SCIENTIFIC COMMITTEE AND EMERGING RISKS UNIT

MINUTES OF THE 11th cross cutting EFSA WG on Uncertainty (WGU)

Teleconference, 14 – 15 December 2020 (2.00-6.00 pm on 14 December; 9.30-12.30 am and 2.00-4.00 pm on 15 December 2020)

(Agreed on 21 December 2020)

Participants

- Panel and external experts:

Dominique Bicout, Andrew Hart, Konstantinos Koutsoumanis, Maarten Nauta, Giuseppe Ru, Heather Wallace, Salomon Sand, Ullrika Sahlin, Wopke van der Werf. Julio Alvarez and Peter Craig.

- Hearing Experts[1]:

Not Applicable

- European Commission and/or Member States representatives:

Not Applicable

- EFSA:

SCER unit : Caroline Merten (chair)

AMU unit : Laura Martino, Olaf Mosbach – Schulz, Fulvio Barizzone (day 2)

1. Welcome and apologies for absence

The Chair welcomed the participants. Apologies were received from Federica Barrucci, Laura Ciccolallo and Elisa Aiassa by the AMU unit.

[1] As defined in Article 17 of the Decision of the Executive Director concerning the selection of members of the Scientific Committee, the Scientific Panels, and the selection of external experts to assist EFSA with its scientific work: http://www.efsa.europa.eu/en/keydocs/docs/expertselection.pdf.

2. Adoption of agenda

The agenda was adopted without changes.

3. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[2] and the Decision of the Executive Director on Competing Interest Management[3], EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process.

4. Support to the implementation of the uncertainty guidance document in ongoing EFSA mandates in 2020

The WG discussed the following matters:

- Feedback by **FAF unit** on the implementation of uncertainty analysis in the revised scientific guidance for the preparation of applications on smoke flavouring primary products. The WG discussed the lessons learnt for future implementations and discussion when and how to do the calibration of the standardised procedure. This was the first time the uncertainty guidance document (UGD) has been implemented in a sectorial guidance document (GD) for applicants in a regulated product. Standard uncertainties have been identified and treated. Ideally a formal "calibration" of the standardised procedure for risk assessment should have been done. Lesson learnt included that it takes time to get used to thinking on uncertainty (especially as integral of scientific assessments), some new experts found it difficult to see the added value of uncertainty analysis and some other experts experienced that the task to identify uncertainties improved the quality of the work. It was found challenging to agree on a level of detail required for describing the standardised procedure as this was seen as a guidance document directed to applicants who will not do the assessment themselves. The lack of examples of implementations (including calibrations) of standardised procedures made it difficult to plan and motivate the implementation. Therefore, it would be very helpful for future implementation of the UGD in sectorial GDs to either create an example of a calibration e.g. by implementing the uncertainty analysis (UA) on a real assessment on smoke flavourings – to support the smoke flavouring WG and to clarify the added value, or to perform a fictive calibration. However, the first option is less useful because it is not a calibration of a standard procedure (which is done on a class of products or assessment problems). Doing a UA on a specific smoke flavouring would illustrate section 3 of the GD (UA for individual standardised assessments) and not of section 6 (calibration of a standardised procedure/GD). Hence, an example of uncertainty analysis on a specific risk assessment could be helpful to FAF for future assessment of individual flavourings, but would not provide an example of calibration. Therefore, the ideal is to do a real calibration. It would be necessary to evaluate the approach taken in this sectorial guidance for future implementation of standard procedures and clarify when and how to do calibration in the process of developing or updating new sectorial GDs. For the least the uncertainty analysis requires a description of the standard procedure. In the planning phase of the work it should be ensured that there are resources to do the calibration

[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[3] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

and be made sure that UA is presented as an integral part of assessments of regulated products. Care needs to be given on how to communicate the uncertainty from a standard procedure. The calibration of the standard procedure should ideally be reported, and the level of certainty needed should at least be documented. There are specific recommendations about the communication of uncertainty from a standard procedure in the guidance.
The uncertainty WG agreed that in order to convince the relevant WG in charge of the development of the sectorial GD to do a calibration exercise it needs to be clear if and how to publish the results from the calibration exercise. The WG members exchanged different views on the word "calibration" as for some of the experts there would need to be a reference procedure against which it could be calibrated and therefore, the chosen terminology may be confusing. Calibration of a standard procedure is a performance requirement to ensure that the method chosen to do risk assessment is judged sufficiently certain to perform as required and is not either over- or under-protective. The uncertainty WG agrees to consider changing this terminology in the future when the UGD would be revised. The WG also agreed that fictive examples are not really helpful as too artificial also in order to get an agreement from the risk managers on the protection goal. Instead an example could be provided from the default value setting to construct a conceptual example to demonstrate the necessity to run a calibration exercise and also the need to have feedback from the risk manager. This example could be presented to the SC for a discussion on the implementation of the UGD in sectorial GDs. The ideal case would be to run a first calibration before the public consultation and if the risk assessment method would be changed due to the feedback from the PC process than, if necessary, another calibration exercise would be needed again. The WG discussed also the feedback relating to uncertainty that was received in the public consultation on the draft smoke flavours guidance.

- Feedback by **PREV unit**: The WG discussed an update on the uncertainty analysis for the Scientific Opinion of the PPR Panel on Developing Integrated Approaches to Testing and Assessment (IATA) on developmental neurotoxicity (DNT) (see uncertainty WG minutes 10 March 2020). The current discussion focused on the stressor based AOP on developmental neurotoxicity: case study on deltamethrin. The uncertainty in the evidence was assessed in a structured way by using the OHAT/NTP tool. A parallel approach was used across study design and the appraisal was done by endpoint. Focus was on risk of bias (RoB) assessment (=internal validity) and it differentiates between a RoB related to poor reporting and a RoB related to methodological quality. The method for screening of molecular initiating event or key events (KE) and adverse outcomes for putative AOP was presented. It involved assessing the evidence and a set of pre-defined set of uncertainties (uncertainty tables) tailored by lines of evidence (invitro, in-vivo, human) The judgement on the possible causal association between deltamethrin and KEs/endpoints was expressed as a subjective probability (below/above 0.66). The concentration/dose triggering the association was also elicited by the experts and expressed either as range (with the assumption of uniform distribution) or as a full probability distribution. The putative AOP network structure was based on expert judgement. A Bayesian network (BN) model was constructed and explained. The outcomes of the BN allow to quantify the strength of the relationship among KEs (by providing a conditional probability distribution), to predict the activation/occurrence of the KEs/AO under exposure to compound X (by providing a marginal probability distribution) and to quantify certainty that all events occur concurrently (by providing a joint probability distribution). Three criteria were used in AOP for assessing KERs: (1) biological plausibility, (2) essentiality and (3) empirical evidence. An influence analysis was done to identify the most influential MIEs/KE on the probability of the AO to occur.
  It was clarified to the WG uncertainty that initially Bayesian network analysis was not described in detail in the UGD partly because it is a special case of Bayesian inference, and partly because it was intended to be added to the weight of evidence GD. However, as the WoE GD does not explain the methods more details on BN should be added to a revised UGD in addition to the

related references that are currently included. It was clarified that all nodes in the AOP BN are binary (I.e. BN is a Bayesian Belief Network). Consequently, the subjective probabilities express pure uncertainty. It was clarified that the model took into account concentration/dose response curve for key events and their concordance across KEs as this was one the criteria (empirical evidence) considered in a narrative way when evaluating the Key Event Relationships. Further it was clarified that despite that the method and the process being quite complex and sophisticated the panel experts became gradually familiar with it. The next steps include a submission of the AOP to OECD and the approach would be to start from the main AOP in the AOP-network, AOP 1 which can also be described as a Bayesian network although a very simple one.

- Feedback by **NUTRI unit**: Update on uncertainty analysis and evidence integration in the assessment of the upper level for sugar intake (please see uncertainty WG minutes 14 July). Current discussion touched upon the final rating of the body of evidence for hazard identification. To establish a final level of certainty in a causal relationship the OHAT NTP approach was adapted. In that approach criteria are used to either downgrade or upgrade the confidence in the body of evidence. Among the adaptations of the approach, the qualitative categories used to grade the certainty in the evidence were turned into approximate probability ranges. It was time intensive to adapt the criteria to fit better to the need of this assessment. A lot of discussion was held on precision, which level of precision is sufficient and which is too large as the threshold set by the OHAT approach did not work for the Nutri WG. Often it was difficult to distinguish between wide confidence intervals due to inconsistency and those due to imprecision, which leads to the question of whether to downgrade once or twice. In most cases, a single downgrade for one of these domains is sufficient. Thus, in most cases where the body of evidence is downgraded for inconsistency in the direction of effect, OHAT will not further downgrade for imprecision. However, it was considered appropriate to downgrade twice if studies are both very inconsistent and imprecise. It was clarified to the uncertainty WG that the hazard characterisation part has not started yet. The mandate has a deadline for end of 2021. It was agreed that not many good examples on quantification of weight of evidence and integration from different lines of evidence are available and that this is an important recommendation for future revisions of the UGD. The uncertainty experts will provide further feedback on how to tackle the challenge on imprecision.

- Feedback by **CONTAM panel** on sub WG uncertainty. The uncertainty WG discussed an update on the prioritisation work on uncertainty. Currently the CONTAM sub WG uncertainty has developed 2 tables of uncertainties that are commonly found in CONTAM opinions, one on exposure and one on hazard identification/characterisation. The challenge is how to make the tables user-friendly and practical to be used for future RA. An excel tool based on the tables is in preparation for the CONTAM WG meeting in January 2021. The uncertainties were then prioritised by evaluating their possible impact based on past opinions. The aim is to start using the tables in the upcoming BFRs opinions. Remaining follow ups include fine-tuning the table for the hazard side by distinguishing the narrative uncertainties from the non-narrative ones. It was clarified that the prioritization is not intended to exclude any uncertainties, but the aim is to separate those for which individually a quantitative method is needed against those ones to quantify collectively.
  Possible next steps for the WG uncertainty is to support the CONTAM WGs when they will start using the tables and may need help in quantifying individual uncertainties. This support could also be suggested to other WGs having an impact on CONTAM work such as the BMD WG or the TTC approach. In addition, the WG uncertainty could also develop a list of methods on how to quantify the list of commonly encountered uncertainties.

- Feedback by **AHAW panel** on uncertainty. Two mandates were discussed with the uncertainty WG. The first one was on the assessment of control measures for Animal Health Law Category

A diseases. In total, measures applying to 14 diseases must be reviewed. 3 ToRs need to be addressed for each of the disease. At the beginning five cat. A diseases were targeted. For ToR 1 and 2 several scenarios were developed: 21 scenarios for ToR 1 on the sampling procedures and 7 scenarios for ToR 2 on the monitoring period. Possible sources of uncertainty were identified in relation with input data and methodology. However, due to extremely tight schedule, quantification of the uncertainty was deemed non feasible and therefore sources of uncertainties are listed and left non quantified. When possible, the direction of their impact was mentioned in qualitative ways.
The uncertainty WG argued that from the indication of the impact of the uncertainty on the assessment the experts seem to have a clear idea about uncertainty. However, without a clear indication of the magnitude of the impact of uncertainty it can be either way and it's not particularly helpful. There is an implicit judgement made that there is a 50 % of chance that the impact is going into either direction. What is meant by "sufficient "? This challenge relates closely to the challenges discussed on the qualitative mandate from BIOHAZ (see point 5 below). It would not cost so much extra effort to attach a probability judgement to the direction of the impact otherwise there remains the issue with implicit judgements. One could agree on a scientific criterion such as a single threshold of concern e.g. 80 % to agree on what is meant by "sufficient" and then there is no need to add the probability bound multiple times. A possible follow up could be a discussion with the AHAW panel on how to implement these mandates in the future along these lines with the time constraints. What could be an objective way of choosing the threshold? As there is an implicit judgment in the conclusion a round table at AHAW panel on which thresholds would be "sufficient" for them could be done to agree on a panel judgement.

The second AHAW mandate was on listing and categorisation of transmissible animal diseases caused by bacteria resistant to antimicrobials, in the framework of the Animal Health Law. The uncertainty WG discussed in more detail the assessment plan for related ToR 2: Summarize the situation in the EU in terms of the actual or potential impact on animal health of the most relevant bacteria in the EU, indicating those for which sufficient data exists and those for which data is not sufficient. EU relevance is to be understood on the basis of practical considerations, such as actual presence in the EU or presence elsewhere but in animal species, age groups or production systems which are widely used in the EU, or similar elements. A 2 steps approach is proposed: First to identify "most relevant bacteria in the EU" and second, for "relevant" bacteria, establish actual or potential impact on animal health. The uncertainty WG discussed how to perform uncertainty analysis in the first step. For the first step, the AHAW WG will consider evidence of EU relevance (non-anecdotal) reports of AMR bacteria presence in the EU or that are present elsewhere in settings/ production systems highly similar to those in the EU. Two options were suggested to the AHAW WG: option 1: to define a yes/no question(s) to be answered (with certainty) based on the same evidence; option 2: to rank pathogens in terms of EU relevance based on presence/prevalence on a scale from 0 to 10 (0=non -relevant) describing along with the score for each pathogen clearly the rationale leading to the score each expert provided. The aim is to rank the AMR pathogens and select them by consensus. The second option seemed currently preferred by AHAW WG. The uncertainty WG discussed how to quantify uncertainty in the assessment of relevance (certainty regarding the non - inclusion of the excluded pathogens? About the included ones? As a whole or individually?). The uncertainty WG made several suggestions/comments to revise the proposed options: e.g. if option 2 was to be chosen and a qualitative scale is introduced it would be difficult to go back to a quantitative assessment at a later stage. In option 1, prevalence is used as a proxy for relevance. In both options, relevance is not well defined and easily understood. Experts should agree on the criteria to define relevance (including prevalence and impact). If they are unable to do this, then the meaning of their judgement's will be unclear, different WG members may consider different factors, and the same rating will have different meaning for different WG

members. In any case experts should provide their rationale for their respective judgements on option 1 or 2. Once the question is well enough defined the experts could express their judgment on the ranking in different ways. More options will be provided by the uncertainty WG experts to support this mandate. It was added that there is a definition for relevance for animal welfare with a clearly defined proportion etc, but the weak point is the impact definition. Another related ranking assessment from AHAW was shared where colour codes give an indication on the quantification of uncertainty. This approach will need to be discussed in more detail at another WG uncertainty.

