

**Approaches
to assess and
manage scientific
uncertainty:
examples from
EU ANSA Agencies**



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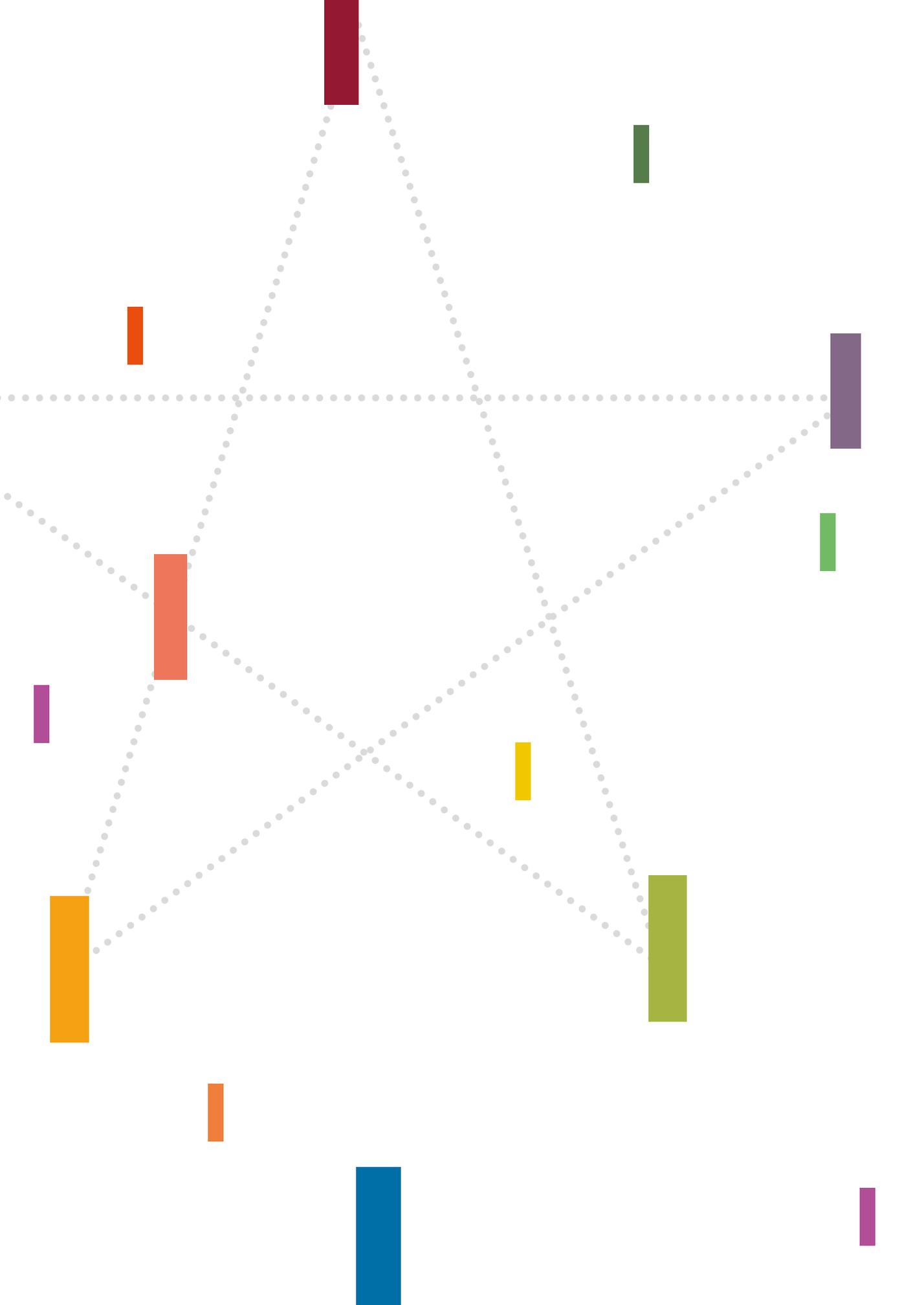


Approaches to assess and manage scientific uncertainty: examples from EU ANSA Agencies

Authors

- Mike Catchpole (Chief Scientist, Office of the Chief Scientist, ECDC)
- William Cockburn (Head of Prevention and Research Unit, EU-OSHA)
- Beatrice Comby (former Director of Capacity Building, Frontex)
- Hubert Deluyker (former Scientific Adviser to the EFSA Executive Director)
- Hans-Georg Eichler (Senior Medical Officer, EMA)
- Joanna Goodey (Head of Freedoms and Justice Department, FRA)
- Paul Griffiths (Scientific Director, EMCDDA)
- Marta Hugas (Chief Scientist, EFSA)
- Demosthenes Ikonomidou (Head of Operational Security Unit, ENISA)
- Derek J. Knight (Chair of EU-ANSA, Senior Scientific Officer, ECHA)
- Erika Mezger (Deputy Director, Eurofound)
- Lars Fogh Mortensen (Head of Group Networks and International Cooperation, EEA)
- Therese Murphy (Head of Operations, EIGE)
- Howard Needham (corresponding author, Expert Scientific Liaison, ECDC)
- Steve Purser (Head of Technical Competence Department, ENISA)
- Antonio Ranieri (Head of Department for Learning and Employability, Cedefop)
- Barbara Schmidt (Monitoring and Evaluation Officer, Eurofound)
- David Stanners (Head of Programme, Partnerships and Network, EEA)
- Agnieszka Szcześniak (Assistant to Director of Capacity-Building Division, Frontex)





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Executive summary

EU Agencies within the EU Agency Network for Scientific Advice (EU ANSA) provide scientific advice to EU policy makers across a broad spectrum of disciplines from public health to gender equality. The primary role of the EU Agencies in ANSA is to collect, use and communicate scientific evidence, and hence there is an onus to identify and communicate the inherent uncertainty that is intrinsic to the scientific process. Doing so ensures that policy makers better understand the strength of the evidence base presented, and that resulting policy is made on the basis of fully informed choice.

This study presents a preliminary exploration of approaches taken by EU ANSA members to address scientific uncertainty in their scientific outputs. It aims to provide a basis to identify common themes and issues, and stimulate further thinking about the definition, identification and communication of scientific uncertainty in scientific advice outputs from the Agencies.

