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Review

Improving Uncertainty Analysis in European Union Risk Assessment of Chemicals

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ABSTRACT

Handling uncertainty in the current European Union (EU) risk assessment of new and existing substances is problematic for several reasons. The known or quantifiable sources of uncertainty are mainly considered. Uncertainty is insufficiently, explicitly communicated to risk managers and decision makers but hidden and concealed in risk quotient numbers that appear to be certain and, therefore, create a false sense of certainty and protectiveness. The new EU chemical policy legislation, REACH, is an opportunity to learn from interdisciplinary thinking in order to evolve to smart risk assessment: an assessment in which awareness and openness to uncertainty is used to produce better characterizations and evaluations of risks. In a smart risk assessment context, quantifying uncertainty is not an aim but just a productive means to refine the assessment or to find alternative solutions for the problem at stake. Guidance and examples are given on how to differentiate, assess, and use uncertainty.

Keywords: 93/67/EEC 91/414/EEC Registration, Evaluation, and Authorization of CHemicals Assessment factor Uncertainty

INTRODUCTION

Environmental pollution of toxic substances has inspired regulation of production and use of chemicals and has led to the development of risk analysis. Usually, such risk analysis process is subdivided into 3 interconnected components (terminology according to the European Commission [EC] 2000): 1) Risk assessment, 2) risk management, and 3) risk communication. General European risk assessment principles for new and existing chemicals are laid down in Commission Directive 93/67/EEC (EC 1993) and Commission Regulation (EEC) 1488/94 (EC 1994), respectively. Similar European Union (EU) risk assessment principles apply for plant protection products in Commission Directive 91/414/EEC (EC 1991). The aim of these regulations is to protect human beings (e.g., workers, consumers, and humans indirectly exposed via the environment) as well as ecosystems in the aquatic (e.g., water and sediment), terrestrial, and air compartments from adverse effects of the production and use of chemicals.

In this paper, it will 1st be illustrated that uncertainty analysis in the current EU risk assessment of new and existing substances is problematic for 3 reasons. First, mainly the known or quantifiable sources of uncertainty are considered, whereas other sources of uncertainty are relevant for risk managers to be informed about. Second, the assessment factors and worst-case assumptions that are applied to derive risk estimates are insufficiently explicitly communicated to risk managers and decision makers but hidden and concealed in numbers that appear to be certain and therefore, 3rd, create a false sense of certainty and protectiveness. Consequently, decisionmakers and risk managers overestimate the reliability of the outcomes of the risk analysis, rendering them vulnerable to distrust of public opinion in case conclusions on risks turn out to be wrong. This idea of certainty and objectivity is understandable in a historic perspective. Since the Renaissance, science has been associated with faith in the infallibility of deterministic interpretation of models and laws of nature. This positivistic paradigm (van Asselt 2000; Krayer von Kraus et al. 2005) has led to the conviction that policy decisions should be grounded in scientific knowledge. This conviction has been transposed on risk assessment as well. Indeed, risk assessors are scientific experts, so risk estimates should also be scientific. However, uncertainty is posing fundamental challenges to the positivistic paradigm by challenging the claim that scientific knowledge can provide certain and objective answers to policy questions pertaining to the safety in the use of chemicals. Uncertainties pertaining to these complex issues are beyond the grasp of traditional scientific methods and require innovative strategies and coalitions in order to solve or manage these issues (Funtowicz and Ravetz 1990; van Asselt 2000; Nowotny et al. 2001; Harremoës 2003; Krayer von Kraus et al. 2005).

Within EU risk assessment, changes are taking place that could be interpreted as indications of a paradigm shift toward the explication of uncertainty. These changes indicate that a valuable reconsideration of dealing with uncertainty is occurring. However, as EU risk assessment still bears witness to an overly positivistic approach, we bring together some of today's insights about risks, uncertainty, and ways of dealing with these to support this development. We argue that current EU

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risk assessment should be improved and develop into a more uncertainty-sensitive risk assessment. Uncertainty information (i.e., recognition of ignorance and characterization of uncertainty) is essential information for risk managers and decisionmakers. Risk assessors should therefore further improve risk assessment by considering the production and interpretation of uncertainty information as an important task.

The last section of this paper explores how risk assessors might be able to improve on this. An unproductive drowning in uncertainty is not advocated. We advance the idea of "smart risk assessment": An assessment in which awareness and openness to uncertainty is used to produce better characterizations and evaluations of risks that can inform decision-making processes in a constructive manner. In such a context, quantifying uncertainty is not an aim but a means. We come up with suggestions to improve the use of worst-case assumptions and assessment factors as illustrations of the further development of EU risk assessment into a smart risk assessment.

THE CURRENT EU RISK ASSESSMENT PROCESS

Risk assessment became the dominant approach in risk policy in the 1980s. Risk assessment quantifies risk and uncertainty and hence suggests objectivity (Porter 1995). Objectivity in turn is a powerful means to obtain legitimacy for policy decisions, especially on contested issues like human health or environmental risks and uncertainties (Souren 2003). This reasoning has provided the grounds for the widespread use of risk assessment in environmental policy both in the United States and in the EU (Klinke and Renn 2002; Halffman 2003; Jasanoff 2005). In fact, what underlies this quest for objectivity is the powerful combination of a realist conception of risk and a positivist methodology. In a realist perspective on risk, risks (and uncertainty) manifest themselves through observable effects. Any difference in perspective concerning a risk is supposed to stem from ignorance, misinterpretation, or the lack of data to describe the effects (Irwin and Wynne 1996; Howes 2005). Contrary to a realist conception of risk is a constructionist conception that recognizes risk as a social construct. In that concept, risk cannot be measured; instead, risk is created through interpretations of historical occurrences and possible hazards. The perception of risk can differ between communities, locations, and situations, and these differences are as legitimate as various observable effects.

The realist conception (risk is real and observable and can objectively be established) is usually accompanied by positivist methodology that values quantitative representations over qualitative quantifications and attaches great value to experimental setup and testing. The conceptualization of risk as the multiplication of chance and effects matches very well with a positivist view on the relation between science and policy. Policy ought to be grounded on observable and objective facts to be disclosed by science. From that view, subjective and contextual factors are secondary or accidental. Revealing facts following such methodology are believed to provide true knowledge, which in turn provides the basis for policymaking. As we will show in the next section, the trend to develop assessment factors and to formulate worst-case assumptions quantitatively is rooted in a realist and positivist perspective and needs to be updated toward a more uncertainty sensitive mode.