5. Methodological development across units

The WG discussed the following matters:

- Structured discussion on examples of BIOHAZ TORS on **qualitative mandates** and how to implement the uncertainty GD in these. The WG discussed the reasons why the UGD recommends that assessors should 'always try' to quantify overall uncertainty. The language used in the ToRs to specify what type of assessment is requested was analysed. An analysis of the wording in a selected list of Biohaz "qualitive ToRs" divided them into 3 categories and indicates that nothing precludes quantification of uncertainty as in the majority of cases the ToRs requires EFSA to provide scientific assessments or conclusions likely to influence risk management. Therefore, UA is relevant, and assessors should try to quantify uncertainty. It was then discussed whether quantification of uncertainty was feasible for the Panel's conclusions on these ToRs. To this end a review of conclusions in the published opinions was shown and discussed if quantification of uncertainty was feasible for these conclusions. The wording in the selected opinions includes qualitative expressions of the level of certainty of several conclusions and /or on risk and risk reduction options. Rigour and clarity could be improved by using terms from EFSA's approximate probability scale. Varying strength of evidence could be expressed with more rigour and clarity using terms from EFSA's approximate probability scale. In some areas of EFSA's work, legislation or risk managers require 'firm' conclusions, without probabilities. This can be accommodated without loss of rigour or transparency by defining what level of certainty (probability) is required for each type of conclusion. The WG discussed the following questions: Does the nature of the evidence or assessment method preclude quantification of overall uncertainty? If EFSA is able to offer a scientific conclusion it is always better to express it using well-defined language – for both the conclusion and its degree of certainty. Does quantifying overall uncertainty require more time/resources? With a little practice, it will require no more time or resources to use defined terms from the approximate probability scale. Being quantitative does not always require formal elicitation – this is an option to be used when appropriate. Quantification expression will improve rigour and clarity even when conducted as informally as current qualitative expressions. What other challenges or concerns are hindering quantification of uncertainty such as differing concepts of probability and its use, or due to the distinction between epistemic and aleatory uncertainty? The uncertainty WG discussed several options to replace the qualitative wording with quantitative expressions of uncertainty. The WG agreed that if one can express the level of likelihood in words one might as well use an explicit probability scale with defined meanings for the verbal expressions of certainty. This will make it clearer what a WG or panel really means when it uses words like "likely", "probably" etc., and it should be clear to the risk manager, NGOs, industry, and all the rest of EFSA stakeholders what is meant with these words. The main advantage of implementing this is that it raises the level of clarity and reduces potential misinterpretation. The issue is that some of the BIOHAZ conclusion comprises multiple bullets and to use probability terms for all of them would be unreasonable as some bullets refer

to the ToRs and others to the reasoning and evidence. Therefore, it would be good to separate the bullets on conclusions and use terms from the approximate probability scale for those only. AHAW and CONTAM uncertainty WG members reported similar challenges in their respective conclusion's sections in the opinions. May be a separate section first on the reasoning and evidence that lead to the conclusions or separate sections on concluding remarks and then conclusions would be a way to address this. Among challenges reported by uncertainty WG members why quantification may be hindered were: some of the adjectives used in the conclusion refer to variability and frequency and to express and report related uncertainty quantitatively is challenging for some experts; some experts are less comfortable becoming more quantitative and numerical, others are more reluctant to provide numbers without a formal process such as EKE as they accept that from data one can derive a confidence interval, but are more reluctant to give a number based on expert judgement. Sometimes experts perceive that the uncertainty does not add much added value to strengthen the conclusion. And it remains to be verified if some of these more quantitative expressions are necessary for the risk managers to inform their decision making. The uncertainty WG agreed to present this topic at an upcoming BIOHAZ, AHAW and CONTAM plenary in 2021 by highlighting all the terms used in conclusions in a vaguer way and provide an alternative that could work to improve clarity.

- Lessons learnt from **virtual EKE**. The uncertainty WG was presented with an overview of the main lessons learnt from passing from physical EKEs to virtual ones due to the ongoing COVID 19 pandemic. The regular EKE using the Sheffield method included an a priori review of the evidence dossier followed by a physical session where an introductory training on the methodology was given, the question and evidence dossier discussed and clarified, individual judgements are given followed by a group discussion and consensus. The impact of doing a virtual EKE was a mixed approach of Delphi and Sheffield where first a virtual group meeting was organized to introduce the group and the method and train the group on the methodology, followed by individual virtual sessions to review the evidence dossier and the individual lines of evidence with the ultimate aim to have the dossier updated by all the experts, followed by a Delphi round where written individual judgements are collected and results are presented. In a second virtual group meeting results are discussed to find a consensus judgement. The lessons learnt are: "Conceptual models" are difficult to develop during virtual sessions. Therefore, individual sessions are helpful to "brainstorm" on possible "lines of evidence", facilitator should guide on the use of "quantitative evidence", exchange should be done in written form as "huge evidence dossiers" and the group sessions are used for "Review". "Uncertainty thinking" is not common for "external experts". Therefore "Low-High-Scenarios" are needed to support the experts, judgements should be "guided carefully" by using a stepwise approach, the group discussions should be "carefully prepared" and the final session should be long enough. In summary: The process needs much longer time, the need of written supporting material is huge, there is the risk to be managed to mix roles "Experts vs. Facilitator" and a strong motivation of the experts is needed, but virtual EKE session with "external" experts are feasible if parts of the Sheffield method are replaced by individual interviews, written procedure and an extended evidence dossier.
  The uncertainty WG discussed the risk of introducing potential new bias or anchoring effects by introducing new approaches in the expert elicitations on their judgments. Further, similarities and differences of the revised protocol in comparison to the IDEA protocol were discussed. Further lessons have been learned from other virtual EKEs in the past year (e.g. the cumulative risk assessment with PREV and an EFSA EKE workshop on GM maize and butterflies), which may be discussed at future meetings of this WG.

6. Any Other Business

- EKE GD revision in 2021: The uncertainty WG was informed that a dedicated session on the revision needs for the 2014 EKE GD will be held at the upcoming SC plenary on 17 -18 February 2021. Inputs are sought on lessons learnt and suggestions for revisions to give the perspective from WG uncertainty.
- Workshop with Risk Managers in autumn 2021: It was noted that preparations for this will start in early 2021, including contacting any key external speakers well in advance.

The dates for the future WG meetings in 2021 are:

- **12th WG uncertainty** 4- 6 hours Teleconference (09.30 – 12.30 and from 2-5 pm) on 29th January 2021
- **13th WG uncertainty** 4-6 hours Teleconference (09.30 – 12.30 and from 2-5 pm) on 8th March 2021;
- **14th WG uncertainty** 4-6 hours Teleconference (09.30 – 12.30 and from 2-5 pm) on 27th April 2021
- **15th WG uncertainty** 4-6 hours Teleconference (09.30 – 12.30 and from 2-5 pm) on 9th June 2021
- **16th WG uncertainty** 4-6 hours Teleconference (09.30 – 12.30 and from 2-5 pm) on 20th July;
- **17th WG uncertainty** 4-6 hours Teleconference (09.30 – 12.30 and from 2-5 pm) on 5th October 2021
- **18th WG uncertainty** 4-6 hours Teleconference (09.30 – 12.30 and from 2-5 pm) on 22nd November 2021

SCIENTIFIC COMMITTEE AND EMERGING RISKS UNIT

MINUTES OF THE 10th cross cutting EFSA WG on Uncertainty (WGU)

Teleconference, 15 October 2020 (02.00 – 05.00 pm)

(Agreed on 23 October 2020)

Participants

- Panel and external experts:

Dominique Bicout, Andrew Hart, Konstantinos Koutsoumanis, Maarten Nauta, Giuseppe Ru, Heather Wallace, Salomon Sand, Ullrika Sahlin, Julio Alvarez and Peter Craig.

- Hearing Experts[1]:

Not Applicable

- European Commission and/or Member States representatives:

Not Applicable

- EFSA:

SCER unit : Caroline Merten (chair)

AMU unit

Welcome and apologies for absence

The Chair welcomed the participants. Apologies were received from Federica Barrucci, Laura Martino, Olaf Mosbach – Schulz, Fulvio Barizzone, Laura Ciccolallo and Elisa Aissa by the AMU unit and by Wopke van der Werf.

1. Adoption of agenda

The agenda was adopted without changes.

[1] As defined in Article 17 of the Decision of the Executive Director concerning the selection of members of the Scientific Committee, the Scientific Panels, and the selection of external experts to assist EFSA with its scientific work: http://www.efsa.europa.eu/en/keydocs/docs/expertselection.pdf.

2. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[2] and the Decision of the Executive Director on Competing Interest Management[3], EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process.

3. Support to the implementation of the uncertainty guidance document in ongoing EFSA mandates in 2020

The WG discussed the following matters:

- Post adoption feedback from the **BIOHAZ panel** on the opinion on the BSE risk associated with collagen and gelatine as ingredients in feed separating uncertainty and variability. Two approaches were applied subsequently: in the first part a probabilistic model was used to estimate the BSE infectivity load; in the second part a subjective quantitative assessment was used to quantify the risks associated with three pathways associated with the use of ruminant collagen/gelatine (C&G), either produced from animals fit for human consumption or from ABP materials, in feed intended for non-ruminant animals, including aquaculture animals. Two separate uncertainty tables were prepared where source, cause, impact on the conclusions were considered with the first table summarizing sources related to the assumptions and factors included in the model and the second table summarizing other sources of uncertainty not related to the model outcomes. This discussion was a follow up with the WG uncertainty on their previous discussion on how to separate uncertainty and variability in the quantitative part. It was clarified to the WG that every probability distribution shown in the model results quantified the uncertainty about the model parameter. Further it was reminded to the WG that the sensitivity analysis was done on uncertainty alone as the variability was found to be negligible. The WG brainstormed about possible standardised methods to separate uncertainty and variability while doing a sensitivity analysis. Experiences have been gained and potential case studies would be good to share with the WG for a technical discussion.

- Feedback from the **CONTAM panel** on ongoing and planned work of implementing the uncertainty guidance document in their opinions. A group of CONTAM panel experts supported by experts from the uncertainty WG developed a risk assessment process roadmap and compiled a list of common uncertainties extracted from previous CONTAM opinions since 2015. These were then categorised in 2 lists, one pertaining to exposure assessment and one to hazard identification and characterisation. The next steps are to prioritise the most important uncertainties in terms of frequency in past CONTAM opinions, magnitude of impact of the uncertainty on the final conclusions and feasibility to quantify the uncertainty. Magnitude was estimated by using a qualitative scale. The feasibility was estimated to determine if all uncertainties can be quantified by EKE or rather to select the most important ones first with highest impact to be prioritised. The aim is to have a dedicated prioritisation meeting in December this year. It was clarified to the uncertainty WG that for each uncertainty the expert is asked to make a personal assessment what they consider a usual impact in a typical opinion and a worst-case impact. The aim is to determine which uncertainties are relevant most often and what is the worst they can be. It will allow to provide a new CONTAM WG with an aid with the most relevant uncertainties, to check this list and decide which ones are relevant and get indications at the beginning of their assessment how

[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[3] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

important they have been in past opinions. It is not the intention that the impact assessment will be taken and transported to their own opinion. Its more an aid memoir to help get people familiar with more common uncertainties. This is the opportunity to have a coherent and consistent way to conceptualise how uncertainties can be identified. The questionnaire to do this prioritisation exercise is under development and it will be shared with the uncertainty WG for their feedback.

- Feedback from the **GMO unit** on the plan for the overall uncertainty assessment of the BriskaR Non-Target Lepidoptera model. The aim is to develop a spatially and temporally explicit model able to provide realistic predictions in terms of risks to NT Lepidoptera for current and future Bt-maize events for cultivation, accounting for ecological and landscape diversity, and newly reported relevant information. Because models are simplified representations of the real world the purpose of the overall uncertainty assessment is to provide risk managers with the information on how reliable the estimates are, how different the real outcome might be and how likely that is taking account of all identifiable sources of uncertainty affecting the model. The model was presented to the uncertainty WG and related input parameters, related uncertainties and its model outputs. The challenges on the framing questions and different options for the EKE for the overall uncertainty assessment were presented to the WG. In particular, conclusions need to refer to well-defined outcomes, which are potentially observable (at least in principle). Further, the method to elicit a probability distribution from the experts was presented. The virtual workshop will be held coming mid-November. The WG asked clarifications on the re phrasing of the question for the EKE workshop. Further it was clarified to the uncertainty WG that the overall uncertainty assessment of any model should ideally always be done unless the modeller specifies that the model output is not influenced by any uncertainties. Otherwise, if the scenario is such a simplification of the real world that would require the risk manager to do an extrapolation to the real world. This kind of extrapolation should not be done by the risk manager, but by the risk assessor.