The methodology involved development of a simple framework to assess; a) overarching guidance on handling uncertainty in each agency, and b) specific scientific outputs from each agency to understand how uncertainty was handled 'in practice'. Participating Agencies were also invited to submit pertinent examples of scientific outputs which illustrate good practice and challenges in handling scientific uncertainty.

This review unsurprisingly revealed differences in approaches and terminologies within the 12 EU ANSA Agencies that were included in this survey, reflecting the differences between Agencies in terms of the policy and subject matter environment that they work within, and the different scientific disciplines that their work is predominantly based upon. For some Agencies, terms such as 'risks' and 'limitations' are commonly used in addition to 'uncertainty'. These terms are not always synonymous, which suggests that a common lexicon of 'uncertainty' does not exist across the Agencies. The review also confirmed that Agencies perception of uncertainty is multifaceted, and hence complex. Some of the components of 'scientific uncertainty' identified include uncertainties arising from underlying policy environment and work planning, study design and methodology, representativeness and reliability of data, interpretation and extrapolation of results and clarity of key messages. This situation also reflects the diversity of EU Agencies' mandates.

The review identified that several Agencies have specific guidance documents on uncertainty in the production of scientific advice. Typically they focus on the proactive identification of sources of uncertainty, with discussion of approaches to the analysis of the magnitude and likely impact on conclusions of uncertainties when they are identified. One of the Agencies, the European Food Safety Authority (EFSA) has recently tested an overarching guidance document to support Agency-wide approaches to the identification, quantification, and communication of scientific uncertainty.

The extent to which uncertainties are elaborated upon in the outputs reviewed varied from detailed assessment of the magnitude of uncertainty in outputs, to a more qualitative highlighting of uncertainty when deemed relevant to the conclusions that might be drawn.

Employing sophisticated frameworks to define and characterise uncertainty with systematic, quantitative approaches is particularly important for some Agencies and their audiences, especially those Agencies that have a regulatory function. However such a framework may not readily lend itself to the work of some Agencies, particularly those that have a non-regulatory mandate and which operate in areas outside the natural sciences. The absence of an ‘uncertainty assessment framework’ does not mean that uncertainty is not addressed; many Agencies invested significant effort to clearly define and communicate methodology approaches and quality control to inform the reader of potential issues that may influence the certainty of resultant conclusions.

This preliminary review provides the basis for further possible reflection. Addressing scientific uncertainty and communicating this is universally recognised among EU ANSA members as important for ensuring that policy makers, and thus policies, are appropriately informed based on available robust scientific evidence. Some Agencies have implemented specific internal practices to support routine assessment and documentation of uncertainty, but there are range of other approaches used across Agencies to address and acknowledge uncertainty in data sets, methodology and resultant advice.

It is likely that a “one size fits all” single standardised approach would not be applicable or useful in all policy contexts, and could be constraining and may not always assist policy making. Ultimately, most Agencies apply a ‘fit-for-purpose’ approach to uncertainty and this may be different for different Agencies and/or within one agency’s various scientific areas, reflecting the differences in mandates.

It was concluded that sharing experiences while developing internal specific guidance documents and/or working practices will allow for an approach that is most appropriate for the mandate and demands of each agency, as well as for their policy stakeholders.

Introduction

The EU ANSA network includes Agencies that address a wide range of topics, from social to physical sciences. All Agencies within the network collate and appraise scientific evidence, integrate current knowledge and communicate this in order to support evidence-based EU policy making.

Uncertainty is found in all disciplines and has various definitions and perspectives. However this review focuses on ‘scientific uncertainty’, which for the purposes of this review is broadly defined as ‘the expression of lack/limitation of scientific knowledge that could be reduced by additional data or information’ [3]. While scientific uncertainty can be characterised and managed, it can probably never be completely eliminated. There are different types of scientific uncertainty and there are many reasons for their occurrence including insufficient data, statistical variability, ‘representativeness’ of data to general populations, or conflicting evidence [5]. It is incumbent on EU Agencies to try to offer a sense of the ‘confidence’ in the evidence and scientific advice that is produced, particularly when this is to be used by decision makers for developing policy. Furthermore, identifying and defining scientific uncertainty is a crucial part of transparency and conveying uncertainty is essential in scientific communication. The increasing drives towards ‘evidence-based’ or ‘evidence-informed’ approaches in policy making also places greater emphasis on a more rigorous approach to collection and presentation of the underlying evidence base, including the uncertainty, in any scientific advice to be used in such policy development. Hence, because uncertainty is an intrinsic part of the scientific process, there is a common interest in approaches to assess and communicate scientific uncertainty in the EU Agencies that provide scientific and technical advice to EU institutions, EU Member States and other EU policy makers.

This summary review aims to target scientific uncertainty from a practical perspective by:

- I. mapping EU ANSA agencies’ approaches to the processes of identifying and managing scientific uncertainty on the one hand, and communicating that uncertainty in scientific advice outputs on the other, and
- II. identifying specific Agency approaches that could be usefully applied in other Agencies with similar mandates.

Methods

Approach

The aim of the review was to better understand the general approaches taken by Agencies to address scientific uncertainty, and to identify common issues and examples of approaches and practices that may guide further thinking in Agencies about how uncertainty may be addressed in future. Hence the working methods used were chosen to obtain some overall sense of how uncertainty is addressed across all EU ANSA member Agencies. It is not the intention to make judgements or compare Agency approaches; ultimately there is no 'right' approach and each agency has its own mandate and working methods that have been developed to meet stakeholder needs.

Data collection

The method of data collection followed a two-step approach:

Step 1:

Independent desk-top review of approaches to addressing uncertainty using a semi-structured review framework. Sources for the review were the following:

A) Policy documents and internal procedures on how to address scientific uncertainty in Agency scientific outputs:

In early January 2016, EU ANSA Agencies were invited to submit technical guidance specifically on handling uncertainty (including internal guidance not in the public domain). 'Official Guidance' refers to institutional guidance that attempts to develop an overarching approach to uncertainty in all scientific outputs, while 'Guidance to authors' refers to guidelines provided to agency staff and external stakeholders on approaches to address uncertainty in specific topic areas or documents.

B) Specific scientific outputs where uncertainty may be addressed:

A 'dip-sampling' method was used to identify and review up to three 'scientific advice outputs' on agency websites that contained some form of scientific assessment or appraisal (and hence which could be used to assess approaches taken to address scientific uncertainty (see Annex 1 for further information on methods to identify relevant documents including Inclusion criteria). The document search was limited to three outputs due to time and resource constraints, and because the focus was to gain rapid insight into practical approaches to address uncertainty across all Agencies rather than assess individual Agencies.