EU risk assessment of chemicals

Guidance on the methodology for conducting risk assessment of new and existing substances is given in the Technical Guidance Documents (TGD; EC 1996, 2003). The TGD serves as the "cookbook" for conducting EU risk assessments and was originally established as a consensus outcome from a multistakeholder harmonization process (Bodar et al. 2002) with experts from member states, nongovernmental organizations, and industry. Risk assessment dossiers are further debated during meetings of the Technical Committee of New and Existing Chemical Substances (TC-NES). Such committees are chaired by the European Chemicals Bureau and bring together all interested parties, such as all EU member states and industry, to discuss the approach and progress and to draw conclusions on the risk assessment. Only member states have a right to vote on issues on the procedure or on the content of the report (e.g., how conservative a particular step should be). One EU member state (typically represented by a national regulatory body or research institute), the rapporteur, is responsible for the draft and final risk assessment report. When the iterating process of commenting and redrafting is completed, the Scientific Committee for Human and Environmental Risks will, independently of TC-NES, provide an opinion on the scientific quality of the report (Bodar et al. 2005).

The main goal of the current risk assessment is to answer the question, "Is it likely that adverse effects will occur to exposed ecological systems or humans due to exceedance of a no-effect level by an environmental concentration?" To answer this question, the risk assessment usually proceeds in the following sequence: Hazard identification, dose–response (effect) analysis, exposure analysis, and risk characterization. The risk characterization comprises of a quantitative comparison of a predicted environmental/exposure concentration (PEC) with a predicted no-effect concentration (PNEC). The PNEC should be protective for a specific environmental compartment and is based on a set of (acute or chronic) toxicity test results (i.e., testing species sensitivity; EC 1996, 2003). A risk quotient (PEC/PNEC) or risk characterization ratio (RCR) is calculated, and a value larger or equal to 1 is interpreted as a potential risk of adverse effects, which is read as a need for further research, testing, and monitoring or as a need for implementation of risk reduction measures. For a risk quotient smaller than 1, the decision is usually taken that there is a need for neither further information and/or testing nor risk reduction measures.

In the calculation of the risk quotient, uncertainties are lumped into assessment factors and worst-case assumptions, implying that the risk quotient contains unexplicated uncertainties. In the following section, we take a closer look at assessment factors and worst-case assumptions and uncover how uncertainty currently gets concealed within the risk quotient.

Dealing with uncertainty: Assessment factors and worst-case assumptions

An "assessment factor" (used in EC 1996) is defined by Vermeire et al. (1999) as "the general term to cover all factors designated as safety factor, uncertainty factor, extrapolation factor, etc and the composite thereof." For most substances in the effect analysis, the pool of data used to predict ecosystem or human health effects is limited. In such circumstances, it is recognized that, while not having a strong scientific validity, pragmatically derived assessment factors must be used (EC

Table 1. Visibility of assessment factors and worst-case assumptions in environmental and human health risk assessment of new and existing substances. *AF* = assessment factor; *RCR* = risk characterization ratio; *PEC* = predicted environmental concentration; *PNEC* = predicted no-effect concentration; *N(L)OAEL* = no (low)-observed-adverse-effect level; *MOS* = margin of safety

Environmental risk assessment	$RCR = \frac{PEC}{PNEC} <> 1$	$RCR = \frac{WorstCaseExposure}{\left(\frac{WorstCaseToxicity}{AF}\right)} <> 1$
Human health risk assessment	$MoS = \frac{N(L)OAEL}{ExposureLevel} <> AF$	$RCR = \left(\frac{WorstCaseExposure}{WorstCaseToxicity}\right)^{-1} <> AF$

1996). This scapegoat to proceed with risk assessment (especially effects analysis) in the absence of sufficient data is in sharp contrast to the embraced realist perspective where policy should be grounded in scientifically established facts. These default assessment factors are dependent on the confidence with which a PNEC can be derived from the available effects data. This confidence increases in the case of the availability of toxicity data from a variety of species covering different taxonomic groups belonging to different trophic levels. In other words, the more data are available and the more they represent a complete ecosystem, the smaller the assessment factor should be. In a next step, the assessment factor is applied to the lowest toxicity level of the relevant available toxicity data to account for the following (EC 1996; Vermeire et al. 1999):

- Intra- and interlaboratory variations
- Intra- and interspecies variations (biological variance)
- Short-term to long-term toxicity extrapolation
- Laboratory data to field impact extrapolation
- The nature and severity of the effect, the dose–response relationship observed and the overall confidence in the database

In principle, an attempt is made to assess the known or quantifiable uncertainties in an assessment factor. In addition, unquantifiable and unrecognized uncertainties are left out, and consequently the estimated assessment factor suggests more certainty (on uncertainty) than actually present.

Although the TGD prescribes that preference should be given to the best and most realistic information (e.g., in the absence of sufficiently detailed data), the exposure or effect analysis is often conducted on the basis of worst-case assumptions, using default, often conservative, values when model calculations are applied. For example, Jager (1998a) found that deviations between defaults and actual measured emission values range from 1 to 1,000.

A closer look at the use of assessment factors and worst-case assumptions in the calculation of RCRs reveals what is so problematic in current EU risk assessment exercises. Although this paper focuses on environmental chemical risk assessment, it is informative to take notice of the way worst-case assumptions and assessment factors appear in human health risk assessment. As it is, both assessments use RCRs containing worst-case assumptions and assessment factors. These 2 assessments differ with respect to the extent to which uncertainties are visible in the calculation (see Table 1). In environmental risk assessment, the RCR inherently contains worst-case assumptions that are incorporated in both the PEC and the PNEC, while the assessment factor is incorporated only in the PNEC derivation. In human health risk assessment, the margin of safety is used and defined as the ratio of a no (low)-observed-adverse-effect level (N[L]OAEL) and the exposure level. The worst-case assumptions are incorporated in both N(L)OAEL and the exposure level. The assessment factor is not incorporated as such but is used as a reference for the calculated margin of safety. The use of the assessment factor is more visible and hence transparent to risk managers in human health risk assessment compared to environmental risk assessment. However, the worst-case assumptions themselves still conceal uncertainties that are kept inside the domain of risk assessors, whereas they pertain inasmuch to the domain of the risk managers and risk communicators. In other words, although visibility is a 1st step toward the explication of uncertainty, the assumptions concealed behind the assessment factor should be explained and hence made informative for risk managers and risk communicators. Risk managers would then realize better that the RCR is in fact no real risk, as the words "risk characterization ratio" suggest, but rather a measure to avoid false negatives.