- Feedback from **FAF panel** on the implementation of uncertainty analysis in the revised scientific guidance for the preparation of applications on smoke flavouring primary products: Lessons learnt for future implementations and discussion when and how to do the calibration of the standardised procedure: This agenda item was postponed to the next meeting due to time constraints

4. Any Other Business

In preparation of next year's planning of the WG meetings the WG suggested to have more frequent and single day meetings and to keep the current cross-cutting compositional nature of the WG.

<u>The dates for the future WG meeting in 2020 are:</u>

- **11th WG uncertainty** – teleconference :14 December 2020 14.00 – 17.00 pm ;15 Dec. 10.00 - 12 00 et from 14.00 – 16.00 pm; this meeting has initially been scheduled as a physical meeting and converted into a TC due to COVID 19.

SCIENTIFIC COMMITTEE AND EMERGING RISKS UNIT

MINUTES OF THE 9th cross cutting EFSA WG on Uncertainty (WGU)

Teleconference, 14 July 2020 (10.00 am-12.00 pm) and (02.00 – 04.00 pm); 15 July (9.30.a.m 12.30)

(Agreed on 22 July 2020)

Participants

- Panel and external experts:

Dominique Bicout, Andrew Hart, Konstantinos Koutsoumanis, Maarten Nauta, Giuseppe Ru, Wopke van der Werf, Heather Wallace, Salomon Sand, Ullrika Sahlin and Julio Alvarez.

- Hearing Experts[1]:

Peter Craig;

- European Commission and/or Member States representatives:

Not Applicable

- EFSA:

SCER Unit : Caroline Merten (chair)

AMU Unit: Federica Barrucci (day 1), Laura Martino, Olaf Mosbach - Schulz

1. Welcome and apologies for absence

The Chair welcomed the participants. Apologies were received from Fulvio Barizzone, Laura Ciccolallo and Elisa Aiassa by the AMU Unit.

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4. Support to the implementation of the uncertainty guidance document in ongoing EFSA mandates in 2020

The WG discussed the following matters:

- Feedback from the **AHAW panel** on the opinion of the Evaluation of public and animal health risks at delayed post-mortem inspection (PMI) in ungulates: to assess the effectiveness (in terms of its sensitivity in detecting the diseases/conditions listed) of PMI when carried up to 24h and up to 72 hours after slaughter or arrival in the establishment in comparison to when it is carried out immediately after slaughter or arrival in the game-handling establishment.
  The WG uncertainty discussed the example of one disease, Mycobacterium tuberculosis complex (M. bovis, M. caprae and M. tuberculosis). Two expert knowledge elicitations (EKE) were held: one to elicit the mean number of carcasses from infected animals per 100 assessed as diseased in a PMI carried out immediately after slaughter (current procedure) that would still be detectable after 24 or 72 hours and one to assess the impact of the delay on the performance of various diagnostic tests. The overall objective was to assess the combination of the effect of the delay on the detection of the lesions and on the performance of diagnostic tests. The WG discussed how the two probability distributions from the 2 EKEs were combined to quantify the desired combined effect of the third parameter. The WG provided several suggestions to improve the understanding and visualisation of the analysis performed and related results e.g. to explain better what is meant by having a correlation of the identified uncertainties, to show results with a cumulative probability. The WG provided some suggestions for alternative expressions of the conclusion.

- Feedback from the **BIOHAZ panel** on the opinion of the Evaluation of public and animal health risks at delayed post-mortem inspection (PMI) in ungulates: Discussion with the WG uncertainty on the expert knowledge elicitation and the output of the Salmonella model, an uncertainty distribution of reduction in sensitivity of Salmonella detection. The conceptual model to assess the impact on the Salmonella detection was presented to the WG. This includes the storage conditions, the influential factors such as the indigenous microbiota and the methods to assess the impact on the sensitivity of the detection, modelling versus literature. An EKE divided into 2 parts was held with 4 experts from the BIOHAZ WG to agree on the model input variables and associated uncertainties. The first part elicited the water activity, the standard deviation of mean initial concentration of Salmonella, the sponging efficiency and the competing microflora. The second part elicited the factors that were expected to have

[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[3] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

greatest impact on the model outcome: the mean initial concentration of Salmonella on carcasses after slaughter before chilling, the minimum number of Salmonella to result in a positive sample after 24 h and the physiological status of Salmonella after 24 h chilled storage. The uncertainty WG asked several clarifications: e.g. uncertainty & variability are separated in the model, how to interpret the reduction of the sensitivity of the method and what is the reason for it, how the final distributions were estimated, the visualization shows the result for a single carcass whereas the objective is to obtain the average over 100 carcasses, the uncertainty to be expressed as a two side bounded distribution. The WG uncertainty agreed to provide further advice and guidance on the interpretation of the model after the meeting.

- Feedback from the **BIOHAZ panel** on the Opinion on the BSE risk associated with collagen and gelatine as ingredients in feed: Discussion with the WG uncertainty on how to separate uncertainty and variability. The Tors should estimate the cattle BSE risk (C-, L- and H-BSE) posed by the use of ruminant collagen/gelatine as feed for non-ruminant animals including aquaculture animals. The TORs are broken down in five assessment questions (AQ) and for the first 3 the related approach was presented in more detail to the WG uncertainty. For AQ 2 (What is the amount of infectivity in collagen and gelatine produced from an infected animal at clinical stage?) and 3 (How many infected animals have to be processed and how many kg of collagen and gelatine have to be produced from infected animals to accumulate 1 cattle oral infectious dose 50 (CoID50)?) a quantitative approach (probabilistic model with worst case perspective used for the model assumptions) was presented and discussed with the WG uncertainty. A sensitivity analysis (SA) was done on the sources of the uncertainties associated with the model. An additional table for other sources of uncertainty not related to the model was presented and their impact on the assessment conclusions was evaluated. Additional clarifications were provided to the WG uncertainty: e.g. in a preliminary SA the contribution of the variability was found to be very low and it was decided to choose the central point without large impact on the model and to concentrate on the uncertainty instead; even when the model was rerun using the upper limit value of the variability the results were very similar within the same order of magnitude. It was clarified what the event expressed in the conclusions was. The WG provided a few suggestions on how to improve the expression of the uncertainty in the conclusions e.g. to express it in terms of the most probable outcome, if language is used from the probability table then the probability range should precede the verbal meaning according to the EFSA GD on how to communicate uncertainty or alternatively, to express instead the probability (quantifying uncertainty) in terms of certainty.

- Discussion with the WG uncertainty on the reasons why it may happen that in the BIOHAZ panel to express quantitatively the overall uncertainty cannot always be an option. One reason is the nature of the assessment question such as to review the literature. However, conclusions from such open questions may still be formulated in well-defined terms so that their uncertainty can be quantified, as stated in section 9 of the Guidance. Another situation where quantification has been considered difficult is when the ToRs ask EFSA to identify factors affecting a certain response. If quantification requires a formal EKE this will not always be feasible due to limitations of time. An informal WG consensus could be reached and quantified but this would be more approximate when the elicitation is informal. It was advised that making informal quantitative judgements, even with few experts, is better than expressing the same judgement qualitatively which makes it ambiguous. When making informal judgements assessors should still try to guard against bias. The WG agreed to discuss a few examples in future meetings.

- Feedback from the **PREV unit** on Cumulative risk assessments for pesticides: Discussion with the WG uncertainty on the public consultation feedback on uncertainty analyses contained in the four published EFSA reports on cumulative risk assessment of pesticides. The possible lessons for future assessments to be retained from the public consolations feedback include:

To guard against possible concerns for reliability/bias of UA/EKE: (1) When the impact of model assumptions will be subjected to uncertainty analysis, consider using realistic rather than worst-case assumptions; (2) When uncertainty analysis results in marked adjustments to estimates from modelling or data, take care to explain well the reasons for this; (3) In all cases, provide detailed information on the evidence and reasoning supporting the assessment of uncertainty – at least for overall uncertainty and, where appropriate, also for individual sources of uncertainty. To increase clarity of reporting: (4) Be more systematic in applying EFSA's Guidance on communicating uncertainty. Public consultation feedback can support the identification of additional sources of uncertainty: (5) Give full consideration to input from public consultation and be prepared to change your assessment and conclusions if appropriate. It was noted that this last point is an example of the importance of ensuring that conclusions in the abstract and summary are consistent with the assessment results. Other comments from the public consultation on the UA were generally positive.

- Feedback from the **PLH panel:** The WG uncertainty discussed some issues encountered with the language of uncertainty and frequency to distinguish well between the frequency of events in the real world and uncertainty on the knowledge about the estimated frequency. These challenges were encountered in past opinions within the commodity risk assessment in the plant health panel. Within this kind of assessment, the PLH panel evaluates the likelihood of pest freedom of imported plant material into the EU territory. The ratings for the frequency of pest freedom is expressed as a probability scale. The assessment questions are framed in terms of pest freedom in 10 000 units as this is a standard production unit in plant consignments. The related certainty on the number of pest freedom plants within the standard unit (10 000) imported into the EU territory is visualised by a descending distribution function. Different versions of possible expressions of the frequency and uncertainty were discussed with the uncertainty WG. For example: "The Panel is 95% confident that at least 9958 bags per 10000 would be free from pest X" versus " The estimated degree of pest freedom varies among the pests evaluated, with pest X being the pest most frequently expected on the imported plants. The Expert Knowledge Elicitation indicated, with 95% certainty, that between 9958 and 10000 bags per 10000 will be free of pest X. On the other hand, an alternative expression using more narratives instead of numbers was rejected by the panel: "The estimated degree of pest freedom varies among the pests evaluated, from "almost always pest free" for three of the species, to "pest free with some exceptional cases" in the case of pest X, the pest most frequently expected on the imported plants. For this latter species, the panel estimated that the number of plants infested with this pest would be in the order of a few tens per 10,000 imported plants." The uncertainty WG agreed that latter expression was not to be recommended for use as the readers don't know the definition of the classes and it was judged too vague. The WG discussed some challenges occurring when drafting the expression of the assessment conclusion and related uncertainty. Among these were:
  (1) Giving such an exact 4-digit frequency as shown above in the example may seem to suggest a high precision which may be misleading considering the evidence and the process used to elicit it. An alternative suggestion to express the frequency as one side bounded with "at least 9958"was not found recommendable neither as a 2 sided interval is better to avoid anchoring on the one sided if only that one is provided. Nevertheless, the implied precision remains a concern as it is derived from a fitted distribution from the expert's judgements and the EFSA communication uncertainty GD does not mention anything about the expression of precision. The WG uncertainty discussed the pros and cons in case the WG/ panel would feel the number as too precise and to readjust the judgment by rounding down the frequency to 9950 and adding" at least". This would make the probability approximate keeping in mind above mentioned risks of anchoring. For other uncertainty WG members the precise number does not seem to be over precise as the imprecision should already be implied by giving a range, communicating that one really does not know within the indicated range where the correct number lies.

(2) The panel itself did not do the elicitation, but the WG did. The uncertainty WG brainstormed about this challenge. Concern was raised about the panel readjusting an estimate derived by a WG EKE. The panel is reviewing the process and raise doubts about the EKE procedures, but if the panel would like to readjust an estimate, they would need to have a strong reasoning for this. The question remains what would be the evidence on which that reason was to be based? The panel adopting the outcome of an EKE is not different from the process on how the panel functions in relation with the WG. It is comparable to the panel adopting the modelling and statistical analysis of one of 2 WG experts. Many assessments are done separately by only a few WG experts and nevertheless the assessment is accepted, adopted and expressed as the panel's view. The process for reviewing and adoption by the panel of the WG work should not be different regarding EKE results.

(3) Assessments sometimes have to be made for up to 20 pest per commodity and it is impossible to put that amount of information into the abstract. Therefore, many statements for several pests were made in a vaguer way without giving the direct number and the full precise statement on the frequency and related uncertainty was done only for the pest with the highest expected frequency. This was a practical solution.

The uncertainty WG agreed that it would be recommendable to try to align the expressions and phrasing of the uncertainty in the assessment conclusions across the panels. To this end the WG will draft several alternative proposals indicating the pros and cons of each of them. The aim is that the WG uncertainty members discuss the options with their respective panel.

Feedback from **FAF panel** on the implementation of uncertainty analysis in the revised scientific guidance for the preparation of applications on smoke flavouring primary products. This GD is destined for the applicants with the aim to clarify the data required from industry, applicable to new and to renewal applications, to explain the approach to be followed in the risk assessment, to take into account cross-cutting guidance/documents and relevant provisions of the new Transparency Regulation. The draft GD is planned to undergo public consultation in autumn. Section 6 of the uncertainty GD applies in this case for UA of standard assessments. Part of this when developing or revising a standard procedure, an uncertainty analysis is needed to assess the standard uncertainties and confirm the provision for them is sufficient (calibrate them). Part of the calibration exercise is to get an agreement of the risk managers protection goal. With regard to human health the standardised procedure will need to 'sufficiently demonstrate' – i.e. with sufficient certainty that products passing the assessment 'do not present risks to human health. 'The added value of the calibration is an improved scientific rigour and improved transparency. With regard to the environmental protection goal there is a need to define the interpretation of the legal objective. An outline of the standard assessment and a table listing the standard uncertainties identified in the standard procedure in the flavouring GD were presented to the WG. The calibration would result in statements of the certainty in the standard procedure expressed by (approximate) probability. The WG also noted that the UA in the standard procedure rely on critical appraisal of data submitted by the applicants combined with e.g. conservative estimates and uncertainty factors.