Step 2:

C) Agency examples of technical outputs addressing uncertainty:

In October 2016, and on the basis of the initial desk-top review, Agencies were invited to submit examples of overarching guidance or specific technical outputs that provided a particularly clear demonstration of how uncertainty had been addressed in order to further understand common practice and examples of approaches used.

This dual approach was selected to ensure that the review considered both; a) the breadth of scientific outputs across the Agencies in order to get a picture of how uncertainty is addressed in general across the EU ANSA network, and b) a detailed consideration of specific outputs with useful examples and illustrations to gain a better understanding of the specific issues being faced.

The methodology deliberately gave opportunity for EU ANSA Agencies to present examples that illustrate both current practice and constraints or challenges in the assessment and presentation of scientific uncertainty. This collaborative approach also ensures that documents or outputs not captured in the initial literature searches could be used in the review; this was particularly relevant for those Agencies which produce primary data and where the criteria used in this study for the initial literature search may have missed relevant content. See results and discussion section.

The desk top review was supplemented with follow-up interviews and fact-finding to further understand approaches to handling uncertainty within the EU ANSA network as necessary.

Assessment framework

All documents identified by the initial search were subject to a preliminary descriptive assessment to determine approaches toward scientific uncertainty for each agency. This initial descriptive review assessed two key elements; a general review of how uncertainty was addressed in the technical outputs identified for each agency from the initial search criteria, and a secondary commentary on how uncertainty is addressed specifically to support policy makers.

The initial descriptive analysis was enhanced and revised based on further inputs from the Agencies to ensure a more complete picture of individual Agency approaches is captured.

The descriptive assessment for each agency is presented in Annex 2, with specific illustrative examples embedded in the main text.

Study Design Limitation/Exclusions

Limitation of the desk top review was the lack of breadth of the analysis which was limited to only three publically-available outputs from each Agency, and the different terminology which meant that potentially relevant content may not have been captured using keyword searches. To overcome this limitation, Agencies were given opportunities to present further information, but ultimately the results from this review are not exhaustive and the small, random sample frame used in the initial assessment may not necessarily be representative of the approaches used in each Agency.

Results and Discussion

Scientific uncertainty: Concept and terminology

The mapping exercise of Agency approaches to uncertainty and subsequent commentary from Agency participants reveals variation in how ‘uncertainty’ is conceptualised. At the outset, the focus of the study was the identification, assessment and communication of ‘scientific uncertainty’ on distilled scientific outputs such as guidelines, scientific advice and other secondary or tertiary content published on Agency websites. However other types of relevant documents, including particularly primary outputs such as survey results or other data sets are equally relevant and reveal Agency practices which clearly demonstrate a commitment to a rigorous qualitative uncertainty assessment of primary data. Hence although Agencies commonly both use and produce qualitative and quantitative data, the context determines how scientific uncertainty is prescribed. For example, some Agencies have greater reliance on empirical data generated under controlled experimental conditions, particularly those Agencies addressing topics from natural or physical sciences. Hence Agencies such as ECDC, EFSA and ECHA tend to produce scientific advice outputs based on construction of tertiary outputs compiled from primary and secondary sources. In this context uncertainty is predominantly related to inherent variance in the pursuit of empirical evidence, and centres on data validity and the confidence that research outcomes are projecting the underlying ‘truth’ about the ‘natural order’, or what is not known, and relates to the limits of research and constraints of scientific endeavour. Other Agencies, typically within the social science domain, including FRA, Eurofound and Cedefop, commonly have greater focus on (often self-generated) large population-based survey data. Statistical validity and confidence is also a crucial element in this context, but uncertainty may be more focused on representativeness of samples and extrapolation of results to wider populations. One can speculate on if these fundamental differences

CASE STUDY 1

European Union Agency for Network and Information Security (ENISA). Article 14 requests for support

The annual Work Program (WP) of ENISA presents in considerable details the specific activities of ENISA each year. Beyond the ‘boundary conditions’ set by the annual WP document introduction of new activities when and as the need arises requires the positive decision of the ENISA Management Board. Obviously in a fast changing field such as ICT Network and Information Security (NIS) this may pose considerable limitations.

The ENISA Regulation (http://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=OJ:JOL_2013_165_R_0041_01&qid=1397226946093&from=EN) introduced in 19th June 2013 gives the opportunity to ENISA to react in fast changing environment such as ICT NIS. Article 14 of the ENISA regulation ‘Requests to the Agency’ allows Member States and EU bodies to send requests to ENISA ‘...for advice and assistance falling within the Agency’s objectives and tasks...’. It is up to the Executive Director of ENISA to accept or decline such requests (on the basis of the availability resources, WP priorities, etc.) and it is also one of the Executive Director tasks to shall inform the Management Board and Executive Board of the requests received, the potential resource implications, and, in due course, of the follow-up to the requests.

Source: ENISA, personal communication

in approaches lead to variance in perception of uncertainty at the level of methods and data collection which are subsequently translated into Agency outputs and communication of results. It is also clear that “scientific uncertainty” has a broader meaning than uncertainty inherent in the scientific processes. For example, for some Agencies scientific uncertainty encompasses the inherent lack of certainty in their policy environments due to unforeseen events, and the need for mechanisms to prioritise scientific work to ensure emerging/urgent activities are addressed (See Case Study 1).

The study also illustrates the divergence in terminology around uncertainty between the ANSA Agencies. Some Agencies give focus to study design ‘limitations’ when describing knowledge gaps or challenges whilst others Agencies use ‘uncertainty’ where the evidence base is imperfect and resultant scientific advice lacks certainty (for more detail see Annex 2) . These terms are not synonymous.

Conversely, the study suggests that there are a range of terms used which are broadly associated with the ‘uncertainty’ as initially defined in the study. For example, some Agencies give focus on addressing ‘risks’ and ‘limitations’ in the underlying evidence. This is clearly addressing uncertainty even if the specific term is not commonly used, and outputs do not include formal uncertainty assessment.

Scientific uncertainty in practise

Guidance documents and prescribed methodology to assess scientific uncertainty

Several Agencies have specific guidance documents to support uncertainty assessment in scientific outputs. Agencies with a regulatory mandate (e.g. ECHA, EFSA and EMA) commonly have well elaborated guidance which illustrates that scope of an Agency is a key determinant in the type of approaches used.