EU risk assessors are genuinely aware of the fact that scientific certainties are not the sole determinants in risk characterizations. Awareness exists that uncertainties play out in a much more subtle way. For instance, when Bodar et al. (2005) discuss that practical considerations are part of risk assessment, they do in fact acknowledge that assessment factors and worst-case assumptions are practical considerations that help translate scientific knowledge into knowledge that can be used by risk managers to develop risk policy and to set risk limits. This is to say that current EU risk assessment is based on a regulatory science rather than on research science. Typical for the distinction between research science and regulatory science is that the latter takes into account the usability of the knowledge for policy purposes (for examples of these differences, see Jasanoff 1990). Regulatory science recognizes the importance of scientific uncertainty for risk management and risk communication and takes an active role in pointing out the dimensions of uncertainty. In her analysis of Dutch soil quality standards, Souren (2006) characterized the scientific knowledge that was labeled as usable knowledge as regulatory science. EU risk assessment has characteristics of such regulatory science practice as well. For the future development of EU assessment, much could be gained from the insights that have been developed about regulatory science, as summarized previously, and about the explication of uncertainty, which will be discussed further.

Another ground for the claim that EU risk assessments are based on regulatory science is that involved parties at the TC-NES meetings often have different views on how much uncertainty is acceptable for them on certain risk assessment elements and how to assess it practically (Bodar et al. 2005 and author's experience). The discussions at these meetings, for instance, concern the size of the assessment factor (as e.g. in the Zn risk assessment; see Bodar et al. 2005) and the

interpretation of "reasonable worst case" versus "unreasonable worst case." Establishing quantitative representations like worst-case assumptions and assessment factors is but 1 way to resolve these discussions. At present, assessment factors and worst-case assumptions are applied in a conservative way in order "to be certain" to avoid false negatives (unsafe chemicals that are assessed to be safe; see Jager 1998b).

In the following sections, we suggest improving risk assessment by developing uncertainty analysis for worst-case assumptions and assessment factors.

Indications for improved uncertainty analysis within the EU risk assessment community

Within the risk assessment community, some recognize the need to address uncertainty more explicitly because this is useful to risk managers (Jager 1998b; Vermeire et al. 2001; Bodar et al. 2002; Kalberlah et al. 2003; Matthies et al. 2004; Verdonck et al. 2005). In addition, several research initiatives are developing and promoting the use of more probabilistic techniques to specifically deal with the quantification and explication of uncertainty, such as for plant protection products (ECOFRAM in the United States and EUPRA, EUFRAM in the EU; Hart 2001; EUFRAM 2005). However, in the EU risk assessment directives and the EU TC-NES meetings, there also seems to be an increasing awareness of the importance to explicate uncertainty, and one is concerned with how to properly deal with this. In this paper, this will be illustrated by 2 examples: The zinc risk assessment (Bodar et al. 2005) and the 2003 update of the EU-TGD (EC 2003).

Although not explicitly requested by the TGD, 2 scenarios with a lower and an upper bound of a certain input parameter are sometimes conducted in ongoing risk assessments. For example, in the environmental zinc risk assessment, a range of the solids-water partition coefficients is considered to quantify the implication of its variation on the final risk outcome. By considering 2 scenarios, the resulting effect of the uncertainty associated with the partition coefficients on the risk conclusions is therefore assessed.

In 2003, based on input from experts from EU member states, nongovernmental organizations, and industry, the European Chemicals Bureau released an updated version of the EU-TGD for new and existing substances (EC 2003). From this revision process, it could be concluded that the basic ideas/principles of the risk assessment process as described in the 1st TGD still hold but that a number of important, mostly technical refinements were included (Bodar et al. 2002). The revised EU-TGD remains intrinsically a deterministic assessment, but there is a tendency to improve uncertainty quantification. Indeed, in the effect analysis, specific guidance on the use of a probability distribution—that is, the species sensitivity distribution (SSD) describing interspecies variability for the derivation of the PNEC for aquatic and terrestrial environments—has now been fully introduced as an alternative to the more traditional approach where default assessment factors were covering interspecies variability. The revised TGD now contains guidance and criteria on when and how to use the SSD in the context of EU risk assessment: If a large data set from long-term ecotoxicity tests is available (at least 10 and preferably more than 15 chronic toxicity data for different species covering at least 8 taxonomic groups), SSDs can be used (EC 2003). Typically, the 5th percentile of the SSD (corresponding to a 95% protection level) is selected as threshold for further propagation in the risk characterization. The use of SSDs is clearly an improvement of the uncertainty analysis because the visibility of the uncertainty on the interspecies sensitivity is improved. This is also recognized in the Zn risk assessment (Bodar et al. 2005). In addition, accepting that 5% of the species are potentially affected recognizes that the concept of zero risk does not hold.

These 2 examples show an increasing awareness of uncertainty and a tendency to make uncertainty more visible in EU risk assessments. However, it could be argued that this is still insufficient and still contains several positivistic concepts. First, not all sources of uncertainty are considered, mainly the known and quantifiable sources, and in case a more elaborate uncertainty analysis is conducted, uncertainty is quantified as much as possible as if it is possible to quantify all sources of uncertainty and as if the uncertainty estimates are true and provide certainty. This can lead to an unproductive drowning in uncertainty. Second, uncertainty is still insufficiently made visible in the risk conclusions. Risk characterization ratios still conceal information on assessment factors and worst-case assumptions. Third, more information leads to "new uncertainties" and additional conservatism because of the search for the certain and hence safe side. For example, after taking the 5th percentile of the SSD, an additional assessment factor between 1 and 5, reflecting further identified uncertainties, needs to be applied on the derived threshold. As a minimum, the following points have to be considered when determining the size of this additional assessment factor (EC 2003):

- The overall quality of the database and the endpoints covered (e.g., covering all sensitive life stages)
- The diversity and representativity of the taxonomic groups (life forms, feeding strategies, and trophic levels) covered by the database
- Knowledge on presumed mode of action of the chemical (also covering long-term exposure)
- Sampling uncertainty and probability distribution or model structure uncertainty
- Comparisons between field and mesocosm studies

These "new" (quantifiable or unquantifiable) uncertainties lead to additional assessment factors and consequently again the pretense of certainty. This tendency of applying additional assessment factors for "new" sources of uncertainty is not robust, as there will always be "remaining" uncertainty that may give rise to the use of additional assessment factors. Moreover, the identification of additional sources of uncertainty does not necessarily mean that the risk is increased. It only means that more uncertainties are characterized.