- Feedback from **NDA panel** on the assessment of the upper level for sugar intake: The uncertainty WG discussed a draft proposal for evidence integration accounting for sources of uncertainty. The purpose of the assessment as stated in the mandate is: 'to investigate whether the intake of dietary sugars may be positively associated with an increased risk of metabolic and other diseases and, in that case, whether an upper level or a safe level of intake can be established'. To assess this two sub questions will need to be answered: (Q1): Is the intake of (total/added/free) sugars or their type (i.e. glucose vs fructose), or sources (e.g. SSBs, 100% FJ) positively associated with the incidence of disease XX at the levels of sugar

intake (only from diet), duration of the intervention/exposure and population subgroups as the ones investigated in the studies eligible for this assessment? (Q2) as above but levels of sugar intake, duration and population as defined in the mandate question. The required evidence is retrieved from two types of lines of evidence: intervention studies for Q1 & Q2 and observational studies for Q2. The approach used for evidence synthesis was: a systematic review with a quantitative summary of the evidence where possible by forest plots graphically displaying study results and their confidence intervals and main characteristics of the studies, pooled estimates, dose-response meta-regression analysis (for a subset of adverse outcomes), linear and non-linear (restricted cubic splines). Uncertainties were identified in the body of evidence within study design and adverse outcome: limitations in the internal validity (i.e. risk of bias tiers across body of evidence and critical domains of risk of bias), unexplained inconsistency (heterogeneity), limitation in the external validity, pooled effect estimate imprecision and impact correlation coefficient, publication bias. For each of the identified uncertainties their possible impact on the results need to be assessed. With regard to the uncertainties in the methodology they were identified within study design and adverse outcome. Those identified for interventional studies and for observational studies were presented with a proposed methodology on how to evaluate their possible impact on the results. Within each Q, randomized controlled trials (RCTs) and prospective cohort studies (PCs) were organised by line of evidence (LoE). The current proposal is to assess the uncertainty on the causality of a positive relationship between the intake of sugars and the risk of disease by following the principles laid down in the OHAT approach, but adapted to this assessment and to express the uncertainty by using the approximate probability scale. An initial rating of the certainty on a positive association will be assigned by design of the studies included in the body of evidence. The plan for the uncertainty analysis in the evidence integration was presented and discussed with the WG uncertainty. Several clarifications were provided to the WG members and they were asked about any experience in combining and integrating different types of study designs with different outcomes for which there is currently rather little guidance.

5. Collaboration process with WG uncertainty

The uncertainty WG was reminded about the EFSA process to ask for support on the implementation of the EFSA cross cutting guidance document. Also the WG members who are supporting various mandates across EFSA with implementing the uncertainty GD were encouraged to give regular updates to the WG uncertainty at various stages of the risk assessment process to ensure the most efficient support can be given by the WG uncertainty to enhance capacity building across EFSA on uncertainty analysis.

6. Output from cross cutting WG uncertainty as additional support

The uncertainty WG was reminded about the revision cycle of the cross-cutting GDs. This revision is usually done after a 3-year cycle of implementation. As the first implementation phase of the uncertainty GD will end by mid-2021 this would be the opportune moment for the uncertainty WG to prepare an output with a proposed list of recommendations for revisions of the current uncertainty GD.

7. Any Other Business

The uncertainty WG was informed that the revised uncertainty check list is now finalised and uploaded into the meeting folder. After an adoption round via email this draft will be the one to be used until the end of the first phase of the implementation.

The dates for the future WG meeting in 2020 are:

- **10th WG uncertainty** – teleconference (3-hour): 15 October 2020 :14.00-17.00 pm
- **11th WG uncertainty** – teleconference :14 December 2020 14.00 – 17.00 pm ;15 Dec. 10.00 -12 00 et from 14.00 – 16.00 pm; this meeting has initially been scheduled as a physical meeting and converted into a TC due to COVID 19.

SCIENTIFIC COMMITTEE AND EMERGINC RISKS UNIT

EFSA cross cutting Working Group

on Uncertainty

Minutes of the 8th cross cutting WG on Uncertainty (WGU)

Teleconference, 17 June 2020 (09.00 – 12.00)

(Agreed on 22 June2020)

Working Group Members:

- **Panel and external experts:**

Dominique Bicout, Andrew Hart, Konstantinos Koutsoumanis, Maarten Nauta, Giuseppe Ru, Wopke van der Werf, and Heather Wallace, Ullrika Sahlin and Julio Alvarez.

- **EFSA:**

SCER unit : Caroline Merten (chair)

AMU unit: Federica Barrucci, Laura Martino, Elisa Aissa, Fulvio Barizzone

- **Hearing expert**

Peter Craig;

Welcome and apologies for absence

The Chair welcomed the participants. Apologies were received by Salomon Sand and from Laura Ciccolallo from the EFSA AMU unit.

1. Adoption of agenda

The agenda was adopted without changes.

2. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2], EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process.

3. Finalisation of the revised uncertainty check list

The WG discussed the revised uncertainty check list. The need for a check list was initially identified after the uncertainty tailor made trainings that started in 2019 with the aim to break the perspective that uncertainty analysis is a separate part from risk assessment in general, and to prompt risk assessors to enquire which methods can be used to do uncertainty analysis. The need was recognized initially for a one pager with a top-level summary of the key things to be done and applicable to all types of assessments. However, in April 2020 the Draft framework for protocol development for EFSA 's scientific assessments was published[3] and will be trialled for 1 year. Acknowledging the need of a priori planning of the assessments the uncertainty WG decided to revise the uncertainty check list to align with the most important elements of the framework from the protocol development.

The WG discussed the following 2 options: option 1 to insert the new flowchart graphic based on the protocol development template into version 4.2 'clean' of the checklist, tidy up the text to align with the graphic, and remove repetition (e.g. delete the second graphic which duplicates part of the first, some information that appears twice, and some text that is covered by the graphic). This would result in a document of 3 pages; option 2 to reformat the document, making the revised flowchart graphic into the primary content and providing the additional information and advice from the text as a series of numbered notes, linked to the relevant points in the flowchart. Option 2 could be done within 2 pages. This revised format does not look like a checklist anymore and probably should be called a flowchart instead. It was clarified to the WG that the end users of this check list are the uncertainty WG members, the EFSA WG coordinators and WG chairs who are implementing the uncertainty guidance document (GD).

The WG in the end preferred option 1, even if that version would be a longer one. The graphic was found a bit complex and not self-explanatory enough, whereas the

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf
[3] https://efsa.onlinelibrary.wiley.com/doi/abs/10.2903/sp.efsa.2020.EN-1843

check list which has been used already by several panels was found to be easily implementable and user-friendly. It was found preferable to have the various steps related to uncertainty when doing the risk assessment listed upfront and the graphic based on the protocol development template later. The WG agreed that in the end the length of the document should not compromise its clarity. The WG supported a practical checklist easy to use. Several suggestions were provided to revise the graph. Then the revised general framework of the uncertainty check list can be used by the various panels to be adapted to their specific needs until the end of the trial phase of the protocol template.

4. Output from the cross cutting WG uncertainty as additional support to implement the uncertainty analysis

The WG discussed a proposal to develop an output to provide support to all EFSA WGs that implement the uncertainty GD on how to assess the overall uncertainty in a conclusion of a scientific assessment. The overall uncertainty in conclusions is the very last step of an uncertainty analysis. The goal is to try to quantify the combined impact of all identified uncertainties on conclusions of a scientific assessment. Ideally it should be attempted in all scientific assessments and requires expert judgement which can be a formal or semi-formal expert knowledge elicitation (EKE). The EFSA EKE Guidance addresses the formal EKE for parameters where the parameter is a quantity that has a fixed value and the experts are asked to express their uncertainty about these parameters. However, the EKE for conclusions involves additional complications and challenges. A conclusion is sometimes a function of multiple parameters. Uncertainty in the parameters must either be assessed individually and then combined, or the combined uncertainty must be assessed directly. Uncertainty in conclusions may already have been assessed for some of the parameters using a quantitative uncertainty analysis. To assess overall uncertainty, the experts must take into account uncertainty in all parameters and uncertainty about the function itself. Some conclusions are based on qualitative assessment with no quantitative parameters. Assessing the overall uncertainty for conclusions is addressed in section 16 of the uncertainty GD, but in an abstract way, without examples and deciding how to combine already quantified & additional uncertainties is new and has proven to be challenging for EFSA WGs. The conclusions sections of EFSA Opinions often contain too many conclusions to conduct even semi-formal EKE on all of them. Therefore, there is a need to prioritise conclusions, but almost no guidance available. There is also the need to provide further guidance to streamline the EKE process and to provide guidance to group or link conclusions. Using more probability bounds may be helpful, but limited guidance is available on this. Some conclusions are based primarily on statistical analysis of data, some primarily on models, some on qualitative review of literature, some on a combination of these. It is often challenging to frame conclusions as well-defined questions for EKE.

Considering all these challenges and the additional challenges the WGs using the guidance face with regard to limited time and resources the Uncertainty WG is proposing to develop additional guidance on assessing the overall uncertainty of conclusions. The main aim of this additional guidance is to provide simple and clear explanation of what is needed, practical options for addressing the various complications and challenges, incorporating experience from recent mandates and examples illustrating how these work in practice. Initial suggestions for content were presented.

The WG welcomed this proposal and confirmed that this additional support would be highly needed by the respective WGs where the uncertainty GD is currently being implemented. It was confirmed that these challenges were encountered many times. It was suggested to go back to past opinions and identify the missing elements in the conclusions. In addition, it was advised to consider also the need for a simplified option for EKE with 2-3 experts. It was suggested to clarify first what is meant by the "overall uncertainty". Indeed, recurring challenges so far have been how to integrate those uncertainties in the final step not having been covered in earlier stages. Other key challenges encountered were how to integrate different study designs, how to integrate results across different adverse health outcomes and endpoints and the need to establish reference values based on different outcomes. The WG agreed that these challenges need to be tackled as well, but they are not an alternative to the initial proposed solution, but an additional complementary support that is currently missing. The WG brainstormed whether enough opinions have already been published where the uncertainty GD has been applied which could be used as examples to illustrate best on how to address above mentioned challenges. A number of examples are so far available, and some additional ones are expected to be published in the coming year which could be used to illustrate the best practice intended to be shown in the additional supporting output. It was agreed to present the additional support proposed by the WG uncertainty to an upcoming SC plenary before proceeding further.

5. Any Other Business

The dates for the future WG meeting in 2020 are:

- **9th WG uncertainty** – teleconference: 14 July 2020 10.00 -12 00 and from 14.00 – 16.00 pm; 15 July .9.30 – 12.30; this meeting has been converted into a TC due to COVID 19.
- **10th WG uncertainty** – teleconference (3-hour): 15 October 2020 :14.00-17.00 pm

- **11th WG uncertainty** - physical meeting (1.5 day): 14 December 2020 14.00 – 17.00 pm ;15 Dec. 10.00 -12 00 et from 14.00 – 16.00 pm; this meeting has been converted into a TC due to COVID 19.

SCIENTIFIC COMMITTEE AND EMERGINC RISKS UNIT

EFSA cross cutting Working Group

on Uncertainty

Minutes of the 7th cross cutting WG on Uncertainty (WGU)

Teleconference, 11 May 2020 (10.00 – 12.00) and (2.00-5.00 pm)

(Agreed on 18 May 2020)

Working Group Members:

- **Panel and external experts:**

Dominique Bicout, Peter Craig, Andrew David Hart, Konstantinos Koutsoumanis, Maarten Nauta, Giuseppe Ru, Wopke van der Werf, Salomon Sand and Heather Wallace, Ullrika Sahlin and Julio Alvarez.

- **EFSA:**

SCER unit : Caroline Merten (chair)

AMU unit: Federica Barrucci, Laura Martino, Elisa Aissa, Fulvio Barizzone and Olaf Mosbach- Schulz

Welcome and apologies for absence

The Chair welcomed the participants. Apologies were received by Laura Ciccolallo from the EFSA AMU unit.

1. Adoption of agenda

The agenda was adopted without changes.

2. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2], EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process.