The European Food Safety Authority (EFSA) has developed an overarching framework and guidance that supports agency-wide approaches to address scientific uncertainty. The guidance, which is currently being tested (April 2016 – May 2017) in a pilot phase, is characterized by its systematic and flexible framework of uncertainty analysis. Various methods are presented to evaluate individual uncertainties either qualitatively or quantitatively with the aim of expressing the overall uncertainty quantitatively (Annex 2). EFSA guidance also includes a dedicated section on communication to different target audiences among which are policy makers. Concrete suggestions on preferred terminologies for efficient and simple communication could not be given yet and will be the subject of a separate companion guidance document on how to communicate on uncertainty in scientific assessments expected to be published by mid-2018. Advice is given on where to address decision makers in the uncertainty analysis process (See case study 4 for application of EFSA guidance in practise).

The guidance documents for authors from EMA (Case Study 2) and ECHA outputs follow similar principles, and include detailed guidelines

CASE STUDY 2

European Medicines Agency. Guidance document on the content of the <Co-> Rapporteur day 80 critical assessment report

The Guidance document is aimed at external stakeholders making applications for medical authorisation. The document presents assessment tools for difficult or contentious cases and problems dominated by uncertainty. It specifies a framework to determine the benefit-risk balance. When displaying the favourable and unfavourable effects in an *Effects Table* a column on uncertainties is available with “brief” comments. In the generic framework for decision making, the source, extent of uncertainty and statistical probabilities are taken into consideration. Multiple conflicting objectives are also of interest when determining a problem. The Guidance proposes that sensitivity analyses can be used to identify the effects on the overall benefit-risk balance. It repeatedly states and comments on the key role of judgement when appropriate. Hypothetical examples are provided [2].

Source: EMA, personal communication

to authors on the need to characterise ‘uncertainty’ rigorously by qualitative and quantitative approaches and present this as a key component of scientific outputs, and guidance on communication of uncertainty to policy makers [6-8] (see Annex 2).

The ECDC guidance promotes the principle of weighing of evidence as an importance element of quality assessment to define and differentiate uncertainty; this then ensures that a broad evidence base can be applied to scientific assessment by ensuring those documents that are considered to be of lower evidence ‘quality’, (and with a greater inherent uncertainty), are not automatically discarded, but are given less ‘weight’ in the underlying evidence assessment. Such an approach is based on quality assessment frameworks such as GRADE – whereby several such frameworks exist to support underlying assessment of the quality of the evidence base. However, in order to be most useful for policy makers, the principles adopted for systematic literature reviews and quality assessment frameworks should also be applied to the scientific documents produced by Agencies. In addition to the Agencies with a regulatory mandate, there are good examples of overarching approaches to uncertainty from non-regulatory Agencies, including from the social sciences. This is commonly conceptualised as data validity, and limitations of extrapolation to general populations rather than scientific uncertainty as defined by the other Agencies. For example Cedefop conceptualise uncertainty in 4 key areas which illustrate a comprehensive approach throughout the scientific process from research design and data gathering to communication of outputs (Case Study 3). Cedefop has no structured framework to reduce uncertainty, but employ several processes and actions to enhance scientific quality and reduce uncertainty. These include expert-led initiatives such as peer review and expert support, inclusion of ‘fail-safes’ in contracted research (minimum requirements for data collection and analysis), and enhancements to scientific processes to improve data confidence (data triangulation and conformational analysis, impact of data variability through alternative scenario ‘modelling’).

European Centre for the Development of Vocational Training (Cedefop). Classification of research activities and uncertainty; four key areas

1. Design and methodology

The research design stage is clearly perceived as a potential source of uncertainty, both for both quantitative and qualitative studies. Bad sampling choices, inadequate modelling choices and, weak quality assurance mechanisms may exist from early stages (e.g. call for tender for contracting-out part of the research activities) may compromise data gathering processes and the use of the data.

2. Representativeness and reliability

Representativeness and reliability of results are dependent on both the quality of the data and the adequacy of the methodology used to analyse and model it. Given the strong context-dependency of policy monitoring and comparative analysis typically carried out at Cedefop, results may also provide limited insight into differences and similarities across national systems, which will affect, in turn, the scope of policy recommendations.

3. Expertise in interpretation and handling of data

Expertise of the project managers and the core research team are the main remedial approaches to reduce uncertainty of the data from qualitative studies. Most measures which can increase reliability of data depend on technical decisions of the project manager and the research team. Both in qualitative and quantitative studies, the choice of models or aspects of models which are used to generate information are critical, and choice is made based on expert knowledge and experience, and is hence is not infallible.

4. Clarity of messages

Cross sectional data interpretations can generate blanket statements due to low sensitivity to real causal factors. Forecasts can generate statements which do not fully acknowledge the role of contextual stability (macroeconomic assumptions, technology). Qualitative research may create general recommendations based on purely local phenomena or highly individual-specific experience. While generation of clear and reliable messages can be a matter of expertise, contamination by the research object is also a risk. A researcher can easily lose perspective and produce recommendations that have no value for policy making.

Source: Cedefop, personal communication

Scientific uncertainty in technical outputs

Process and methodology

The desk-top review of agency outputs based on key word searches found evidence that scientific uncertainty was addressed explicitly in outputs from the majority of Agencies. Examples of systematic approaches to evaluate uncertainty using both qualitative and quantitative approaches were also identified. As described above, EFSA has developed an elaborate framework for addressing uncertainty in EFSA scientific outputs; an example of the application of EFSA's framework in a specific output is presented in Case study 4.

European Food Safety Agency.

Main elements of an uncertainty analysis as proposed in the EFSA guidance document:

- Dividing the scientific assessment into parts for uncertainty analysis (when appropriate)
- Ensuring the outcomes considered in the assessment are well-defined
- Identifying uncertainties affecting the assessment
- Prioritising uncertainties for analysis within the assessment
- Expressing uncertainties
- Combining uncertainties (when needed)
- Characterising overall uncertainty
- Prioritising uncertainties for future investigation (when needed)
- Conclusions and Reporting

Illustration: EFSA opinion on Animal welfare aspects in respect of the slaughter or killing of pregnant livestock animals (cattle, pigs, sheep, goats, horses) (EFSA 2017) <http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2017.4782/pdf>

Background Information on Mandate and TOR

The mandate comprised of 5 ToRs, two of which involved uncertainty analyses: ToR1) to assess the prevalence of pregnant livestock animals slaughtered (methods and results are shown hereafter); ToR3) to assess the scientific evidence available on the capacity of fetuses to experience pain.