This criticism to the EU risk assessment could be elaborated much further. However, we like to focus in this paper on the improvements that are being made already from within the risk assessment community and provide support for further motivation to proceed with the explication of uncertainty in EU risk assessments. We will do this by bringing in insights from interdisciplinary studies on uncertainty and risk in the next section and by suggesting a further improvement in uncertainty explication in the following sections.

Further support for improved uncertainty analysis

As indicated previously, the actual working practice within EU risk assessments already contains elements of a regulatory practice; there is room for exchange of views and arguments

between science and policy. Illustrative of this is that the strict distinction between risk assessment, risk management, and risk communication begins to fade. Jasanoff has showed in her analysis of the use of environmental standards in the United States in the 1980s and 1990s that this fading is crucial for the development of a robust risk assessment. The demarcation and maintenance of boundaries between science and policy and hence between risk assessment, management, and communication is artificial and unproductive. Regulatory practices and the assessments they produce do become more robust if involved parties have access to all steps in the process. We would like to interpret this development in EU risk assessment as an improvement and a step toward smart risk assessment. A further improvement toward smart risk assessment is to recognize subjective judgment as decisive for the outcome of the risk assessment. From this recognition it follows that this subjectivity must be explicated, providing all actors with more insight into the dimensions of uncertainty and risk at play.

One of the further improvements we would like to encourage is the inclusion of uncertainty analysis into the EU risk assessment process. With this we mean that not only the risks but also the uncertainties and the different types and sources of these uncertainties should become explicitly part of risk assessment process. In addition, not only technical, scientific uncertainties should be explicated but also uncertainties related to decision making and implementation. This encouragement is grounded in several studies. For instance, Jasanoff (1995) argued already in the 1990s that the uncertainties related to environmental risks do not only concern scientific uncertainties but also include uncertainties and values related to interests of all stakeholders. The significance of this work for our argument here is that these interdisciplinary studies have revealed that the distinction between objective and subjective elements in risk assessments is not only illusory but unproductive as well. For instance, in their correspondence to *Nature* in March 2002, Hoffmann-Riem and Wynne (2002) made clear that the interactions in complex systems like ecosystems are simply beyond our capacities to be modeled and predicted with certainty, providing a fundamental obstacle to obtain objective and certain knowledge. Put differently, the assessment of environmental risks is fraught with ignorance, that is, the most fundamental uncertainty. Such complex systems and interactions are beyond "normal" or research science. Science alone cannot satisfactorily deal with these fundamental uncertainties. While encountering such fundamental uncertainties, Funtowicz and Ravetz (1992) aptly phrased the inadequacy of research science when they state that "in the light of such uncertainties, scientists become amateurs." Funtowicz and Ravetz (1992) have sketched the outlines of what they consider adequate "problem-solving capacity" for such situations. Without discussing their proposals in detail here, the core of their proposal is to broaden the number of actors involved in formulating and evaluating strategies to cope with the risks society encounters. A broadening up is required to ensure that the various stakes are represented and taken into account. The broadening up we observe in current EU risk assessment is promising in the light of these interdisciplinary studies.

This perspective has already inspired analyses of risk assessment practices on risk-related issues like agriculture and pesticides (Halffman 2003), food quality (Frewer et al. 2003), genetically modified food (Fischer et al. 2005; Borrás 2006), and antibiotics in food (van Asselt and Vos 2006). For future direction, EU risk assessment could benefit from the experiences gained in these fields.

Besides the encouragement to proceed with involving more actors, the main issue we want to address in this paper is the explication of uncertainty as an important step toward smart risk assessment. The explication of uncertainty is motivated from 2 bodies of literature. First, the concepts of risk and uncertainty have been studied from different angles and have led to a differentiation of risk and uncertainty types (Renn 1992; van Asselt 2000; Klinke and Renn 2002). The increased scientific knowledge base for risk assessment has revealed that uncertainties can be classified as inexactness, unreliability, and border with ignorance (Funtowicz and Ravetz 1990). The latter class has been further subdivided, resulting in uncertainty typologies that are useful for the purpose of our paper; the further development of EU risk assessment. We would encourage the implementation of these typologies and discuss these typologies in more detail in the next section. Second, and besides this recognition to differentiate between level, location, and nature of uncertainty, there is further support for an improved uncertainty analysis. Such support originates from risk perception and risk communication studies that have revealed that the public can deal with information on risks and uncertainty in a very genuine way and in a much better way than was assumed before (e.g., Frewer 2004). This is an argument that favors the explication of uncertainty and risk. Related to this is that that public trust in science and risk assessment will increase with transparency and openness about risks and uncertainties in risk communication (compare Löfstedt 2005). In order to maintain and increase trust in science and risk assessment, it will be crucial for the EU to develop a more explicit risk and uncertainty analysis.

Explicit risk and uncertainty analysis within a regulatory practice provide the 2 essential ingredients of what we call "smart risk assessment" (see next section). Smart risk assessments are geared toward a transparent and informative assessment that enables risk managers, risk communicators, and all involved stakeholders to be able to weigh both the risks and the uncertainties. In addition, smart risk assessment includes the development of strategies to reduce or mitigate eventual risks.

TOWARD SMART RISK ASSESSMENT

The EU chemicals program has been heavily criticized for its slowness in finalizing risk assessment for priority chemicals and for the lack of outcome in terms of implemented risk reduction measures (Bodar et al. 2002). In the light of the previous discussion, it could be interpreted that the EU has not yet developed a risk assessment process that meets the need of current decision-making processes on chemicals. The generation of scientific certainties and facts has become a time- and resource-consuming activity that has not sufficiently paid off in terms of relevant information for risk managers. As a response to this criticism, the EC has initiated a process of reforming the EU chemicals management. As we see it, uncertainty analysis can improve EU risk assessment at this point. Uncertainty analysis enables risk managers to take more robust decisions basically because more information is available. This new chemical policy, REACH, for Registration, Evaluation, and Authorization of CHemicals (CEC 2003),

involves delegation of the responsibility of data compilation, risk assessment, and risk reduction (management) of chemicals from the authorities to industry. In addition, risk/safety assessment and risk management will be more integrated. REACH will involve the evaluation of tens of thousands of chemicals for which, in most cases, only a limited set of information is available. These circumstances are called data poor. When more information is available, the circumstances are called data rich.