3. Use of TEAMS in between meetings to share info on ongoing activities

The WG was given a short overview on the main functionalities of the new collaborative platform "TEAMS" that will from now onwards be used to collaborate in preparation of, during the WG meetings and in between. Among those functionalities the tag function to add posts either for the entire WG or targeted at a subgroup of the WG seem to be promising to keep the history of exchange in one place and diminish email exchange and screening to find back information from the past. The WG brainstormed about how best to use TEAMS for a focused cross horizontal support to certain panels and their various mandates. It needs to be verified if channels can be split further into sub channels instead of subfolder within the same channel. The aim is to keep the structure as simple as possible with the aim to have a structured environment to see what is going on in the various panels and mandates. The WG discussed the option to grant access to external experts from other EFSA WGs on their particular mandate. The particularity and possible granularity of permission granting within one TEAMS groups and across channels needs to be checked. One option could be that external WG experts involved in only one mandate are tagged individually. The WG proposed as a possible way forward to have one channel for all the WG meetings with subfolders per meeting and one channel per panel that is supported by the WG uncertainty with subfolders for the various mandates. The experts can use the pin button to prioritize the number of channels presented when entering TEAMS. The WG discussed the necessity to have a collaboration process discussed and defined that would enable the WG early on in the process to discuss the uncertainty plan for the analysis early in the process at protocol development stage and not later on in the process once uncertainty analysis has already started and recommendations can only be given a posteriori. This process could define what to report and at which stage in each mandate in the respective channel. Each WG member following specific mandates is reminded to send out information upfront and at regular intervals to ensure best support can be given a priori.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf

[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

4. Support to the implementation of the uncertainty guidance document in ongoing mandates in 2020

The WG discussed the following matters:

- Feedback from **AHAW panel** on the ongoing mandate on Evaluation of public and animal health risks at delayed post-mortem inspection in ungulates. The aim is to assess the effectiveness (in terms of its sensitivity in detecting the diseases/conditions listed) of post mortem inspection (PMI) when carried up to 24h and up to 72 hours after slaughter or arrival in the establishment, in comparison to when it is carried out immediately after slaughter or arrival in the meat-handling establishment. To this end a disease matrix was developed, lesions subjected to possible changes with delayed PMI were selected, a lesion map was drafted, a questionnaire was sent to the meat inspectors and the results from that survey was used in the evidence dossier in preparation of the expert knowledge elicitation (EKE) with the AHAW sub WG in which nine diseases/group of diseases were evaluated. For each disease the WG was asked to assess the mean number of carcasses from infected animals per 100 assessed as diseased in a PMI carried out immediately after slaughter (current procedure) that would still be detectable after 24 or 72 hours. In this context, assessed as diseased by the inspector means that the inspector is detecting lesions compatible with the presence of a disease (without necessarily diagnosing the disease itself). The WG was asked to give their individual judgment on the median for that mean value ahead of the meeting. Their judgements were then discussed at the WG meeting, and a consensus median was then agreed upon. Then individual judgments for Q1 and Q3 at 24 and 72 hours were elicited followed by a discussion and consensus on a distribution for each delay. This evaluation was completed for the initial 9 diseases/groups of diseases, and the remaining ones will be done in a second exercise. The method was presented during the AHAW plenary to serve as an example for other opinions.

The uncertainty WG was reminded that the scale used in the survey for the meat inspectors to assess their certainty on their judgements (from 1 to 10) was not the optimal one as it is too arbitrary and the WG needed to translate it in a meaningful way as the meat inspectors may interpret the scale differently. The uncertainty WG was reminded to try to avoid using this kind of scale. Because of these limitations the individual scores on certainty were only incorporated in the plots generated in the evidence dossier showing the individual answers from the meat inspectors, and not taken into consideration more formally during the EKE. Plots and tables summarizing the answers from the meat inspectors on the effect of the delay on the different lesions relevant for each disease were used for the evidence dossier in addition to information on other lesions not included in the survey, and were available

to the AHW sub WG experts to inform their judgment during the EKE exercise. Shorter sessions for the remaining diseases are planned now that the experts are better trained and more experienced in the method. Further it was clarified to the Uncertainty WG that due to the available time it was decided not to ask first for the plausible range (as advised by the EKE GD and in more detail by Oakley and O'Hagan 2016) and instead it was set to the maximum range (0-100%). The experts were asked to divide the range 0-100% into equally probable parts, which should provide some protection against anchoring around the median. In this case this compromise was deemed acceptable as a natural bound existed and asking for the minimum and maximum (the plausible range) was not absolutely needed. Also, the experts were provided with judgements made by meat inspectors for the individual lesions, which already occupied nearly all of the range. In recognition that it might not prove possible to elicit judgements for all the diseases, a strategy was formulated for prioritising them and for assessing collectively any that could not be assessed individually in the time available (by eliciting a single judgement for the probability that one or more of the remaining diseases would suffer more loss of lesions than the worst of the diseases assessed individually). This may not be necessary in practice, as the AHAW subWG decided to schedule additional EKE sessions. The experiences gained in this mandate may serve as a lesson learnt for future EKEs with a high amount of questions to be addressed. The WG discussed further what to present in the opinion and supplementary materials. The preference was given to show the full distribution and not only the tails of the distribution.

- Feedback from the **BIOHAZ** panel on taking stock of first experiences gained so far by implementing the uncertainty GD in BIOHAZ opinions since 2019. The BIOHAZ panel has discussed this at their May plenary meeting 2020. Since the training in March 2019 the BIOHAZ panel has been drafting a list of minimum requirements for implementing the uncertainty GD and the subject has become a standing item on their plenary agenda. The GD was applied in 3 BIOHAZ mandates, all three recently adopted in March 2020: (1) Campylobacter control options in broilers at primary production; (2) Listeria monocytogenes in frozen fruits, vegetables and herbs; (3) Use of tubs for transporting and storing fishery products. Respective TORs, uncertainty analysis, conclusions and added value and challenges encountered were discussed. For (1) the EKE added an important conclusion on risk reduction that would not have been possible without EKE and the conclusions were more precise in comparison with the 2011 opinion. For (2) & (3): the approach allowed a detailed discussion on uncertainties. Among the challenges reported for all were the increased resource need in terms of WG meetings and the high workload for experts and EFSA staff. Questions were raised with regard to the reproducibility of the EKEs in general. For (2): Not all the WG experts can always be involved in EKE as they are lacking the required background; despite EKE initiated due to time constraints it was not possible to finalise it and finally an expression of the

probability was proposed through individual expert judgement and agreed with the WG and panel. Could a more pragmatic and faster way initially have been proposed and utilized to express the uncertainty? For (2) & (3): It takes a lot of time to discuss in the WG the uncertainty tables. To plan the uncertainty analysis from the start was found challenging as it is an iterative process. The BIOHAZ panel is committed to the implementation of the uncertainty GD and the awareness and discussion of uncertainties and translation of their impact on the conclusions has certainly improved. The panel urges to develop an alternative (simpler) approach to EKE.

The WG brainstormed whether in the second mandate a rough sensitivity analysis on the model prior to the risk assessment could have been done to evaluate the impact of the uncertainties on the input parameters. For the sake of saving resources, it is up to each panel to decide on the level of simplification. It is also understandable that the panel necessitates time to learn and apply a new methodology to solve the problem. It was advised to be transparent about the limitations available for the assessment: if no time was available and if only one expert was available to elicit a probability range this should be clearly recorded and justified. Even if only one WG expert was able to provide an estimate it is the task of the entire WG to understand the model used by the modeller and the probability range provided by the single expert was given in consensus with the WG. Although it was advised that in this case it should not be named an EKE, but an expert discussion instead.
The WG discussed about a possible standardised approach for 2–3 experts which could be agreed by the WG and then by panel. This could be considered in a future output from the WG uncertainty.

- Feedback from the EFSA **CLEFSA (Climate change as a driver of emerging risks in the EFSA's remit)** project team: Discussion with the WG uncertainty on the approach used to rank climate change related emerging issues, allowing to take into consideration individual expert uncertainty. The WG was given a short overview on the various steps applied in the CLEFSA project to identify emerging issues in relation to climate change. The project is in its final step in which the final report is reviewed. In previous steps identification criteria were defined to identify emerging issues (EI) in relation to climate change. EI were gathered via a list of issues previously identified by EFSA, via a CLEFSA working group, via literature search and via a survey to the general public. This was followed by defining the criteria to characterize the EI: impact, likelihood, risk management measures, other qualifying criteria. Expert knowledge was used to evaluate each EI identified. This was done by using Shiny tool. In total 129 issues were evaluated, and 60 experts participated remotely to the characterisation exercise. Experts were asked to assess for each EI the impact in terms of the following criteria: how many units are affected, magnitude of symptoms, fatality or mortality rate, production or yield loss and likelihood in the "reference period" (1981-2010). Experts were asked to assess the same

criteria in the "near future" period (2021- 2050) for each EI. Experts were asked to express their uncertainty on their estimates by providing a credibility range and the most probable value on an ordinal scale that was converted into a quantitative scale with the assumption that the various criteria scales are equally spaced. Individual uncertainty distribution for one issue was derived assuming a Pert distribution on the numerical scale and deriving probability associated to each level in the ordinal scale. Individual uncertainty distributions were averaged over all experts and over subcriteria. This resulted in the expression of a bivariate uncertainty per issue expressed on the impact and likelihood due to the assumption that they are independent. The EI are visualized in terms of their probability weighted average impact and probability weighted average likelihood. In addition, dispersion was used as other criteria to characterise the distribution of the uncertainty. Additional sources of uncertainty at the characterisation step such as ambiguity of possible different understanding and interpretation of the issues or expert group composition etc and analysis step such as the choice of the probability distribution or possible dependency between sources of uncertainty etc were identified.

The WG agreed that it is important to come up with a different methodology to assess uncertainty in this kind of very data limited assessments in the area of emerging risks. How to treat uncertainty in this type of assessment is different from the typical risk assessment. It was clarified to the WG that although the initial aim was to use MCDA in the end this was not used as both criteria impact and likelihood were not combined. Further it was clarified that the probability weighted average indicates the central tendency of the distribution. It was chosen as a quick method to compile and compare the estimates of 60 experts on the 129 issues. The WG discussed additional comments to the presented methodology and other potential sources of uncertainty that may not have been considered yet.

The WG was not convinced about the assumption on the likelihood scale used on the equal spacing of the ordinal scale when converted to a numerical scale. As a consequence, the results may be most driven by the mapping of the ordinal scale that was used. Each expert could have interpreted the criteria and its scale differently. Instead the ordinal qualitative scale could have been used to inform the judgments in a follow up step. How could the information from the ordinal scale be used to inform better defined conclusions?

Further it was clarified to the WG that for the impact scale definitions were given to the survey participants for the units that were provided in the pick list. However, as these definitions were hazard specific it remains questionable how comparable they then are on the impact scale. Would this not require a definition by or an agreement with the risk manager? Also, it will be challenging to say something practical on the impact of the uncertainty on the conclusion. It was clarified that a conclusion will be drawn for each individual issue and for groups of issues belonging to the same area

investigated such as animal health or plant health. It was agreed that the WG uncertainty will have the opportunity to review the uncertainty section of the final draft CLEFSA report.

5. Output from cross cutting WG uncertainty as additional support

This agenda item was postponed to the next meeting.

6. Any Other Business

- It was proposed to have an additional WG meeting in June to discuss and agree on the pending items.
- It was proposed to open a channel for the general template on the uncertainty check list and use the chat in teams to continue the process to finalize it in preparation for the next WG meeting.

<u>The dates for the future WG meeting in 2020 are:</u>

- 8th WG uncertainty - teleconference (3-hour): 17 June 2020: 09.00 - 12.00
- 9th WG uncertainty - physical meeting (1.5 day): 14 July 2020full day - 15 July ½ day am; this meeting will be converted into a TC due to COVID 19.
- 10th WG uncertainty – teleconference (3-hour): 15 October 2020 :2.00-5.00 pm
- 11th WG uncertainty - physical meeting (1.5 day): 14 December 2020 ½ day pm -15 Dec. full

SCIENTIFIC COMMITTEE AND EMERGINC RISKS UNIT

EFSA cross cutting Working Group

on Uncertainty

Minutes of the 6th cross cutting WG on Uncertainty (WGU)

Teleconference, 10 March 2020 (2.00-5.00 pm); 11 March 2020 (9.30 – 12.30 am)

(Agreed on 19 March 2020)

This meeting, originally scheduled as a physical meeting, was converted into a teleconference to avoid travelling to EFSA in line with the measures established to reduce the risk of coronavirus infection.

Working Group Members:

- **Panel and external experts:**
  Dominique Bicout, Peter Craig, Andrew David Hart, Konstantinos Koutsoumanis, Maarten Nauta, Giuseppe Ru, Wopke van der Werf, Salomon Sand and Heather Wallace, Ullrika Sahlin and Julio Alvarez.

- **EFSA:**

  SCER unit : Caroline Merten

  AMU unit: Federica Barrucci (day 1), Laura Martino(day 1), Elisa Aiassa (day 1) and Fulvio Barizzone (day 1)

1. Welcome and apologies for absence

The Chair welcomed the participants. Apologies were received by Laura Ciccolallo from the EFSA AMU unit.

2. Adoption of agenda

The agenda was adopted without changes.

3. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2], EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process.

4. Proposal to align the uncertainty check list with the template proposed in the draft report on protocol development

The WG discussed a revised uncertainty check list where most important elements of the template from the protocol development were integrated. More focus should be given on the a priori planning of the assessment. The need for a check list was initially identified after the uncertainty tailor made trainings with the aim to break the perspective that uncertainty analysis is a separate part from risk assessment in general, and to prompt risk assessors to enquire which methods can be used to do uncertainty analysis. The need was recognized for a one pager with a top-level summary of the key things to be done and applicable to all types of assessments. The challenge is now to reconcile this need with the desire to align with the protocol template that has just been adopted at the February 2020 SC plenary for a trial period.

The WG discussed several additional suggestions: to put more focus on the appraisal and internal validity of the studies; in terms of process there is a need to align better such as eg data extraction, data appraisal, evidence synthesis; part A and B of check list: to give more detailed guidance tailored by approach used to deal with the evidence (i.e. using data from literature, from other databases, conducting primary research studies, performing an EKE) as given in the protocol template.
The WG agreed to rewrite the annex on supporting information of the check list by recognizing the four types of approach to deal with the evidence as shown in the protocol template and by putting references to the framework of protocol

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf

[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

development and different methods in section A, B & C of the check list. B1 and C1 need to be revised.
The WG agreed to take on a step wise approach in the future to evaluate whether and how to merge the two templates once more experiences will have been gained by trialling the protocol template across EFSA.

