, A.
- **European Food Safety Authority (EFSA):**
  Tarazona J.(Co-chair), Auteri D., Court-Marques D., Kass G. (Co-chair), Schoonjans, R., Arena, M.; Barmaz, S.; Rauch, M.; Serafimova, R.; Terron, A.; Streissl, F.

1. **Welcome and adoption of the agenda**

   The meeting was hosted and chaired by EFSA. The Chair welcomed the participants and a tour de table was initiated. The agenda was adopted without changes, specifying that agenda item 1 will be kept as short as possible; chapter 4 will be discussed before chapter 5 because the participants from the JRC have to leave the meeting on Wednesday.

2. **Common understanding of the proposed criteria**

   The common understanding of the mandate and guidance was recapitulated. The guidance is supposed to serve three purposes:

   1. As specified in the mandate, the Guidance is intended as a regulatory guidance for applicants, Member States and both agencies in the area of biocides and pesticides. As added value, the Guidance can also support other

assessments, e.g. by EFSA or ECHA, requiring the identification of endocrine substances or the risk assessment.

2. The Guidance is intended to be used together with the other regulatory guidance documents applicable to pesticides and biocides, and not in isolation.
3. The guidance will not include recommendations on the data requirements applicable to pesticides and biocides. Nevertheless, once the Guidance is finalised, ECHA and EFSA may prepare specific proposals, in line with the guidance principles, regarding the update of the data requirements for biocides and for pesticides, respectively. However, such recommendations on the update of data requirements are neither part of the guidance document nor part of the guidance drafting task.

3. Chapter 4 of the ED Guidance document

The draft of chapter 4 was presented, commented and partly rephrased by the drafting group. Moreover, it was decided who will further elaborate on certain parts of chapter 4. It was agreed that the template developed by the JRC to summarise the available studies should be used.

4. Chapter 5 of the ED Guidance document

The draft of chapter 5 was presented, commented and partly restructured and rephrased by the drafting group. JRC presented a summary table in form of an Excel-Spread-Sheet. This table was welcomed by the participants and it was proposed to add an example in the GD on how to fill this table with respect to the steps described in Chapter V. JRC will assemble the final table. Drafting groups were formed and the individual steps were further discussed and developed. Actions to finalise the text for each step and work distribution to achieve this were agreed.

5. Discussion on how to conclude

The drafting group discussed the elaboration of the overall conclusion. A preliminary approach was agreed on. Plans to finalise these parts of the guidance have yet to be drafted.

6. Conclusion and discussion of the timelines

The participants discussed the timelines of the drafting process and of the finalisation of the guidance. The first consultation period will be postponed to after Easter due to additional time required to finalise chapters 4 and 5, and the consultation phase was planned to take place from April 18 to May 2. The drafting

work will continue with the planning for finalising the document by addressing the next work packages: harmonising the terminology, preparation of examples, finalization of chapter 4 and 5.

Minutes of the

EFSA/ECHA/JRC ED Guidance drafting group meeting

Held on 8 and 9 December 2016
(Agreed on 23 January 2017)

Participants

ECHA: Andersson N., Lepper P. (Chair of the meeting), Pellizzato F.

EFSA: Auteri M., Court-Marques D., Tarazona J., via Webex: Kass G. (8 Dec. only, morning) and Reinhilde Schoonjans

JRC: Munn S., Van der Linden S. and Grignard E (9 Dec. only, via Webex)

DG Sante: Laura Fabrizi (8 Dec. only, via Webex)

1. Welcome and adoption of the agenda

The meeting was hosted and chaired by ECHA. The Chair welcomed the participants. The agenda was adopted without changes.

2. Discussion of annotated Table of Content (ToC) for inclusion in the outline document

The participants worked together to revise the draft ToC starting from the draft document that had been worked on and developed since the previous face to face meeting by both Agencies and JRC. The participants agreed on the main content of the ToC to be included in the outline document. It was agreed that further editorial amendments to the ToC would be done in written consultation after the face to face meeting.

3. Internal and external consultations

3.1 EFSA/ECHA Consultation group (stakeholder involvement – recruitment process; consultation and documentation thereof)

On ECHA's side the Members of the Endocrine Disruptor Expert Group (EDEG) will be part of the Consultation Group. In order to ensure that experts with expertise in Plant Protection Products (PPP) are appropriately represented in the Advisory Body, EFSA has launched a call for MS experts and will select a number of members representing MS risk assessment organisations. There is also the intention to involve on EFSA's side stakeholder experts from industry and public interest organisations, and potentially academia. In this regard EFSA will consider which recruitment process for these stakeholder experts would be appropriate.