It sounds as if these initiatives will speed up the process; however, it is still unclear how these developments will affect the treatment and consideration of uncertainty. The preliminary TGD (RIP 2005) remains on the one hand positivistic in the sense that uncertainty (partly quantified in worst-case assumptions and assessment factors) is still hidden in risk estimates. Improved uncertainty analysis concerns the further quantification of what is assumed to be quantifiable (i.e., certain uncertainties). As it is stated explicitly in the draft TGD, EU risk assessment favors the quantification of uncertainty over a qualitative analysis: "The qualitative analysis [of uncertainty] is a simple method to provide insight in the influence of uncertainty on the RCR. However, it does not deliver a single number that can be used to objectively assess the magnitude of the uncertainty. This is unsatisfactory, both from a scientific point of view and from a practical point of view" (RIP 2005, p. 437). The delegation to industry also has a positivistic nature. It assumes that who conducts the risk assessment does not matter and that every actor will reach the same risk conclusions. Only the risk assessment procedure (as specified in the TGD) and the fact that industry has better access to information and data matter. The subjective position of industry and its risk assessment is overlooked. On the other hand, the preliminary TGD for REACH has taken up some of the insights from interdisciplinary thinking and increases room for a broader perspective on risk and uncertainty explication: "It may be advised to always perform such an assessment [qualitative] even if probabilistic methods are employed" (RIP 2005, p. 83). Uncertainty is made more explicit and visible "in order to assist decision-making in the light of the uncertainty associated with the outcome of the risk assessment" (RIP 2005, p. 428). It is recognized (Bodar et al. 2005) that practical considerations play an important role in establishing assessment factors and hence RCRs. This is an indication that current EU risk assessment acknowledges that risk assessment bears resemblance to a regulatory practice. It also contains the promise of a further improvement and development of EU risk assessment in that direction. In regulatory practices, constructionist perspectives on risk and uncertainty prevail.

Given the lessons learned and the insights from interdisciplinary thinking about scientific uncertainty, some directions can be formulated toward smart risk assessment, an assessment in which awareness and openness to uncertainty is used to produce better characterizations and evaluations of risks. In such a context, quantifying uncertainty is not an aim but just a means. It will be further illustrated here how guidance should be and is given in the current draft TGD for REACH on how to differentiate, assess, and use uncertainty.

Differentiating uncertainty

A 1st prerequisite in smart risk assessment is to differentiate uncertainties. As indicated previously, our suggestions for improvement of EU risk assessment are based on a recent review of uncertainty typologies (Walker et al. 2003). These authors have distinguished 3 dimensions of uncertainty. The level, location, and nature of uncertainty are the 3 dimensions to be distinguished in any smart risk assessment. From that review, it seemed also that it is important to differentiate between uncertainty due to variability (ontological uncertainty) and uncertainty due to limited knowledge (epistemological uncertainty; van Asselt 2000; Walker et al. 2003). Funtowicz and Ravetz (1990) describe uncertainty as a situation of inadequate information, which can be of 3 sorts: Inexactness, unreliability, and border with ignorance. However, uncertainty can prevail in situations where a lot of information is available (van Asselt and Rotmans 2002). Furthermore, new knowledge on complex processes may reveal the presence of uncertainties that were previously unknown, hidden, or understated. In this way, more knowledge illuminates that our understanding is more limited or that the processes are more complex than thought before (van Asselt 2000). This broader uncertainty perspective and awareness makes a risk assessment smarter. The previously mentioned insights from interdisciplinary analyses of uncertainty have also revealed that uncertainty due to variability (ontological uncertainty) should include not only this inherent randomness of nature but also the variability in human behavior (behavioral variability) as well as societal variability, including the development of technological systems (Walker et al. 2003). Therefore, future EU risk assessments should broaden its conceptions of uncertainty and variability and try to consider behavioral variability as well as societal variability (e.g., variability in risk acceptability and risk perception). However, this additional extension, which can be considered an even smarter risk assessment, will not be further extended here.

In current EU risk assessment, a similar terminology is applied, albeit in a different way. Uncertainty is often used as an umbrella term for variability and reducible uncertainty. Variability represents inherent heterogeneity or diversity in a well-characterized population. Fundamentally a property of nature, variability is irreducible through further measurement or study. Variability can only be better characterized. Variability emerges at the exposure side of risk assessment, as the temporal and spatial variations of chemical concentrations in the environment and as the variability in the human population (e.g., variability in diet and consumption pattern, differences in duration and in route of exposure). At the effects side of environmental risk assessments, variability can, for example, be captured in an interspecies sensitivity probability distribution (SSD). Other forms of variability are intraspecies variability, differences in endpoints (reproduction, growth, survival), and life-stage variability (e.g., larvae and adults). Reducible uncertainty comes under the forms of sampling uncertainty, short-term to long-term toxicity extrapolation, laboratory data, and field impact extrapolation. As it is, uncertainty in EU risk assessments at present refer exclusively to the physical, natural system, that is, where species and organisms are exposed, and where effects are observed, measured and modeled. This illustrates that uncertainty and variability as concepts in current EU risk assessment still bear witness to the realistic conception of risk.

Several guidances have been developed in response to the notion that in the daily practice of science for policy, there is a pressing need for guidance in assessing and communicating the broad spectrum of uncertainty types (van der Sluijs et al. 2003;

Krayer von Kraus 2005). The so-called RIVM guidance recognizes that this need extends beyond the quantitative assessment of (known) uncertainties in model results per se and focuses therefore on the entire process of environmental assessment, running from problem framing to reporting the results of the study (van der Sluijs et al. 2003). Arguably, with the development and implementation of the guidance, RIVM sets a best practice standard in environmental management. The uncertainty matrix is a useful aid in making an inventory of where ("location") the most policy-relevant uncertainties are expected and how they can be characterized in terms of a number of uncertainty features (van der Sluijs et al. 2003; 2004; Walker et al. 2003; Krayer von Kraus 2005). In the draft TGD for REACH (RIP 2005), a checklist is proposed to systematically check and list the different sources of uncertainty and variability for each step in the risk assessment procedure.