5. Support to the implementation of the uncertainty guidance document in ongoing mandates in 2020

The WG discussed the following matters:

- Feedback from **PREV unit** on mandate and related plan for uncertainty analysis (UA) for the Scientific Opinion of the PPR Panel on Developing Integrated Approaches to Testing and Assessment (IATA) on developmental neurotoxicity (DNT): The WG was presented with the mandate outline: To develop AOP informed IATA case studies using a DNT risk assessment-based problem formulation using selected active substances as examples considering the level of uncertainties associated with the available evidence and to integrate the outcomes of a new in-vitro testing battery for DNT (outsourced by EFSA) in the AOP informed IATA case studies and re-analyse uncertainty to guide on the use and interpretation of the in-vitro DNT testing battery. Two case studies were selected: Deltamethrin and Flufenacet using DNT and focusing on the hazard assessment only. The template for protocol development was followed to dealing with evidence and analysing uncertainty. The WG was presented with part 1 of the protocol: the upfront definition of the problem formulation, the methods for data collection and for evidence appraisal. This part has been finalised. Then, the WG discussed part 2 of the protocol: upfront definition of methods for synthesising and integrating evidence, including uncertainty analysis. This is still work in progress. The WG discussed in more details the proposed analysis for each evidence stream following the hierarchy in the evidence: specific endpoints followed by apical categories as defined in the OECD guidelines.

  The WG asked clarifications about the questions posed to assess the association between exposure and adverse outcome. It was clarified that the questions are posed by evidence stream for each specific endpoint by using a screening approach with the aim of grouping the endpoints and that questions in the presentation were simplified from the detailed versions being used by the DNT WG. The WG provided a few suggestions such as changing the probabilities of 0.6 to 0.66 for yes answers, to attempt alignment and consistency of the questions for the two steps presented, to ask for an approximate probability instead of a probability distribution for yes/no questions, other approaches

were discussed and need to be further explored with the WG. It remains to be clarified how to quantify the overall uncertainty at the end. In case approximate probabilities are used for the various AOP components, one option could be defining a logical model that links all the questions together.

- Feedback from **CONTAM** panel on the follow ups since the tailor-made training on uncertainty in November 2019: The panel recognized the added value of applying the uncertainty GD and are committed to implement the uncertainty GD in future new mandates. The plan is to set up a subgroup meeting with CONTAM panel members to establish an approach for uncertainty analysis in CONTAM. The objective of that subgroup is to identify common issues across opinions, to develop a default list of uncertainties, and method/principles for how to handle them and to revise the checklist for CONTAM. The aim is to draw up plans for uncertainty analysis for all new mandates.

- Feedback from the **BIOHAZ** panel on taking stock of first experiences gained so far by implementing the uncertainty GD in Biohaz opinions since 2019. The BIOHAZ panel will discuss this at their April plenary meeting 2020. A challenging aspect is the nearly continuous need to do an expert knowledge elicitation to characterise the overall uncertainty at the end of the assessment with a limited number of experts able to take part in the elicitation because of lacking expertise.

- Feedback from **FAF** panel on a new mandate on updating the guidance document for submission of applications on smoke flavouring primary products and the plan for addressing the uncertainty GD. The WG clarified the following: the meaning of standardised and non-standardized uncertainties in the context of an assessment, that it is recommended to ask for information that can support the characterisation of uncertainty (including variability) when asking for data, which may include errors of estimates (or sufficient statistics to be able to estimate this) of toxicity and, information about how samples have been selected in assessments of batch to batch variability, and uncertainty in parameters supporting the exposure assessment; in the context to look at how uncertainty analysis could be done in future assessments the WG discussed tools to support MC-simulations. The WG agreed that the weight of evidence GD should also be applied when integrating the uncertainty analysis and uncertainty should not be a separate chapter but integrated in each respective chapter of the GD.

- Feedback from **AHAW** panel: The WG was presented with uncertainty analysis for an ongoing mandate (BIOHAZ-AHAW-CONTAM) on the Evaluation of public and animal health risks at delayed post-mortem inspection (PMI) in ungulates. The terms of references are to assess the effectiveness (in terms of its sensitivity in detecting the diseases/conditions listed) of PMI when carried up

to 24h and up to 72 hours after slaughter or arrival in the establishment, in comparison to when it is carried out immediately after slaughter or arrival in the game-handling establishment. Part of the AHAW tasks included to implement a survey to meat inspectors to evaluate the effect of the delay in detecting the listed diseases by assessing the impact of the delay in the probability of detection of compatible lesions/patterns. The WG provided suggestions to improve the questions for future surveys and to ask the questions in a more objective way. The WG also provided suggestions for further analysis. The differences in the results from the surveys can be used to reflect the uncertainty about the true value of the quantities of interest. An EKE is proposed as a potential way to do so. It remains to be clarified how the probability of the overall conclusion can be estimated.

The WG also discussed the potential usefulness of the approach used to quantify uncertainty in easiness of application of killing methods in the rabbit welfare opinion. In that survey the questions were asked using the Likert scale, while in this case (national reference laboratories survey) a probability was directly elicited. The WG suggested to directly use the estimates received in the survey to express uncertainty.

6. Any Other Business

Improvement of communication with cross cutting WG: The WG was informed that the WG will be moved to TEAMS, a platform aimed to increase collaboration between WG members. The WG was encouraged to also ask for support and questions in between meetings and to share the plans for UA before they are implemented to increase the chance of getting feedback still implementable during the ongoing respective mandates.

<u>The dates for the future WG meeting in 2020 are:</u>

- 7th WG uncertainty – teleconference (3-hour TC): 11 May 2.00-5.00 pm
  It is proposed to prolong this TC to a 6-hour TC with an additional morning 3 hours session from 9.30 am to 12.30 pm (TBC)
- 8th WG uncertainty - physical meeting (1.5 day): 14 July full day - 15 July ½ day am
- 9th WG uncertainty – teleconference (3-hour): 15 October 2.00-5.00 pm
- 10th WG uncertainty - physical meeting (1.5 day): 14 December ½ day pm - 15 Dec. full

SCIENTIFIC COMMITTEE AND EMERGINC RISKS UNIT

EFSA cross cutting Working Group

on Uncertainty

Minutes of the 5th cross cutting WG on Uncertainty (WGU)

Teleconference, 19 December 2019 (14.00-17.00)

(Agreed on 13 January 2020)

Working Group Members:

- **Panel and external experts:**

Dominique Bicout, Peter Craig, Andrew David Hart, Konstantinos Koutsoumanis, Maarten Nauta, Giuseppe Ru, Wopke van der Werf, Salomon Sand and Heather Wallace, Ullrika Sahlin

- **EFSA:**

SCER unit : Caroline Merten, Jean -Lou Dorne

AMU unit: Federica Barrucci, Laura Martino, Olaf Mosbach- Schulz, Elisa Aiassa

COMCO unit: Anthony Smith

1. Welcome and apologies for absence

The Chair welcomed the participants and the new members to the WG, Elisa Aissa from the AMU unit and the external expert Ullrika Sahlin. Apologies were received by Laura Ciccolallo, Fulvio Barizzone from the EFSA AMU unit and by Julio Alvarez.

2. Adoption of agenda

The agenda was adopted without changes.

3. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management, EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process.

4. Integration of uncertainty analysis into the scientific assessment process

The WG was presented with an overview of the 4-step approach (plan, do, verify and report) for EFSA's scientific assessments based on (EFSA, 2015, 2018). Uncertainty analysis goes through all the steps of the scientific assessment process. It starts at the protocol development step where first an explicit description of the mandate or question that must be answered is given (problem formulation). For broad questions, this involves defining as clearly as possible all possible potential underpinning sub-questions and their relationship. Then, in the data collection and analysis part uncertainties in the methods and in the evidence need to be identified and assessed. It is important to have a process in place to identify systematically the evidence that is relevant for the formulated problem/question. Clear eligibility criteria should be established upfront to justify how bias has been minimised in this step of the process. If only key studies/specific datasets are selected, a defendable rationale should be provided. Uncertainty in the evidence retrieved from literature can be assessed by looking into internal and external validity, precision which can be assessed either at individual level or at the level of the body of evidence. Publication bias and unexplained inconsistency of results are assessed at the level of the body of evidence. One example of a critical appraisal tool is the OHAT/NTP tool. At the evidence synthesis step possible ways to account for uncertainty in the evidence are (modified from Higgins and Green 2011): (1) to restrict primary analysis to studies with lower risk of bias and perform a sensitivity analysis to show how conclusions might be affected if studies at high risk of bias were included; (2) to present multiple (stratified) analysis; (3) to present all studies and provide a narrative discussion of risk of bias; (4) to quantify uncertainty on domains most affected by risk of bias. It was highlighted that experience in EFSA to assess uncertainty in the evidence extracted from databases is less advanced. Tools that supports assessment of

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf

metadata are lacking and often the reference document to the databases are more focused on promoting best practices in handling, documenting and exchanging digital data than on assessing the quality of the data. The WG was reminded of the ongoing initiatives in EFSA on evidence appraisal and the SC WG on the draft framework for protocol development which provides recommendations on how to cover uncertainty analysis in the planning phase.

The WG discussed the challenge to evaluate the risk of bias and the need to encourage experts to do so. Although it may be resource intensive there are options to prioritize with tiered approaches or doing a sensitivity analysis at sub question level. It was also noted that in some panels such e.g. the plant health panel the problem is not about having too many studies, but not having enough standardized studies. They rarely exclude studies because of bad quality. Therefore, internal validity is not a problem, but external validity is. The WG agreed to exchange experiences on the use of CAT in the future and they agreed that an alignment of the current uncertainty check list and the current draft report on protocol development is needed.

5. Support to the implementation of the uncertainty guidance document in ongoing mandates in 2019

The WG discussed the following matters:

- Feedback from the **AHAW panel** on:
    - *Template on implementation of uncertainty:* The uncertainty template's aim is to keep track of the implementation of the uncertainty analysis in all EFSA scientific opinions according to the guidance document. To this end the creation of a "database/repository" is planned that helps to keep track of how UA has been conducted in the context of different opinions to help build capacity for panel and WG experts in the future. It is proposed to publish the repository. The template was aimed to be short without adding/replicating work for the unit and to be as standardized as possible. AHAW panel provided feedback on the proposed template which need further clarifications before being usable. Potential users/beneficiaries of the template (and repository of the filled templates) were identified to be the AHAW panel (i.e., source of information for future opinions on how UA was performed/could be performed), EFSA (other panels and staff dealing with this matter) and the general public at large (how EFSA is tackling uncertainty). The panel advised to keep the template to a minimum and use drop-down menus if possible.

The WG agreed with the suggestions from the AHAW panel and to follow up on these. In addition it was suggested to add an entry regarding lessons learnt from the applied uncertainty analysis.

- *Communication on uncertainty*: It was highlighted that, when using probabilities for expressing uncertainties, the recommendation provided in the guidance document (EFSA, 2019) on communication on uncertainty (i.e. to provide the quantitative estimate before the qualitative description) is not always followed.

  The WG was encouraged to remind their respective panel about the existing guidance document on how to communicate best on uncertainty to various target audiences. The communication colleagues will receive training in 2020 on this guidance document to ensure full alignment between the risk assessors and communicators on how to report on uncertainty.

- Feedback from the **BIOHAZ panel** on how uncertainty is addressed in the mandate on Update and review of control options for Campylobacter in broilers at primary production (EFSA-Q-2018-00676). In particular, feedback was provided on the expert knowledge elicitation (EKE) to rank the preventive measures. The first step in the EKE was to assess what the probability was that, if the specified control option was implemented by all broiler producers in the EU that are not currently using it, average annual incidence of campylobacteriosis cases in the whole EU population caused by Campylobacter in broiler meat produced from chickens raised in the EU would reduce by more than 10% (compared to the current level), other things being equal? This first step allowed to prioritize the 21 risk reduction options. In a second step, specific control options were evaluated further by a second EKE where the following question for each prioritized control option was answered: If the specified control option is implemented by all broiler producers in the EU that are not currently using it, what will be the resulting % reduction (compared to the current level of implementation) in average annual incidence of campylobacteriosis cases in the whole EU population caused by campylobacter in broiler meat produced from chickens raised in the EU, other things being equal?

- Feedback from **COMCO unit** on communication activities on uncertainty: The WG was presented with an overview of EFSA opinions published in 2019 and planned to be published in 2020 where uncertainty analysis has been addressed. It was clarified to the WG that news stories are not necessarily developed for each published output. A few examples were provided e.g. a section on frequent asked questions (FAQs) on the EFSA draft outputs on cumulative assessment groups of pesticides for the thyroid and nervous

system. In that section questions such as e.g. -What is an uncertainty analysis? Why did EFSA carry out an uncertainty analysis? How does EFSA express uncertainty? - were answered.

6. Towards a new OECD Harmonised Template to implement EFSA horizontal guidance documents in the chemical risk assessment area - feedback from outsourced contract

The WG was provided with the context for the development of a new OECD Harmonised Template to implement EFSA horizontal guidance documents in the chemical risk assessment area within the framework of an outsourced contract to develop further the EFSA OpenFoodTox Database. Parts of new developments are to design a template for weight of evidence, biological relevance and uncertainty analysis and to update mechanistic (OHT 201) and toxicokinetic OECD template.

The WG agreed to review the template to ensure alignment with the uncertainty guidance document.

7. Any Other Business

A tailor-made training on uncertainty was held in November 2019 for the CONTAM panel. Some follow up actions from this training are planned for 2020.