3.2 Information event at the start of public consultation

The participants discussed the possibility to organise a public information event in order to present the draft guidance at the beginning of the public consultation. The event could be organised in form of a Webinar or as a physical event in

Brussels. Some organisational aspects with regard to administrative preparation needs and programme were discussed, a decision on the form of the event however was postponed.

3.3 Public consultation

It was confirmed that the public consultation on the draft guidance will be conducted by both Agencies together (details still to be defined).
The report addressing the comments received during the public consultation will also be jointly prepared and published.

3.4 Workshop with Member States experts

It was agreed that the envisaged workshop with MS experts in ED assessment should take place (shortly) after the end of the public consultation. With this timing, it may be possible to already take main comments received in public consultation into account when discussing and testing together with the MS experts the applicability of the guidance. A report on the outcome of the workshop will be jointly prepared and published.

4. Endorsement procedure for guidance

The participants discussed the endorsement procedure of the guidance. EFSA and ECHA procedures are in this respect different, so it was agreed that there is a need for further discussion with DG SANTE to develop an ad-hoc procedure for endorsement of a common guidance.

5. Timelines

The participants discussed the timelines of the drafting process and of the finalisation of the guidance after the start of the public consultation. Two separate timelines should be included in the outline document for those two major parts of the work. The reason for the split into two periods is that the guidance will undergo public consultation only after there is certainty that the ED criteria will not be changed anymore in the formal endorsement processes of the legislative acts implementing the criteria.

6. Finalisation of the outline document

The participants worked together in order to finalise the content of the draft outline document, based on the outcomes of discussion during the meeting. It was agreed that further suggestions for editorial amendments should be included in the draft by 12 December. Thereafter the document should be finalised for submission to DG SANTE on 16 December.

7. Drafting process

There was a discussion on the internal organisation and timing of the actual drafting work starting in January, including assignment of tasks across Agencies and organisation of the internal commenting rounds.
It was agreed that the drafting of the guidance should start from the core of the guidance, i.e. from the specific sub-sections of section IV (Information sources for ED identification), subsequently followed (or in parallel, as appropriate) by the corresponding sub-sections of section V (Hazard identification strategy for endocrine disrupting properties). Each Agency will in January 2017 commence working on specific sub-sections and prepare first draft text by the end of January, followed by a short period for the other Agencies to comment. For begin of February 2017 a teleconference

of the drafting group is envisaged in order to discuss the comments on the first drafts and how to proceed further with the drafting.

The coordinators of the drafting group will in January 2017 set up a detailed work-plan for developing the first draft Guidance for public consultation, including a detailed time plan for particular steps, milestones, deliverables, drafting-group internal commenting and discussion and consultation of the Consultation group during the drafting process. In addition, a structure of the S-CIRCABC folder for drafting group internal exchange of documents will be developed that is suitable to facilitate and support the drafting process.

Minutes of the kick-off meeting on development of Guidance for Endocrine Disruption hazard identification

Held on 27 October 2016, Parma

(Agreed on 30 November 2016)

Participants

- **European Chemicals Agency (ECHA)**

Andersson N., Lepper P., Pellizzato F.

- **European Commission:**

Munn, S. JRC

Other JRC colleagues followed the discussion by videolink

- **EFSA:**

Auteri M. (PRAS), Court-Marques D. (PRAS), Kass G. (SCER), Tarazona J. (PRAS, chair for this meeting)

Terry S. (RISKCOM) participated in agenda point 5 and 6

Other EFSA colleagues followed the discussion by telelink

1. Welcome and apologies for absence

EFSA hosted and chaired the meeting. The Chair welcomed the participants.

2. Adoption of agenda

The agenda was adopted without changes.

3. Topics for discussion

1.1. Table of Content for the scoping paper

Following an introductory discussion, the following draft table of content for the scoping paper was agreed. This ToC may be modified and adapted as needed.

PROVISIONAL DRAFT TABLE OF CONTENT FOR THE SCOPING PAPER

i. Introduction
ii. Proposed Table of Content for the guidance document
iii. Workplan, timelines, milestones and task distribution
iv. Procedures for participation and consultation with MSs
v. Procedures for consultation with other stakeholders
vi. Procedures for adoption of draft for consultation and final guidance
vii. Template for the guidance document
viii. Final remarks

1.2. Brainstorming on scope of the guidance and elements to be included

During the brainstorming, the following issues were agreed

i. Definitions, in principle no need for development of new definitions is anticipated. It presumably will be possible to draw on existing ones.