Practically, a structured matrix or checklist, covering all sources of uncertainty, should be added to the risk assessment report. In addition, it should be specified whether uncertainty can alter the risk conclusions. The environmental risk assessment of zinc, for example, successfully described a number of (mainly known) uncertainties related to natural background concentration, release factors, bioavailability correction, assessment factors, and so on in a separate section (Bodar et al. 2005). However, an uncertainty matrix would further add a number of uncertainty issues. To give an example, the dimension on value ladenness could be added. This concerns, among other things, the way in which 1) the problem is framed vis-à-vis the various views and perspectives on the problem (member states, industry, nongovernmental organizations), 2) the knowledge and information (data, models) are selected and applied, and 3) the explanations and conclusions are expressed and formulated. If the value ladenness is high for relevant parts of the assessment, then it is imperative to analyze whether the results of the study are highly influenced by the choices involved and whether this could lead to a certain arbitrariness, ambiguity, or uncertainty of the policy-relevant conclusions.

Uncertainty matrices and checklists allow the risk assessor and manager to have a broader perspective on uncertainty instead of focusing only on quantification as such. Consequently, this is a productive and necessary way forward in EU risk assessments. Recognized but unquantifiable uncertainties are, in this way, made more transparent.

Assessing uncertainty

One needs to recognize that all uncertainties can never be quantified. However, it would be counterproductive to conclude that quantification of the known uncertainties is useless. For example, if the same uncertainty sources are assessed in different chemical safety dossiers, uncertainty information can still be used for comparative purposes in risk management. The most important point in assessing uncertainty is to recognize that all uncertainties are not quantifiable, and therefore they should be separated from the risk characterization. The quantified part of uncertainty should be seen as a best estimate that can be used as a means (see next section).

In the draft TGD for REACH (RIP 2005), a tiered procedure has been proposed from a qualitative uncertainty analysis to a simple probabilistic analysis or a full quantitative probabilistic analysis, depending on the level of complexity of the assessment, resource intensity, and data needs. Uncertainty can be assessed in both data-poor (through the use of assessment factors and worst-case assumptions in a scenario analysis) and data-rich conditions (through the use of probability distributions in a probabilistic analysis). The data-poor circumstances will occur predominantly in REACH, and hence assessment factors and worst-case assumptions are predominant. In the remainder of this section, an approach is proposed to improve the unraveling of uncertainty that is inherent in worst-case assumptions and assessment factors.

If only the known uncertainties are to be quantified, it should be done independently from risk quantification. For this, variability (ontological uncertainty) should be separated from epistemological uncertainty, as variability contributes in the risk characterization. After all, the risk aims to assess whether the spatially and temporally varying PEC exceeds the interspecies varying chronic effect thresholds. By separating variability from epistemological uncertainty, risk management can be improved, for example, because it allows judging the expected outcome of additional efforts for a reduction of uncertainty and enables proper decisions for such an engagement (see also Kalberlah et al. 2003). Consequently, the probability distributions of exposure and effects are made up of a variability distribution (the cumulative probability; S-shaped curves in Figure 1) and an uncertainty (epistemological) distribution (the gray bands in Figure 1, representing the 90% confidence interval of this epistemological uncertainty distribution). Figure 1 reveals how mean exposure and mean effects relate conceptually to the worst-case exposure and worst-case effects, which are currently used, respectively, as PEC and PNEC values. Mean exposure and mean effects are at the 50% of the cumulative probability (visualized as squares), while the worst-case exposure estimate (the PEC) used in actual risk assessments can be seen as an upper percentile of both the variability distribution and the epistemological uncertainty distribution (visualized as a circle). The actual worst-case effects or toxicity estimate (the PNEC) can be seen as a lower percentile of both its interspecies variability and its epistemological uncertainty (visualized as a circle).

When insufficient data and knowledge are available to describe the variability and epistemological uncertainty distributions, assessment factors (AF in the following equation) and worst-case assumptions are used to estimate the epistemological uncertainty and variability (as illustrated by the arrows at the bottom of Figure 1). The actual worst-case exposure estimate (the PEC) can then be seen as a mean exposure estimate multiplied with extrapolation factors due to worst-case assumptions from both variability and epistemological uncertainty. The actual worst-case effects or toxicity estimate (the PNEC) can be seen as a mean effects or toxicity estimate divided by assessment factors and worst-case factors from both variability and epistemological uncertainty. This can also conceptually be formulated as

$$WorstCaseExposure = MeanExposure \cdot FactorExp_{worstcase,\mathrm{var}} \times FactorExp_{worstcase,unc}$$

$$WorstCaseToxicity = \frac{MeanToxicity}{(AF_{\mathrm{var}} \cdot FactorTox_{worstcase,\mathrm{var}}) \cdot (AF_{unc} \cdot FactorTox_{worstcase,unc})}$$

Efforts to distinguish between different sources of epistemological uncertainty and variability in assessment factors have