<u>The dates for the future WG meeting in 2020 are:</u>

- 6th WG uncertainty - physical meeting (1.5 day): 10 March ½ day pm -11 March full day
- 7th WG uncertainty – teleconference (3-hour TC): 11 May 2.00-5.00 pm
- 8th WG uncertainty - physical meeting (1.5 day): 14 July full day - 15 July ½ day am
- 9th WG uncertainty – teleconference (3-hour): 15 October 2.00-5.00 pm
- 10th WG uncertainty - physical meeting (1.5 day): 14 December ½ day pm - 15 Dec. full

SCIENTIFIC COMMITTEE AND EMERGINC RISKS UNIT

EFSA cross cutting Working Group

on Uncertainty

Minutes of the 4th cross cutting WG on Uncertainty (WGU)

Physical meeting, 03 October 2019 (09.00-18.00)

(Agreed on 10 October 2019)

Participants

- Working Group Members:

  Dominique Bicout, Julio Alvarez, Peter Craig (pm only), Andrew David Hart, Konstantinos Koutsoumanis (via TC), Maarten Nauta, Giuseppe Ru, Wopke van der Werf, Salomon Sand and Heather Wallace (via TC)

- EFSA:

  SCER unit: Caroline Merten

  AMU unit: Federica Barrucci, Laura Martino, Fulvio Barizzone and Olaf Mosbach- Schulz

1. Welcome and apologies for absence

The Chair welcomed the participants. Apologies were received by Laura Ciccolallo from EFSA AMU unit.

2. Adoption of agenda

The agenda was adopted without changes. Due to time constraints the agenda items on Uncertainty training and Integration of scientific assessment process into the uncertainty check list had to be postponed to the next WG meeting.

3. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process

4. Feedback from discussion at Scientific Committee (SC) plenary in 13th September on the status of the implementation of uncertainty guidance across EFSA

The WG was presented with a feedback on this agenda item from the SC plenary on 13th September 2019. The SC was reminded of the implementation plan of the guidance on uncertainty in scientific assessments that was agreed in 2018 after the publication of both, the guidance on how to analyse uncertainty in scientific assessments and its companion opinion detailing the principles and methods behind the guidance. It was agreed to start the implementation in RASA after the renewal of the panels (by mid-2018) and to implement the guidance in REPRO only gradually from 2021 onwards, apart from single outputs per unit previously agreed with DG SANTE. It was further agreed with the RASA units to start the implementation in the RASA department in autumn 2018 by first providing panel specific tailor-made trainings to the AHAW (last trimester 2018), BIOHAZ (first trimester 2019) and CONTAM panel (last trimester 2019). Hence the implementation is only in its very early phase with very few opinions published (except for plant health) where the guidance had been applied. Also, the capacity within the panels to apply the guidance without support varies highly. The different RASA panels (PLH, AHAW, BIOHAZ and CONTAM) reported back to the SC on their current implementation status of the uncertainty guidance and highlighted in which area they would need additional support. Also, the benefits of having applied the guidance and related challenges were discussed. It was concluded to repeat this update on the implementation status once per year at the SC.

5. . Support to the implementation of the uncertainty guidance document in ongoing mandates in 2019

The WG discussed the following mandates where the uncertainty GD has been implemented:

- AHAW panel: Feedback on how uncertainty is addressed in the following four mandates:
  - Slaughter of animals for human consumption (domestic birds) (EFSA-Q-2018-00715) and Killing for other purposes than slaughter (domestic birds) (EFSA-Q-2018-00716): both opinions were adopted in AHAW September 2019 plenary meeting.
  - Slaughter of rabbits for human consumption and the killing of rabbits for other purposes (EFSA-Q-2018-00909) and Health and welfare of rabbits farmed in different production systems (EFSA-Q-2018-00593): both opinions are planned for adoption in the AHAW November 2019 plenary meeting.
  - African Swine Fever (ASF) Risk assessment in south eastern Europe (EFSA-Q-2019-00049): TOR 1 (to estimate the risk of spread of ASF in the south-eastern countries of Europe after introduction; and to identify the main risk factors (indicators) for the spread of the disease) of this opinion was adopted in AHAW September 2019 plenary meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

The WG discussed and exchanged on how uncertainty was implemented in these risk assessments and how uncertainty was reported in the conclusions of these mandates. The WG provided suggestions for possible improvements of addressing the uncertainty in the assessments and also on how to express uncertainty in the scientific assessment's conclusion. These suggestions included additional considerations on uncertainty in problem formulation, model conceptualization and clearer expression of uncertainty in the conclusion. Uncertainty analysis should be focused on what the risk manager needs to know most importantly for their decision making.

- BIOHAZ panel: Feedback on how uncertainty is addressed in the mandate on Update and review of control options for Campylobacter in broilers at primary production (EFSA-Q-2018-00676)

The WG discussed and exchanged on how uncertainty is planned to be implemented in this opinion. Next steps include implementing and running the models with quantified uncertainties to estimate the effect on public health by reducing flock prevalence and concentrations in intestinal content in broilers, finalising the evidence tables and related uncertainty and preparing for an expert knowledge elicitation planned for November 2019 with the aim of weighting model predictions with expert opinion on their validity and to rank all control options on the basis of their contributions to reducing risk.

- PLH panel: The WG was presented with the methodology to provide a quantitative assessment of pest related criteria required to rank candidate priority pests as defined by regulation (EU) 2016/2031.Within this context 28 pests with 74 pest-host combinations were ranked by eliciting expert knowledge on 3 to 4 questions per combination. It is expected that additional 50 to 100 new candidate pests need to be ranked by 2022 and additional 100 -200 high risk plants. To manage this workload a revised workflow and protocol was presented to the WG: the steps cover among others performing an extensive literature search, listing the limitations of the evidence, summarizing the uncertainties, eliciting the distribution of possible scenarios from the experts and agreeing on consensus scenarios and final judgment with fitted distribution. For each step of the revised protocol responsibilities between EFSA staff and WG members were specified.

The WG appreciated the impressive progress made in PLH and suggested distinguishing more clearly between risk and uncertainty in the expression of the conclusions. The WG agreed on the need to try to assess the uncertainty on the evidence in a harmonised way by using standard approaches as far as possible within the time and resource constraints.

6. Any Other Business

The WG discussed the format of future WG meetings to support the implementation of uncertainty guidance in 2020. It is planned to keep current mixed composition of the WG as implementation is still in its early phase and the WG members benefit from each other's experiences and feedback on implementing uncertainty analysis in their respective panels. It was decided to switch between physical 1 day meetings and teleconference 4 hour meetings next year to allow more time for this exchange to happen.

7. Next meeting(s)

The date for the remaining WG meeting in 2019 is the following:

- 5th meeting cross cutting WG uncertainty: (physical 1 day meeting) –December (exact date to be confirmed)

SCIENTIFIC COMMITTEE AND EMERGINC RISKS UNIT

EFSA cross cutting Working Group

on Uncertainty

Minutes of the 3rd cross cutting WG on Uncertainty (WGU)

Teleconference, 24 June 2019 (14.00-17.00)

(Agreed on 02 July 2019)

Participants

Working Group Members:

- **Panel and external experts:**

Dominique Bicout, Julio Alvarez, Peter Craig, Andrew David Hart, Konstantinos Koutsoumanis, Maarten Nauta, Giuseppe Ru, Salomon Sand.

- **EFSA:**

SCER unit: Caroline Merten

AMU unit: Federica Barrucci, Laura Martino and Fulvio Barizzone

COMCO: Tony Smith (for agenda item 3)

1. Welcome and apologies for absence

The Chair welcomed the participants. Apologies were received by Laura Ciccolallo and Olaf Mosbach from EFSA AMU unit and Heather Wallace and Wopke van der Werf.

2. Adoption of agenda

The agenda was adopted without changes.

3. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management, EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process. Additional interests were declared by Andy Hart orally at the beginning of this meeting. No conflict was identified.

4. Guidance for risk assessors on how to report the different expressions on uncertainty

The WG was presented with an overview on the recently published guidance document on how to communicate and report best on uncertainty[2].
In particular, the discussion focused on the recommendations for risk assessors on how to communicate on uncertainty. It was agreed that the WG members remind their respective panels about these recommendations to ensure alignment in the reporting on uncertainty. The WG agreed that it was important to collaborate with the newly established EFSA WG on social science.

5. Ad hoc support requests on ongoing & new mandates in 2019

The WG discussed the three following mandates where the uncertainty GD has been implemented:

- Mandate on Scientific opinion on dietary references values (DRVs) for sodium (EFSA-Q-2011-01224): The WG was provided with an overview on the main

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] https://www.efsa.europa.eu/en/efsajournal/pub/5520

feedback points from the public consultation in relation to the uncertainty analysis. The WG discussed the expected advantages of proactively publishing the evidence dossier used during an expert knowledge elicitation and a comprehensive description of the process of the exercise. They also acknowledged though that publication of both reports would have implied additional time and resources that were not available in the case of sodium exercise. The revised opinion along with the technical report on the public consultation will be discussed at the Nutri panel in the first week of July 2019.

- Mandate on the African Swine Fever Risk assessment in south eastern Europe & risk ranking matrices (EFSA-Q-2019-00049): The WG discussed how uncertainty was implemented in this mandate and the WG provided suggestions for possible improvements. The opinion will be discussed at the AHAW panel in the last week of June 2019.

- Applying uncertainty analysis to cumulative risk assessment to pesticides: The WG was presented with a summary on how uncertainty was addressed in the following reports: (1) Scientific report on establishment of cumulative assessment groups of pesticides regarding their combined effects on the nervous system (EFSA-Q-2017-00434) and (2) Scientific report on establishment of cumulative assessment groups of pesticides regarding their combined effects on the thyroid (EFSA-Q-2017-00436). The outputs aimed to be well aligned with the following EFSA Guidance document: Uncertainty Assessment, Weight of Evidence, Expert Knowledge Elicitation and Communications on Uncertainty. It will provide a good example for a case-specific assessment involving 2D MC including quantification of overall uncertainty associated with model outputs. The two outputs are planned to be published by end of September 2019.

6. Any Other Business

The agenda item on Integration of scientific assessment process into the uncertainty check list was postponed to the next WG meeting due to time constraints.

The dates for the remaining WG meetings in 2019 are the following:

- 4th meeting cross cutting WG uncertainty: (1day physical meeting) 3 October
- 5th meeting cross cutting WG uncertainty: (TC: 4 hours) – 10 December

SCIENTIFIC COMMITTEE AND EMERGINC RISKS UNIT

EFSA cross cutting Working Group

on Uncertainty

Minutes of the 2nd cross cutting WG on Uncertainty (WGU)

Teleconference, 3 April 2019 (9.30-12.45)

(Agreed on 08 April 2019)

Working Group Members:

- **Panel and external experts:**

Dominique Bicout, Julio Alvarez, Peter Craig, Andrew David Hart, Konstantinos Koutsoumanis, Maarten Nauta, Giuseppe Ru,

- **EFSA:**

SCER unit: Caroline Merten

AMU unit: Federica Barrucci, Laura Martino and Fulvio Barizzone

1. Welcome and apologies for absence

The Chair welcomed the participants. Apologies were received by Laura Ciccolallo from EFSA AMU unit.

2. Adoption of agenda

The agenda was adopted without changes.

3. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management, EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process. Additional interests were declared by Andy Hart orally at the beginning of this meeting. No conflict was identified.

4. Monitoring implementation of uncertainty Guidance document

The WG discussed and reviewed a template to capture the information to report on each mandate in which the uncertainty guidance document has been implemented. The template contains information on the different methodologies used to characterise the individual uncertainties and the overall uncertainty. The template will be filled out by either the WG chair or scientific coordinator before a mandate's outputs will undergo public consultation and when the output will be adopted as final for publication. The aim of this information is to serve as a repository for illustrative examples on how uncertainty analysis has been assessed within the implementation of the new EFSA guidance document on uncertainty[2].

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf

[2] https://www.efsa.europa.eu/en/efsajournal/pub/5123

5. Ad hoc support requests on ongoing & new mandates in 2019

The WG discussed two ad hoc requests to support the implementation of the uncertainty GD in the following mandates:

- Mandate on Scientific opinion on dietary references values (DRVs) for sodium (EFSA-Q-2011-01224): The WG discussed how the overall uncertainty was characterised for that mandate. The opinion was published for public consultation on 5 April 2019.
- Mandate on Scientific opinion providing an update and review of control options for Campylobacter in broilers at primary production (EFSA-Q-2018-00676): The WG discussed the general plan on how to address uncertainty in relation to the different control options.

6. Support on panel tailored training materials

- Biological hazard (BIOHAZ) tailored training: The training took place 5- 6 March 2019. The WG discussed the feedback from the plenary discussion on the break out and required follow ups. The case studies developed for this specific training will need to be revised to serve best as illustrative examples for the BIOHAZ panel and working group experts.

- Animal Health and Animal Welfare (AHAW): The WG was informed about the finalisation of the case study and subsequent discussion of it and the checklist at the AHAW Panel plenary on 21 March 2019.

The WG agreed to use the same version of the checklist (version3.1) in both panels (AHAW and BIOHAZ) in the future when implementing the guidance document in the respective working groups. It was agreed that the checklist is a working document. The current version is shown in annex 1. It was also agreed that potential updates to the checklist would be discussed at the regular WG meetings.

The WG agreed to discuss at their next meeting an agenda item on the communication aspects on how to report best on uncertainty based on the recommendations for risk assessors from the recent EFSA guidance document on how to communicate on uncertainty[3].