Methods and Results

For ToR1, the prevalence of slaughtered pregnant animals was elicited by an expert knowledge elicitation (EKE) meeting involving 10 external experts who conducted slaughterhouse surveys; TOR1 (prevalence of slaughtered pregnant animals in EU)

1. PLAN THE ASSESSMENT

a survey was outsourced to experts from 10 EU countries to convenience sample 10 slaughterhouses - 4 for cattle, 3 for pigs, 2 for sheep, 1 for goats and 1 for horses, when possible. The survey asked for estimates about the prevalence of pregnant livestock animals slaughtered and the fetal stage of development (1st, 2nd or 3rd term of gestation).

The experts were invited to the [EKE] meeting and asked, based on the estimates collected through the surveys, to give probability judgments per species about the overall prevalence of pregnant animals slaughtered at European level and respective proportions for terms of gestation. Finally, a collective view per each livestock species in Europe was agreed upon.

2. ASSESS UNCERTAINTY

Uncertainty is represented using a probability distribution which expresses the likelihood of possible estimates.

3. SUMMARY OF CONCLUSIONS ON UNCERTAINTY

Estimated prevalence (median) of mature female animals that are pregnant at the time of slaughter in Europe (example below for overall prevalence irrespective of stage of gestation), including the uncertainties expressed as probability distribution. The latter is described by the percentiles (P) which define the 50% uncertainty range (P25 – P75), as well as the 98% uncertainty range (P1 – P99).

All pregnandes	P1	P25	median	P75	P99
Dairy cows	2 %	9 %	16 %	27 %	60 %
Beef cattle	1 %	7 %	11 %	18 %	40 %
Pigs	0 %	3 %	6 %	9 %	20 %
Sheep	0 %	5 %	10 %	14 %	40 %
Goats	0 %	2 %	4 %	6 %	10 %

Source: EFSA, personal communication

Examples of other approaches were also identified, including outputs that gave focus to the magnitude and statistical probabilities of predicted uncertainties occurring and suggests the use of sensitivity analysis to identify the effects on the overall assessment of benefit-risk [9]. Many Agencies clearly had an existing foundation in discussing uncertainty and ‘limited evidence’, even though in some cases no evidence of internal guidance or overarching policy on uncertainty was identified. This suggests that the assessment of uncertainty may be embedded in the culture of some Agencies and is an implicit element of all Agencies ‘scientific processes’ even in the absence of formalised approaches.

CASE STUDY 5

Eurofound: Implicit uncertainty review through assessment of methodology and quality control in technical reports

Eurofound includes methodology in all reports. For surveys, there is extensive information published on methodology and quality control. In addition, quantitative analysis is commonly presented with commentary on the statistical limitations. In effect, this explicit assessment of methodology and quality control acts as an implicit statement of the certainty level of the findings in the report.

Examples:

a) Disclosure of surveys methodologies: EWCS 2015 – Methodology: <https://www.eurofound.europa.eu/surveys/european-working-conditions-surveys/sixth-european-working-conditions-survey-2015/ewcs-2015-methodology>

b) Quality control in Technical report of the European Company Survey:

https://www.eurofound.europa.eu/sites/default/files/ef_files/surveys/ecs/2013/documents/ecs2013docs/3rdECS2013TechnicalReport.pdf

https://www.eurofound.europa.eu/ef/sites/default/files/ef_files/surveys/ecs/2013/documents/ecs2013docs/3rdECS2013Qualitycontrol_2.pdf

CASE STUDY 6

European Union Agency for Fundamental Rights (FRA) – Reporting on all stages of data collection and analysis for the purpose of scientific rigour and the identification of possible limitations

FRA undertakes large-scale quantitative EU-wide surveys on groups and issues that are typically under-researched at Member State and EU level; such as violence against women, the situation of ethnic minorities and immigrants in the EU, and LGBTI communities.

FRA survey reports are accompanied by detailed technical reports concerning each survey’s development and implementation, which cover the subject of ‘uncertainty’ using a range of terms and tests; typically including sections on: the survey pre-test; piloting the survey; questionnaire development; sampling; fieldwork; response rate; quality control; data cleaning and data validation; weighting; sensitivity analysis; and confidence intervals. Examples include:

Violence against women: an EU-wide survey - survey methodology, sample and fieldwork

<http://fra.europa.eu/en/publication/2014/violence-against-women-eu-wide-survey-survey-methodology-sample-and-fieldwork>

EU LGBT survey: technical report – methodology, online survey, questionnaire and sample

<http://fra.europa.eu/en/survey/2012/eu-lgbt-survey>

Source: Eurofound & FRA, personal communication

Many Agencies, including those working in the physical and the social sciences, assess reliability of primary data, and provide extensive information on methodology and quality control on all reports. For example FRA's technical reports and annexes accompanying survey outputs apply a quantitative assessment of 'limitations' through use of confidence intervals, sampling weights etc. when reporting on how data was collected or on how to interpret research findings. Eurofound and FRA also pursue similar approaches (see Case study 5 and 6).

Presentation and discussion of uncertainty for policy makers

The document search revealed several examples of agency outputs that undertook uncertainty assessment of the underlying evidence base and methods and which included commentary in methods but which then did not extrapolate this to final conclusions, meaning caveats on data quality and possible limitations were not emphasised. The reason for such omission is unclear, but may be for fear of diluting the potency of conclusions, and introducing additional complexity to those that interpret and use such outputs for policy development. In some cases Agencies may need to balance the efforts put into the identification of uncertainty in the underlying evidence base, on the one hand, against providing commentary on how such uncertainty should be interpreted by providing contextual understanding to the topic and guidance to the reader through the assessment. Ultimately a pragmatic approach may be needed to find the balance between giving uncertainty due consideration in scientific outputs, including high level conclusions, while ensuring Agency outputs remain concise and key messages do not 'drown in a sea of uncertainty'. Examples of such pragmatism were seen in outputs from several Agencies (ECHA, Eurofound, EFSA, EMA and FRA) [13][34] (Case study 7).