ii. The guidance should focus on the data and information needed for the ED hazard identification rather than making an attempt to build the assessment exclusively on the current data requirements for pesticides or biocides. It should indicate the minimum essential information needed to allow a conclusion that there is currently no indication that the substance assessed would be an ED in accordance with the criteria. The assessment approach should be holistically taking available toxicological or ecotoxicological information into account and identify indicators which would trigger further investigation across the human health or environmental domains if indications are seen in one of the domains. It further should provide guidance and criteria for the identification of further information and testing needs in order to close identified data gaps.

iii. Regarding the groups of (non-target) organisms to be considered in the guidance, it was agreed that, although endocrine effects are relevant and have been reported in different invertebrate groups, the coverage for the guidance should be limited to vertebrates, including mammals, fish, birds, amphibians and reptiles. Main reason for this limitation is the short timeline provided by the mandate for drafting. For the amphibian and reptile vertebrate groups input may be obtained from the current EFSA PPR Panel WG.

iv. With regard to population relevance of adverse effects it was discussed that generically the nature of the adverse effect(s) observed could be considered for this purpose. Any assessment beyond this point would be inadequate for ED identification as it would require the consideration of specific conditions of use. Specific exposure and hence population relevance of the specific degree of adversity of the effect seen might however differ between uses of the same substance for

instance as pesticide, biocide or industrial chemical, which consequently could lead to inconsistency in ED identification.

v. It was proposed that the guidance couldoffer two different starting points for the ED identification to ensure compatibility with the available information for different substances. One approach would consider starting the assessment with apical studies indicative for ED effects and would set out how to assess if indeed an endocrine mechanism would be the cause for the adverse effect seen; the second approach would consider starting the assessment with ED relevant mechanistic information and set out how to investigate whether the observed endocrine activity would result in adverse effects in intact organisms.

vi. A key issue regarding the assessment of adverse effects is to describe, for the endpoints measured in standard test guidelines, which apical effects could be considered as diagnostic of ED effects and which could be considered as indicative for ED mechanisms, i.e. possibly but not exclusively linked to ED mechanisms, and those that in principle are not related to ED mechanisms. These descriptions will be based on the OECD 150 guidance document, updated with additional information sources and considering the JRC methodology. In this context the currently ongoing revision of OECD GD 150 needs to be taken into account as well as the results of the workshop on thyroidal ED effects, which will take place in March 2017.

vii. Approaches on how to determine further testing needs in case of inconclusive assessments/data should to the extent possible be part of the guidance.

viii. Case studies: Although the inclusion of case studies in a guidance document could be a useful tool, it was considered not feasible, due to the short timelines, to produce full case examples supporting the guidance. Instead, generic examples based on case studies but not indicating specific chemicals, are envisaged to be included. The assessments by the ECHA ED EG, the ED assessments in the EFSA conclusions and the screenings conducted according to the JRC methodology will be used in addition to other sources for compiling these generic examples.

ix. It was considered that specific recommendations for updating the data requirements for pesticides and biocides could be collected during the work on this guidance, but would not be part of the guidance. (The recommendations may be compiled in a different document prepared jointly by the agencies. Such activity would however be a separate task beyond the guidance drafting mandate.)

1.3. Draft table of content for the guidance document

During the discussion, the following first preliminary draft for the Table of Content of the guidance document was agreed; this draft will be updated during the development of the scoping paper as needed.

1. Introduction and Regulatory background

2. Scope
3. Definitions and general issues including reference to other guidances
4. Information sources for ED identification
    a. Guideline tests for identification of ED relevant effects
        i. Ecotoxicology
        ii. Human health
    b. Mechanistic information
        i. Standard tests (test guidelines, lists and relevance)
        ii. Non-standard tests (protocols)
    c. (Q)SAR and Read across approaches
    d. Scientific literature (through systematic review)
5. Assessment elements for weight of evidence determination
    a. Consistency, etc.
    b. Secondary effects
    c. Biological plausibility
    d. Human relevance
    e. Population relevance
    f. Limit dose
    g. Weight of evidence
6. Hazard identification strategy (holistic: eco and human-using decision tree and identification of additional information needs; combining #4 and #5)
    a. Identification of Concern - starting with
        i. Apical studies (adverse effects) including mammalian, fish, amphibian/reptiles, birds
        ii. Mechanistic information
7. How to conclude (i.e. meeting the criteria, combining #5 and #6) – 3 elements (i.e. endocrine MoA, adverse effect and biologically plausible link)
8. Recommendations (general recommendations, as necessary).
9. References

1.4. Procedural issues

The following specific processes were discussed and will be the bases for preparing the drafts on the proposed procedure. The involvement of SANTE is essential and a trilateral will be organised for getting SANTE input.