[3] https://www.efsa.europa.eu/en/efsajournal/pub/5520

Further support from the WG will be needed in the second and third trimester 2019 to develop case studies for tailored panel training materials for the panel on contaminant hazards.

7. Any Other Business

The agenda item on Integration of scientific assessment process into the uncertainty check list was postponed to the next WG meeting due to time constraints.

The dates for the remaining WG meetings in 2019 are the following:

- 3rd meeting cross cutting WG uncertainty: (1day physical meeting) – 24 June
- 4th meeting cross cutting WG uncertainty: (TC: 4 hours) - 3 October
- 5th meeting cross cutting WG uncertainty: (TC: 4 hours) – 10 December

ANNEX 1: CHECKLIST FOR APPLYLING EFSA'S UNCERTAINTY GUIDANCE IN A CASE-SPECIFIC ASSESSMENT – Version 3.1

Note: iteration of some steps may be required. *GDn.n: see section n.n of the EFSA Uncertainty Guidance.

☐ A. When Interpreting the Terms of Reference (ToRs) for the assessment (except for open questions)

☐ 1. **Check the ToR questions are well-defined. If not, make a well-defined interpretation, consulting with the Panel and/or requestor if needed.** A *well-defined question or conclusion* (GD10*) refers to an outcome or quantity that could (in principle) be observed or measured without ambiguity in the real world, or obtained from a defined scientific procedure. Check each word has a defined meaning and that the population, region & time period of interest are specified. For a *variable* quantity, specify which statistic(s) and/or quantile(s) are required. Also define the question the assessment will actually answer, if it differs from that posed by the ToR, so that this can be taken into account when assessing overall uncertainty in step C5.

☐ B. When planning the data and methodologies for the assessment

☐ **1. Consider the data and methodologies you plan to use in the assessment and identify any major uncertainties associated with them.** See next page #1 for types of uncertainties to look out for (GD7).

☐ **2. Decide whether it would be beneficial to quantify any of these uncertainties within the assessment calculations or procedure, rather than later when assessing overall uncertainty.** If the former, decide how to express (GD11,12) and combine (GD13-15) these uncertainties and integrate this into the planning and implementation of your assessment. Seek specialist support if needed.

☐ **3. Consider including sensitivity or influence analysis in your uncertainty analysis (UA), to help when prioritising uncertainties and/or when assessing overall uncertainty** (GD8).

☐ **4. Make a plan for the assessment & UA** and seek feedback from the Panel if appropriate. **Include meeting time for assessing overall uncertainty** (C5 below).

☐ C. When carrying out the assessment and uncertainty analysis

☐ **1. Be alert for additional sources of uncertainty and add them to your list.** See next page #1 (GD7).

☐ **2. If the assessment involves calculations, review the preliminary results and consider again whether it would be beneficial to quantify any (more) uncertainties within the calculations** (GD4.2-4.4) **or subject them to sensitivity analysis** (GD8)**.** If so, integrate this into a revised plan for the remaining steps of your assessment & UA.

☐ **3. When developing draft conclusions on the ToRs, ensure they are well-defined** (see A1 above for explanation). When a conclusion *directly* answers a ToR that is already well-defined, this should be sufficient.

☐ **4. Review all uncertainties which were not yet quantified and list or tabulate them concisely, ordered or grouped in a way that will be helpful for readers. Decide whether to quantify some of them separately (individually or in groups) before assessing overall uncertainty.** It may be easier to make separate judgements for uncertainties affecting different parts of the assessment (GD9), or separate uncertainties affecting model inputs from those about how model outputs relate to real outcomes. If you do this, decide how you will express the contribution of each group (GD11,12) and whether to combine them by calculation or expert judgement (GD13-15).

☐ **5. Quantify the overall uncertainty of each conclusion.** If there are many conclusions, prioritise those where the uncertainty will have most impact on decision-making, if this is known; otherwise, prioritise those conclusions that address the ToRs most directly and/or are more uncertain. If no uncertainties were quantified in earlier steps, assess the combined impact on each conclusion of all the identified uncertainties by expert judgement

(GD4.1, Figure 6, steps C-E). If any uncertainties were quantified in earlier steps, take the results of that into account together with all the other uncertainties you have identified, either by expert judgement (GD16,16.1) or by a combination of expert judgement and calculation (GD16.2). **Use a formal or semi-formal expert knowledge elicitation procedure for the judgements required to quantify overall uncertainty.** For options and basic procedure, see next page #2.

☐ **D. When reporting the assessment and its conclusions**

☐ **1. Report the methods and results of the uncertainty analysis in the same way as other parts of the assessment**, making sure they can be easily found by readers of the Opinion or Report (GD17).

☐ **2. Report each conclusion with your quantitative expression of its overall uncertainty**, making clear this involves expert judgement**. Report also the rationale for the assessment of uncertainty** with the conclusion and/or in the body of the Report or Opinion. **Highlight any sources of uncertainty you were unable to include in the quantitative expression, and state what assumptions were made about them** (GD17). **If unable to quantify any uncertainties, report that the probability of the conclusion is unknown.** If legislation or risk managers require firm conclusions, define the level of certainty required for these and report only conclusions for which this level is met (GD17 #5).

SUPPORTING INFORMATION (#1) Types of uncertainties to look for in an assessment (GD 7)

The Uncertainty Guidance offers the following table of general types of uncertainties. Use the table to help *identify* uncertainties; it is not necessary to classify them. Over time, EFSA Panels are encouraged to develop lists of specific types of uncertainties which they commonly encounter in their work. Lists provided by other methodologies (e.g. EFSA's framework for evidence based scientific assessments, GRADE, etc.) should be used where relevant (GD7.2).

Uncertainties associated with data	Uncertainties associated with assessment methodologies
1. Ambiguity	1. Ambiguity
2. Accuracy and precision of the measures	2. Excluded factors
3. Sampling uncertainty	3. Distributional assumptions
4. Missing data within studies	4. Use of fixed values
5. Missing studies	5. Relationship between parts of the assessment
6. Assumptions about inputs	6. Evidence for the structure of the assessment
7. Statistical estimates	7. Uncertainties relating to the process for evidence from literature
8. Extrapolation uncertainty (i.e. limitations in external validity)	8. Expert judgement
	9. Calibration or validation with independent data
9. Other uncertainties (including uncertainty due to conflicting evidence)	10. Dependency between sources of uncertainty
	11. Other uncertainties

SUPPORTING INFORMATION (#2) Basic principles for quantifying overall uncertainty by expert judgement

The Guidance uses probability judgements to quantify overall uncertainty about whether a conclusion is correct, and about estimated quantities. The Guidance recommends that these judgements should be obtained by formal or semi-formal 'expert knowledge elicitation' (EKE) methods, (GD12.6). Formal EKE methods are described in EFSA's 2014 Guidance on EKE and require weeks to months to implement. Semi-formal EKE can be done within a single Working Group (WG) meeting and should follow the steps below, to support good quality judgements and guard against biases (request advice/support from EFSA AMU or Standing WG on Uncertainty if needed):

- Ensure each conclusion or estimate to be considered is expressed in well-defined terms (see A1 in Checklist).
- Decide which WG members will participate and invite additional experts (e.g. from Panel) if appropriate.
- Identify a suitable form for expressing overall uncertainty: a probability distribution (GD12.1) or probability bounds (GD12.2) for an estimate; a probability (GD12.1), approximate probability (GD12.2) or the approximate probability scale (GD12.3, see Table below) for a conclusion, or for an estimate falling in a specified range.

- Plan the agenda for the elicitation session, allowing at least 2 hours per judgement and including appropriate elements to guard against bias (e.g. eliciting plausible limits before central estimates; ask for advice if needed).
- Add 1 hour for training in probability judgements unless all participants are already familiar with it.
- Identify a suitable person who is not making judgements to facilitate: their job is to keep to time and ensure a balanced discussion based on evidence and reasoning. Identify a second person to take detailed notes.
- In the meeting, after training (if needed), for each conclusion or estimate in turn:
  - Have a summary of the evidence and uncertainties to hand (e.g. from the draft opinion or report)
  - Each participant makes their own judgement(s) privately, taking account of the evidence and uncertainties
  - Display the individual judgements together, discuss reasons for differences, and discuss whether higher or lower judgements could be plausible (to guard against over-confidence)
  - Facilitated discussion to elicit a consensus judgement: what a rational impartial observer would judge, having seen the evidence, uncertainties and individual judgements and heard the discussion
  - It is essential to elicit also the group's rationale for the consensus judgement.
  - If there are any uncertainties which the experts cannot include in their quantitative judgements, agree and record what assumptions will be made about them
  - Record the *consensus judgement*, the *consensus rationale* for that judgement, and *which experts contributed*
  - If individual judgements and discussion are recorded, do not attribute them to the individuals involved.

Approximate probability scale recommended for harmonised use in EFSA, where appropriate (GD12.3):

Probability term	Subjective probability range	Additional options	
Almost certain	99-100%	More likely than not: >50%	Unable to give any probability: range is 0-100% Report as 'inconclusive', 'cannot conclude', or 'unknown'
Extremely likely	95-99%		
Very likely	90-95%		
Likely	66-90%		
About as likely as not	33-66%		
Unlikely	10-33%		
Very unlikely	5-10%		
Extremely unlikely	1-5%		
Almost impossible	0-1%		

EFSA cross cutting Working Group

on Uncertainty

Minutes of the cross cutting WG on Uncertainty (WGU)

Teleconference, 23 November 2018(9.30-12.30)

(Agreed on 29 November 2018)

Working Group Members:

- **Panel and external experts:**

Dominique Bicout, Peter Craig, Andrew David Hart, Konstantinos Koutsoumanis, Maarten Nauta, Giuseppe Ru, Salomon Sand, Wopke van der Werf, Heather Wallace

- **EFSA:**

SCER unit: Caroline Merten

AMU Unit: Laura Ciccolallo, Laura Martino, Olaf Mosbach, Federica Barrucci

1. Welcome and apologies for absence

The Chair welcomed the participants. Apologies were received from Julio Alvarez and Barizzone Fulvio (AMU unit).

2. Adoption of agenda

The agenda was adopted without changes.

3. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management, EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

4. Terms of references of cross cutting WG uncertainty

EFSA has developed a harmonised approach to assessing and taking account of uncertainties in food safety, and animal and plant health. This approach aims at increasing the transparency of the resulting scientific advice and make it more robust for decision-making. The EFSA Scientific Committee (SC) guidance on Uncertainty in EFSA's scientific assessments offers a diverse toolbox of scientific methods and technical tools for uncertainty analysis (published in January 2018)[2]. It is sufficiently flexible to be implemented in such diverse areas as plant pests, microbiological hazards and chemical substances. A separate opinion has been published separately describing in detail the principles and methods supporting the concise Guidance Document[3].

The long-term goal is that the new guidance on uncertainty will be an integral step in all EFSA's scientific assessments. EFSA will implement the approach in two stages. In general scientific areas, the guidance will apply from autumn 2018 after the renewal of the Authority's scientific panels. In regulated products areas such as pesticides, food additives or food contact materials it will be phased in later on, in light of the experience gained in the 'non-regulated' areas.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] https://www.efsa.europa.eu/en/efsajournal/pub/5123
[3] https://www.efsa.europa.eu/en/efsajournal/pub/5122

To support the implementation of the above-mentioned EFSA SC Guidance document, EFSA has established a cross-cutting EFSA Working Group on uncertainty (cross-cutting WG uncertainty).

Terms of reference:

The objective of the cross-cutting WG uncertainty is to support EFSA panels and units and, in particular, those from the Risk Assessment and Scientific Assistance (RASA) department in implementing the EFSA guidance on uncertainty by:

(i) Providing scientific advice and support to ad hoc requests on how to apply the uncertainty guidance document across the various EFSA opinions, guidance documents, technical and scientific reports ;

(ii) Providing scientific advice and support to the development of panel tailor made training materials;

(iii) Ensuring a sustainable capacity building across the panels on uncertainty analysis;

The chairmanship of the cross-cutting WG uncertainty remains within the SCER unit.

The composition of the cross cutting Working Group is available on the EFSA website.

The WG discussed and agreed on the terms of references and working process of the cross cutting WG.

5. Monitoring implementation of uncertainty GD

The WG agreed to develop a template to capture in which upcoming EFSA opinions the uncertainty GD has been implemented and how. This information will be published next year in the EFSA knowledge junction[4].

6. Ad hoc support requests on ongoing & new mandates in 2018

The WG discussed two new ad hoc requests to support the implementation of the uncertainty GD in the following mandates:

- Mandate on Scientific opinion on dietary references values (DRVs) for sodium (EFSA-Q-2011-01224): The WG discussed a template to record in a structured way the uncertainties identified on the evidence and on the methods used for the scientific assessment.

[4] https://zenodo.org/communities/efsa-kj?page=1&size=20

- Mandate on Scientific opinion providing an update and review of control options for Campylobacter in broilers at primary production (EFSA-Q-2018-00676): The WG for this mandate will meet for the first time in early December.

7. Support on panel tailored training materials

The WG discussed the next steps in facilitating the implementation of the uncertainty analysis in the Animal Health and Animal Welfare panel: checklists on what to consider at the different steps of the risk assessments process to integrate uncertainty analysis will be developed.

Further support from the WG will be needed:

- in the first trimester of 2019 to develop case studies for tailored panel training materials for the panel on biological hazards;
- in the second trimester 2019 to develop case studies for tailored panel training materials for the panel on contaminant hazards;

8. Any Other Business

3 teleconferences and one physical meeting will be organized in 2019. The dates will be fixed in early January 2019.