CASE STUDY 7

European Union Agency for Fundamental Rights (FRA). Cost of exclusion from healthcare: the case of migrants in an irregular situation

http://fra.europa.eu/sites/default/files/fra_uploads/fra-2015-cost-healthcare_en.pdf

Alongside the collection of primary data through large-scale surveys, FRA also undertakes analysis of existing secondary source material. FRA's report on the cost of exclusion from healthcare of migrants in an irregular situation uses an economic model to look at hypertension and pre-natal care. In reporting the results, 'uncertainty' is referred to under different sections of the report with respect to 'sensitivity analysis', 'limitations of the model' and 'limitations of the analysis'. The back cover of the report also states 'Although results must be interpreted with caution . . .'

Source: FRA, personal communication

The presentation on the eventual effects of uncertainties on the outcome also varied. Examples ranged from outputs that mentioned “potential effects on outcome” to more elaborated descriptions of under- and overestimation of outcome. Generally, the inclusion of some commentary on the effect on outcome is likely to be beneficial (although there are circumstances where presentation of uncertainty in the outcome conclusions may be regarded as unhelpful, such as where Regulators are required to make decisions on Agency-led recommendations for product authorisation). Clarifying the magnitude and impact of uncertainty facilitates judgement and can also provide an understanding of the importance of knowledge gaps in relation to the topic which can be used to prioritise future research. Overall, inclusion may strengthen the content of EU ANSA scientific advice documents.

Addressing scientific uncertainty: Scientific communication

Risk communication is outside the scope of the paper, but it is clear that communication of uncertainty is a key issue to many Agencies. There are examples where communication of uncertainty is clearly addressed; for example the new EFSA guidance on how to communicate on uncertainty will provide clear recommendations on how to communicate uncertainties depending on the different expressions of uncertainty depending on the scientific outputs (to be published by mid-2018).

In the EU context, this review has illustrated that a common EU lexicon on uncertainty that can be used by ANSA Agencies is currently lacking, and comments also suggest that even within Agencies, the different professions in the different functions (science/research on the one hand and 'Communication' professionals on the other hand) have quite different perspectives on this topic, which are played out in particular when it comes to communicating scientific uncertainty.

Hence there may be a need for more in-depth joint conversations between 'scientists / researchers' and 'communication' professionals within each agency. From an EU perspective, there may also be value in engaging EU-ANSA and the EU Agencies Head of Communications Network around this topic to gain mutual understanding of the complexity and develop some shared understanding and appreciation of this topic.

Ideally, there should be a balance in communicating the magnitude and effect of uncertainties to policy makers, such that uncertainty is addressed adequately while avoiding unhelpful complexity. In some cases, underlying uncertainty may not impact greatly on conclusions, and clear explanation on research process and methods to support transparency is likely to be sufficient. In such cases, Agencies communication focus is the research and findings and uncertainty is addressed within this context; caveats are stated, but as an inherent part of scientific research. Other Agencies' reported that their policy areas are by nature uncertain, and hence key messages rely on evidence-based opinion. In this context, uncertainty is implied, and if it is overstated, it may present an alibi for damaging policy inertia and inaction. Conversely the explicit presentation of uncertainty may illicit the opposite effect; risk managers may feel greater obligation to take more stringent risk mitigation measures in the face of uncertainty due to the

precautionary principle. Clearly Agencies need to exercise judgement and have a clear understanding of the policy environment and policy makers attitudes to risk in order to meet expectations and to avoid uncertainty being used negatively as a driver for either overregulation or inertia. Ultimately, balancing the need to convey enough information around uncertainty to support clear communication and decision making, while not overburdening policy makers and other stakeholders with superfluous detail remains a challenge for many Agencies.

One approach used in some Agencies is the inclusion of clear disclaimers, or similar general statements regarding inherent limitations of research and data collection and analysis. This is published online across all channels and included as a standard element in all reports. It could also be systematically included in any description of the agency's working methods in terms of ensuring high-level scientific credibility and reputation. Generic statements can always be further enhanced with more detailed commentary and communication on specific actions to characterise uncertainty if warranted, or where the policy context demands more detailed communication on uncertainty analysis conducted. However while using such a general statement may ensure the key messages are not diluted, in some contexts the underlying uncertainty in Agency advice is a key message itself. In such cases, it is important that policy makers understand the uncertainty in order to make informed policy decisions, including sanctioning targeted research actions to improve the quality of the evidence base. Hence uncertainty communication requires a deep understanding of the topic, policy environment and audience needs, and approaches adopted that are appropriate to the context and audience.

Conclusions and Recommendations

The aim of scientific endeavour is to reduce uncertainty and enhance knowledge. However uncertainty is an ever-present in the scientific process, and includes limitations in knowledge, in the quality of data, representativeness to general populations, methodological constraints, limits in data interpretation and clarity of communication. All such issues can impact on the underlying ‘confidence’ in Agencies scientific outputs.

Overall the review has revealed some variation in how scientific uncertainty is addressed across EU ANSA. This is not surprising as EU ANSA Agencies cover a broad spectrum of topics and disciplines, and have different mandates, and this ‘context’ defines the mechanisms by which uncertainty is identified and addressed; for some scientific uncertainty is predominantly related to inherent variance in the pursuit of empirical evidence, and centres on data validity and the confidence that research outcomes are projecting the underlying ‘truth’ about the ‘natural order’. For others, uncertainty is about what is not known, and relates to the limits of research and constraints of scientific endeavour. For example, some Agencies are heavily reliant on empirical data generated under controlled experimental conditions, particularly those Agencies addressing topics from natural or physical sciences. Hence Agencies such as ECDC, EFSA and ECHA tend to produce scientific advice outputs based on construction of tertiary outputs compiled and distilled from primary and secondary sources. In this context data sets and result conclusions may be amenable to systematic quantitative approaches to define and characterise uncertainty in the process of developing scientific advice. Other Agencies, typically within the social science domain, including FRA, Eurofound and Cedefop, commonly rely on large population-based survey data. Statistical validity and confidence is also a crucial element in this context, but uncertainty may be more focused on representativeness of samples and extrapolation of results to wider populations. These differences in approaches lead to variance in perception of uncertainty at the level of methods and data collection which are subsequently translated into Agency outputs and communication of results.

The review has also revealed that Agencies conceptualisation of scientific uncertainty is broad, and expands beyond the confines of the ‘production’ of advice and encompasses such issues as work planning and prioritisation in the face of emerging risks.