A. Drafting group and additional support for drafting

Due to the short timelines and the different approaches established by ECHA and EFSA for drafting scientific guidance documents an *ad-hoc* approach has been agreed.

The drafting group is composed by staff from ECHA, EFSA and JRC, SANTE is involved as observer. The drafting group will compile the relevant available information, draft the guidance text and identify needs for

additional information or for specific scientific advice. After the public consultation, the drafting group will consider the comments and update the draft as needed.

The drafting group may be supported by additional staff members providing support for specific points.

If needed, the drafting group will prepare questions or requests to be answered by existing bodies in ECHA and EFSA, such as the ECHA ED EG or the EFSA SC, Scientific Committee and Panels and their WGs.

B. Template for the guidance: A single document with ECHA and EFSA logos produced and published by both agencies was proposed. As EFSA has more constrains due to the involvement of an external publisher for the EFSA Journal, EFSA proposed to use the template for EFSA guidance documents as starting point and adapted to cover ECHA needs. ECHA will consider this proposal.

C. Involvement of MS experts through an Advisory Body or "Sounding Board". Alternatives and proposals for creating this advisory body were discussed.

POSTMEETIG NOTE: After the meeting, ECHA has indicated that they will use the ECHA ED EG and no additional nomination is needed. EFSA will proceed with a call for nomination for MS experts to cover expertise on pesticides. The experts proposed by ECHA and EFSA will be merged in a single advisory group. No physical meetings are anticipated for this advisory group. The consultations will be agreed by the drafting group. Further details to be discussed.

D. Involvement of other stakeholders.
    - Considering the short timelines, a public consultation of the final draft was considered the only feasible option.

E. Public and Targeted consultations
    - Public consultation: It was agreed to envisage running one single public consultation by ECHA or EFSA, the selection would be done after comparing the tools available in each agency for collecting and compiling the comments. The other agency would include a link to the public consultation.

      Targeted consultation with MSs. It has been discussed and considered pertinent to organize during the public consultation a workshop with MSs experts for testing the applicability of the draft guidance document using real case studies prepared from the updated screening assessment, EFSA conclusions and ECHA ED EG specific discussions. Ideally, the case studies will be on a.s. used as pesticide and biocide, which could be retrieved from the screening and updated to consider additional information and assessments.

The comments and proposals provided at the workshop will be considered together with the comments received during the public consultation for revision and enhancement of the draft guidance. EFSA has already experience from dedicated PSN meetings for discussing draft documents as part of the PSN mandate, the details will be further elaborated.

F. Approval procedure (for draft for public consultation and for final guidance)

- The approval of the draft for public consultation is similar (internal decision by the agency management). Once the draft group, to which DG SANTE is observer, agrees on the content, the final draft will be sent to the management of both agencies for approval for public consultation. Any proposal for modification will be discussed with the other agency and only agreed changes will be incorporated.
- The procedure for approval of the final document and for the consultation with risk managers for endorsement as mandatory regulatory guidance is very different for ECHA and EFSA guidance. ECHA organizes a consultation with CARACAL and risk managers before the formal approval and once approved by ECHA becomes mandatory. EFSA approves the document as EFSA outcome, and then SANTE organizes the consultation with risk managers in the PAFF Committee for their endorsement as regulatory guidance. The group considered that a consultation with SANTE is needed before moving forward on this procedural issue.

1.5. Communication alignment

ECHA and EFSA may collect feedback from MSs and other stakeholders using their own channels, e.g. the ECHA ED Expert Group and the EFSA peer-review expert meetings and Pesticides Steering Network. EFSA organized a joint Tox-Ecotox peer-review meeting and the input from MSs was considered, and the proposals will be compiled with additional feedback received from MSs. The proposals will be taken into due consideration.

Due to the short deadlines, a consultation process with MSs of the draft outline paper is not feasible; obviously the same applies to other stakeholders. For transparency, it was proposed to discuss with DG SANTE the possibility of publishing the outline paper once it is finalized and submitted to COM.

Full alignment between SANTE, ECHA and EFSA regarding communication activities is envisaged and preliminary discussions are on-going, JRC will be informed. Four communication events have been identified:

a) Acceptance of the mandate
b) Publication of the Scoping paper
c) Publication of the Draft guidance for consultation
d) Publication of the final guidance including information on how the comments have been addressed

4. Next steps and tasks distribution

A. EFSA will draft the minutes of the meeting

B. ECHA will organize a telemeeting of the drafting group in November

C. ECHA will organize and chair the next physical meeting in Helsinki (8 and 9 December)