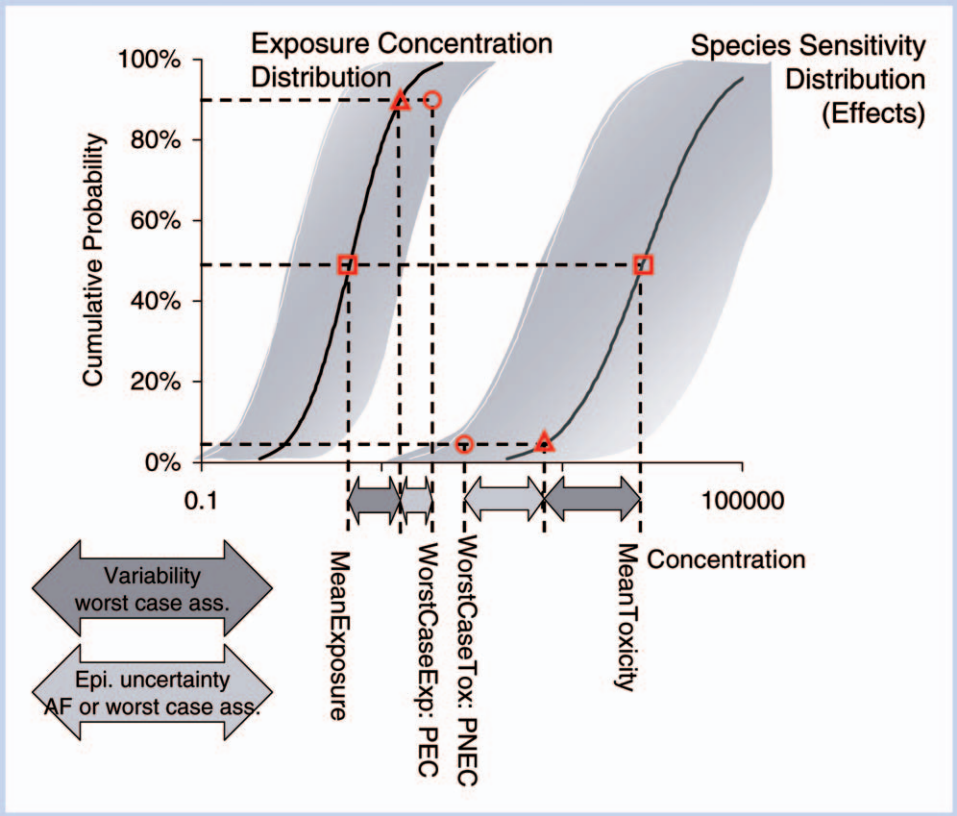

Figure 1. Cumulative probability distributions describing variability in exposure (exposure concentration distribution) and effects/toxicity (species sensitivity distribution [SSD]) with grey bands describing 90% confidence intervals of the epistemological uncertainty distribution. Below the *x*-axis, the arrows represent assessment factors/worst-case assumptions describing variability or uncertainty in environmental risk assessment (AF = assessment factors).

already been made in human health risk assessment (Vermeire et al. 1999; Kalberlah et al. 2003). However, the high level of detail in categorization was found to be difficult in practice (Vermeire et al. 1999). Nevertheless, a distinction in 2 categories (epistemological uncertainty and variability) will most likely be more feasible. This can be done by thoroughly reasoning and interpreting the different types of uncertainty (typically by experts). For example, the observed variation in sensitivity between different species cannot be reduced through additional observations or further research. It can, for this reason, be interpreted as variability. However, in case it is unknown how large the variation between species can be and one estimates its variation, it should be interpreted as uncertainty. In general, average database-driven assessment factors on intra- and interspecies variability, on acute to chronic extrapolation, and from insensitive to sensitive subpopulation can be attributed to variability, whereas assessment factors on overall confidence in the data set can be attributed to (epistemological) uncertainty.

In data-poor conditions, the risk assessor can conduct 3 scenarios without the need to characterize the entire probability distributions (summarized in Table 2). The 1st scenario is an "uncertain worst-case" estimate scenario that accounts for all worst-case (parameter or modeling) assumptions and assessment factors caused by sources of both variability and epistemological uncertainty. A 2nd scenario, the "realistic worst-case" estimate scenario, accounts for the worst-case assumptions and assessment factors caused by sources of variability only. The 3rd scenario, the "average" estimate scenario, does not account for sources of variability and epistemological uncertainty. The difference in RCRs between the "uncertain and realistic worst-case" estimate

Table 2. Risk characterization ratio (RCR) formula for several scenarios in data-poor conditions. See Table 1 for definitions

Scenario	Formula risk characterization ratio
"Uncertain worst-case" estimate scenario (accounts for both variability and uncertainty)	$RCR = \frac{MeanExposure \cdot FactorExp_{worstcase,var} \cdot FactorExp_{worstcase,unc}}{\left(\frac{MeanToxicity}{AF_{var} \cdot AF_{unc} \cdot FactorTox_{worstcase,var} \cdot FactorTox_{worstcase,unc}}\right)}$
"Realistic worst-case" estimate scenario (accounts only for variability)	$RCR = \frac{MeanExposure \cdot FactorExp_{worstcase,var}}{\left(\frac{MeanToxicity}{AF_{var} \cdot FactorTox_{worstcase,var}}\right)}$
"Average" estimate scenario	$RCR = \frac{MeanExposure}{MeanToxicity}$

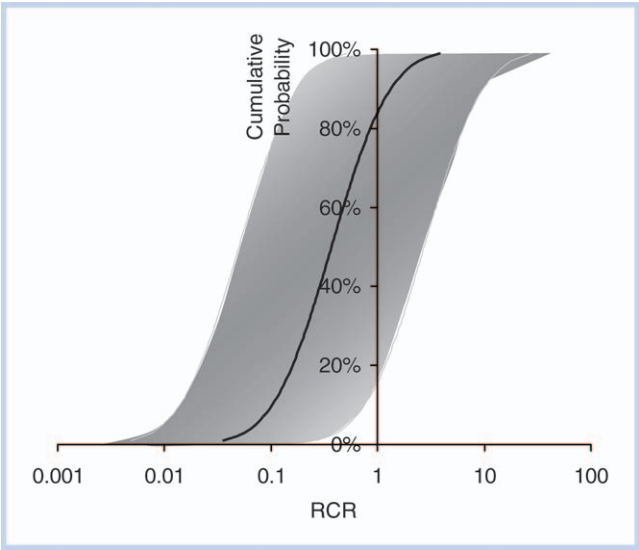

Figure 2. Risk characterization ratio (RCR) cumulative distribution function with 90% uncertainty/confidence band summarizing several scenarios.

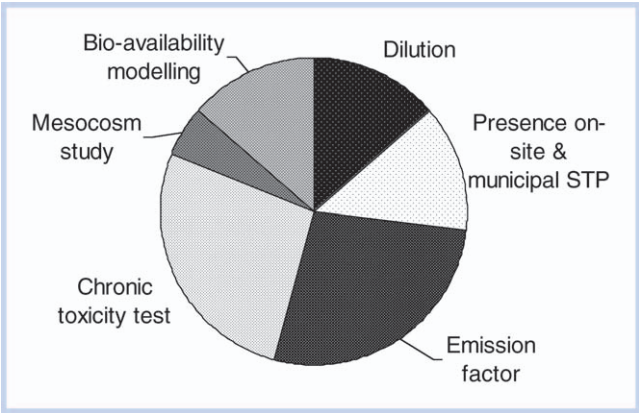

Figure 3. Effect of uncertainty sources on the risk outcome (hypothetical example using sensitivity analysis, STP = sewage treatment plant; Verdonck et al. 2006).

scenario can be considered as a measure for epistemological uncertainty. The difference in RCRs between the "realistic worst-case and average" estimate scenario can be considered as a measure for variability. The "average" estimate scenario is not necessarily sufficiently protective for the environment but is useful obtaining a quantitative estimate of the variability. The terminology (as "realistic worst case") is positivistic, as again a false sense of certainty is suggested (as if it is possible to calculate the "realistic worst case" exactly). Nevertheless, the terminology is kept because of its widespread use within the community. The quotation marks are added to remind the reader of its potential, misleading character. A similar scenario analysis has been proposed in the draft TGD for REACH (RIP 2005), where a best-case/worst-case analysis is recommended as a simple way for checking the influence on the risk conclusions and the usefulness of collection of additional information.