This review also identified that there is variable use of terminology, particularly in respect of references to ‘uncertainty’ and ‘limitations’. There may be value in trying to harmonise terminology and develop a common understanding of definitions and terminology related to uncertainty.

However although the mandate and focus for uncertainty differ between Agencies, ultimately, all attempts to define and reduce uncertainties are likely to be beneficial to all Agencies. The challenge remains to strike the right balance between comprehensiveness and fitness-for-purpose. Hence it is important to present scientific results and advice objectively with uncertainty clearly stated, while ensuring salient points in any

scientific output remain clearly understandable and sufficiently emphasised to support clear policy making, and are not wrapped up in endless caveats that may overwhelm decision makers. Agencies need to find a balance when communicating 'truthful' uncertainties without risking a fixed interpretation of 'nothing is known' which then devalues the hard work and scientific rigour that is the basis of EU ANSA Agencies work. Finding this balance is a primary focus of risk communication and is of fundamental importance in all Agencies. There may be a need for more in-depth joint conversations between scientific researchers and communication professionals within each agency in order to present uncertainty in a clear and transparent manner, and maintain trust in the scientific method and in the EU Agencies charged with applying it.

The work already initiated by some Agencies illustrates a range of possible approaches to addressing uncertainty and an opportunity for further strengthening the utility and consistency of scientific advice for policy making within the EU; there are examples of well elaborated guidance to support the consistent approach to uncertainty, and many agencies have demonstrable focus on uncertainty through practises such as identification of data limitation and explicitly statement on constraints in primary data collections. The case studies illustrate some of the various approaches taken, and are presented to support understanding of diversity in concept and approach in addition to supporting internal reflection on current approaches. This is an evolving field, and the speed and direction of this evolution is unique to each Agency. There are likely to be several competing drivers which shape the approach of every Agency including agency mandate, scientific culture, policy maker expectations, institutional 'need', and willingness to invest in processes to characterise and communicate uncertainty.

Given the range of topics, mandates, policy contexts and other variables within the EU ANSA network, adopting a 'one-size-fits-all' model to address uncertainty across all EU Agencies is unlikely to be appropriate. It is therefore preferable for Agencies to share experiences while developing guidance documents and/or working practice practices best suited to identify, address and communicate uncertainty based on their own needs and mandates. This allows for an approach that is most appropriate for the demands of each agency and their policy stakeholders.

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END

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Annex 1:

Desk top literature review:

Detailed methodology

Scientific advice output assessments fulfilling one or more of the inclusion criteria were scrutinized. The inclusion criteria were: document, guidance, review, full report, description of limitation or uncertainty, grading evidence and scientific uncertainty. Literature on rating quality of evidence and strength was also included. Keywords used were as follows: uncertainty, uncertainties, science, decision making, risk and Europe. While the searches were initially restricted to the term 'uncertainty' this was subsequently expanded to also include 'limitation' as it became apparent that 'limitation' was used synonymously with 'uncertainty' in several agency outputs.

The searches were restricted to cost-free documents in English from publication year 2013 onwards. 2013 was used to limit the searches to only topical literature in the area of scientific uncertainty. Official guidance and similar documents were included regardless the year of publication, but Workshops, training or other activities dealing with uncertainty were not included as they were considered to be outside the scope of the desk-top review.

The literature search of Agency websites was conducted in March 2016, and hence only documents that were publically available at that time were admissible. Due to time and resource constraints, only a maximum of three outputs were analysed from each Agency. Hence this 'dip sampling' methodology was not able to generate representative sample of all Agencies' approaches with consequential risks of misrepresentation and bias in the selected Agency outputs and the resultant analysis.

Annex 2: Agency's approaches to uncertainty - Descriptive analysis

The method used to develop this analysis are summarised in Annex 1, and is based on a random 'dip sample' of selected search terms. This work was undertaken at the outset of the project to get some sense of Agency approaches, but it cannot claim to show a representative sample of all Agencies' approaches to uncertainty that incorporate other terms. Other examples – which were not identified through the dip sample search, are outlined in the case studies contained in the paper.

European Centre for Disease prevention and Control (ECDC)

Description of general approach identified in initial document trawl

Formal frameworks for assessing the quality of evidence in defined types of scientific advice outputs are defined in guidance for the production of those types of output, but no overarching guidance to assess scientific uncertainty in all types of ECDC outputs was identified. The three examples of scientific outputs that were reviewed included one instructional document which included practical guidance to address uncertainty [11] and examples of assessments of uncertainty (or limitations, as termed in one document) with respect to the source evidence used [18][12]. Formal frameworks for assessing the quality of evidence were advocated or used in these documents, in order to provide transparency, including GRADE, SIGN, and HASTE. One report also includes a specific section on implications for future research which emphasizes weaknesses in the evidence base used, including descriptive assessment of the underlying evidence base for the interventions considered. However, the documents included little guidance or information on how the uncertainties or limitations in the source evidence could impact on the output conclusions, or provided much information to policy makers on how to communicate uncertainties identified.

European Chemical Agency (ECHA)

Description of general approach identified in initial document trawl

The Agency has a number of Guidance documents for authors to support uncertainty assessment (*Chapters on uncertainty analysis within the Guidance on information requirements and chemical safety assessment; Guidance on the preparation of an application for authorisation 2015; Application of the regulation on classification, labelling and packing of substances and mixtures*). The underlying principle in the reviewed guidance is that the detail of the analysis should be proportionate to the level of uncertainty and potential impact on risk characterisation. Hence one document includes a review of the necessity for uncertainty assessment, and if needed, recommends a stepwise, risk assessment algorithm to identify when specific uncertainties should be addressed based on level of inherent hazard from a chemical substance and its use. Specific techniques for making qualitative, deterministic and probabilistic analysis to review uncertainty were also identified in the documents, including the use of both quantitative and qualitative methods with discussion on limitations on the proposed approaches, and practical tools such as checklists to identify the main sources of uncertainty were also identified. Approaches for reporting and communicating uncertainty were also suggested and several illustrative examples on the approaches were given [6][7][8].

European Environmental Agency (EEA)

Description of general approach identified in initial document trawl

The approach to uncertainty was predominantly descriptive and qualitative in the three scientific outputs assessed; this was presented as general comments such as caveats in regard to uncertainty and risk of over-interpretation in output conclusions (*European Environment Agency. Air quality in Europe – 2015* [19]) *National monitoring, reporting and evaluation of climate change adaptation in Europe 2015* [20]; *Trends and projections in Europe 2015-Tracking progress towards Europe’s climate and energy targets 2015* [21]. There was little evidence of detailed quantitative uncertainty assessment or limits on data confidence, but explicit commentary on methodological challenges with suggested approaches to reduce methodological uncertainty was identified.

European Food Safety Authority (EFSA)

Description of general approach identified in initial document trawl

EFSA was unique in this survey in that it has adopted formal overarching guidance on how to assess uncertainty that is currently in a pilot phase (April 2016 – May 2017). The EFSA guidance document includes a detailed framework on uncertainty analysis, and a companion document will provide recommendations on how to communicate uncertainty (by mid-2018). The draft EFSA guidance provides a framework and principles for uncertainty analysis along with the flexibility of choosing a method. There was a recurrent focus on the role of the decision-maker and assessors, several approaches are presented to facilitate sound decision-making. The guidance states that associated uncertainties should always be clear and unambiguous to reduce misunderstandings, while ultimately the decision maker decides on the acceptable level of uncertainty [3]. Communication between the two parties should also be clear. The overall uncertainty should be assessed quantitatively and if not possible, one should avoid qualitative statements (e.g. “likely”) if they are not clearly linked to a probability scale (probability table). The strength in a quantitative expression of the uncertainty lies in expressing the magnitude of an individual uncertainty and relative contribution to the overall uncertainty [3].

Of the documents reviewed, there was evidence that the principles of the Agency guidelines were seen in some outputs including explicit identification of sources of uncertainty and some qualitative assessment of the potential impact (magnitude) on outcome with suggested ways to decrease it. Other outputs were more descriptive and made less elaborate qualitative statements on uncertainty and data ‘weakness’ [14] [15]. It should be noted that the principles of the EFSA guidance document on uncertainty was not applied yet in the two outputs of this review [14, 15] as they were published before the guidance document was finalized and published for the testing phase.

European Institute for Gender Equality (EIGE)

Description of general approach identified in initial document trawl:

Literature keyword search only identified one document for the assessment (*Study to map the current situation and trends of FGM*). The cited studies and associated commentary in the document identified a number methodological and statistical limitations, including the inability to produce an estimated prevalence from a qualitative survey as a primary limitation. Attempts to reduce limitations inherent in the document were described. [22].

European Medicines Agency (EMA)

Description of general approach identified in initial document trawl

The Agency provided internal guidance documents that assist stakeholders and assessors to support or review medicine safety and efficacy (e.g. *Guidance document on the content of the <Co-> Rapporteur day 80 critical assessment report*). As a regulatory agency using empirical data to assess drug safety and efficacy, uncertainty is well elaborated and approached in a number of ways, including through explicit guidance on benefit- risk assessment, discussion on known and unknown uncertainties and sources of bias on methodological and systematic procedures. The document also suggested to examine the impact on outcome (magnitude) from a favourable versus unfavourable aspect, and discussions on key messages are promoted [2].

Documents identified from the Literature review also demonstrated evidence of a quantitative approach to uncertainty, including emphasis on the importance of statistical methodology and making explicit uncertainty due to statistical variability. However the mechanisms used to identify uncertainty in some documents were not always clear to external. An example of an approach used by EMA is presented in the main document- see (Case study 2) [9].[23].

European Monitoring Centre for Drugs and Drug Addiction (EMCDDA)

Description of general approach identified in initial document trawl

Two Documents identified by the literature search provided evidence of quantitative assessment of confidence in a primary dataset, and commentary on limitations of data quality, reporting coverage, missing values and validity. [10]. [24]. One document also identified data uncertainty and consistency, and explicitly cautioned again over interpreting associations between datasets.

The third identified document was excluded as being outside the scope of this review [25].

European Union Agency for Network and Information Security (ENISA)

Description of general approach identified in initial document trawl

Documents identified by the literature search included descriptive analysis of data limitation in study design and interpretation, including risks from a lack of detail in the primary dataset and constraints on data collection. An approach to possibly overcome the limitations from the legislative framework was also suggested. One document also explicitly identified a lack of resource as a cause of uncertainty due to inability to capture all relevant datasets as part of the analysis [26]. [27].[28].

In general, it was difficult to find scientific outputs using the terminology 'limitation' or 'uncertainty' (none using the latter). When found, it was mostly used outside the scope or briefly mentioned.

European Agency for Safety and Health at Work (EU-OSHA)

Description of general approach identified in initial document trawl

Documents identified by key word searches included descriptive acknowledgement of the limitations of the evidence base used in outputs, and some more detailed review of potential impact was also identified, including assessment on impact due to evolution/ progress in the field, general lack of available data, and restricted access to non-English datasets. The identified documents included the importance of addressing policy makers to improve comprehension of the outcomes and related uncertainty [17]. [30], [29]].

European Foundation for the Improvement of Living and Working Conditions (Eurofound)

Description of general approach identified in initial document trawl

Documents identified by key word searches include descriptive acknowledgement of statistical variability and a clear summary of data limitation due to lack of statistical power. Limitations due to data reliability and collection were also identified. Conclusions included some commentary on risk of over interpretation based on identified limitations, and also evidence of provision of targeted communication to support policy maker understanding. However, in general uncertainty and limitations was given little attention in overriding conclusions. [31]. [32]. [33]. [34].

European Union Agency for Fundamental Rights (FRA)

Description of general approach identified in initial document trawl

Documents identified by key word searches include outputs with some description of data limitation and commentary on impact on output conclusions and recommendations for improvement and interpretation of data collection. In general the potential limitations or uncertainty in the data presented and the associated conclusions was not always fully elaborated, although risks of over interpretation were implicitly included in high level conclusions, and the documents included suggestions how improvements to reduce inherent uncertainty could be made. [35]. [36]. [13] (see case study 6).

European Agency for the Management of Operational Cooperation at the External Borders of the Member States of the European Union (FRONTEX)

Description of general approach identified in initial document trawl

The documents identified by the literature search were rather unrelated to the scope of the literature review, but did reference the practical challenges and time constraints in data collection may impede meaningful analysis and conclusions [37]. [38]. [39].



Approaches to assess and manage scientific uncertainty: examples from EU ANSA Agencies



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