In data-rich conditions, a probabilistic risk assessment can be conducted to account for both variability and epistemological uncertainty of the input parameters. Probabilistic risk assessment is similar to the previous "what if" scenarios in that it generates a number of possible scenarios. However, it goes 1 step further by effectively accounting for every possible value that each variable could take and weighing each possible scenario by the probability of its occurrence. Probabilistic risk assessment achieves this by modeling each variable by a probability distribution. In this way, all possible scenarios are simulated, including "realistic and uncertain best-case" estimate scenarios but also even worse scenarios than the "uncertain worst-case" estimate scenario. Exposure and effects are then represented as an exposure concentration distribution and an SSD, as in Figure 1. The result is an RCR probability distribution (Figure 2). The black line represents the estimated variability of the RCRn whereas the gray band represents the epistemological uncertainty of the risk. Examples on probabilistic risk assessment in the EU framework on new and existing substances can be found in Vermeire et al. (2001) for phtalates and Van Sprang et al. (2004) for zinc. In addition, a comparison of model predictions with monitoring data can also indicate how large the lump sum of parameter, model, and monitoring uncertainty is.

In this way, uncertainty is not hidden in risk estimates but is made visible through "uncertain versus realistic worst-case" estimate scenarios or through probability distributions and confidence intervals. This is an improvement because it increases the transparency of the risk assessment, which is an essential feature for robust risk assessment procedures. It is a step forward, but further effort and analysis are needed to develop a complete integrated example to work out more precisely the implications of uncertainty explication for risk management. For policy instruments to be effective, they must be consistent with the principles underlying policy development. The required development in EU risk assessment toward smart risk assessment must therefore include a reconsideration of the adequacy of the policy instruments that are available to risk managers. For example, risk decisions that are based on the information provided by uncertainty analysis must be flexible enough to allow for revisions or adaptations once uncertainties disappear or turn out to be larger or smaller than expected. In other words, the flexibility of the policy measures, rules, and procedures available to risk managers must be tuned to this uncertainty explication.

Uncertainty analysis as a means

Besides uncertainty differentiation and assessment, the 3rd prerequisite in smart risk assessment is to use the uncertainty information as a productive means to refine the assessment or find alternative solutions for the problem at stake (to take smart decisions). The draft TGD for REACH considers addressing uncertainty for further iterations of a risk assessment (RIP 2005) as illustrated in the following examples.

First, REACH (and the current EU chemicals policy) is based on the "no data, no market" principle. Missing data/information are replaced by conservative, default worst-case assumptions and assessment factors. In general, a lot of resources have to be allocated for collection of information/data in order to obtain realistic risk estimates. It would therefore be resource efficient to identify and to collect information/data for those uncertainty sources having the largest effect on the risk outcome only. Sensitivity analysis is a widely known and accepted technique to allocate output uncertainty to several input uncertainties. In the hypothetical example of Figure 3, it is most resource efficient to refine the

potential risks associated with a local site to collect chronic toxicity tests and/or site-specific emission factors. Large uncertainty contributions from model predictions are a driver to collect additional monitoring data. In this way, uncertainty is used as a means for further risk refinement or better characterization of the risk (Verdonck et al. 2006).

Second, uncertainty analysis will uncover the expected effects of further efforts to reduce or characterize uncertainties. In case further reduction is judged to be impractical (too time consuming or prohibitively expensive), a mixed strategy should be followed. Precautionary measures could be taken, and at the same time investments should be taken to make the social system more adaptive to live or coexist with uncertainties and the possible adverse effects of risks when they occur. Key words for such strategy are resilience (Klinke and Renn 2002), coping (Morgan et al. 2001), and information. These strategies are based on the results of studies on risk perception (Slovic 2000). That work has revealed that personal control over risky situations, together with information about the occurrence, the assumed effect, and the mechanism causing this effect, reduces the perceived dread of a risk. This empowers society to cope with these risks. The positive side effect of this is that it reduces the unrealistic pressure on governments to control and reduce those risks that are characterized by high and irreducible uncertainties.

The previous examples illustrate an approach whereby uncertainty is not used as a mathematical artifact to obtain a false sense of certainty but is used to obtain a better risk estimate. Admitting uncertainty as postulated by Hoffmann-Riem and Wynne (2002) additionally builds up trust and credibility toward the risk manager.

CONCLUSIONS

In the current EU risk assessment of new and existing substances, uncertainty analysis is problematic for several reasons. First, mainly the known or quantifiable sources of uncertainty are considered. Second, although partly discussed in the risk assessment report and TGD, uncertainty is insufficiently made visible in the risk conclusions to risk managers. Uncertainty is actually concealed in risk characterization ratios. Third, uncertainty is considered a mathematical artifact that can be quantified such that a false sense of "certainty" and "protectiveness" is reached. This way of dealing with uncertainty can be characterized as positivistic. Consequently, decision makers and risk managers overestimate the reliability of the risk conclusions outcome.

The new EU chemical policy REACH is an opportunity to learn from interdisciplinary thinking in order to evolve to smart risk assessment, that is, an assessment in which awareness and openness to uncertainty are used to produce better characterizations and evaluations of risks. The preliminary TGD already provides some useful steps in this direction but still bears witness to an overly positivistic approach. In a smart risk assessment context, quantifying uncertainty is not an aim but just a productive means to understand the impact of uncertainty on conclusions and recommendations, to refine the assessment, and to develop alternative solutions or additional policies for the problem at stake or as a basis for monitoring and evaluation that can inform policy adjustment over time. Guidance was given on how to differentiate (e.g., through an uncertainty matrix or checklists), to assess (e.g., through scenarios or probabilistic assessment), and to use uncertainty (e.g., for risk refinement or to search for alternative solutions). The application of such comprehensive uncertainty analysis on a risk assessment case would further illustrate the potential and benefits of a smart risk assessment. A subsequent challenging question is concerned with the adequacy of the policy instruments available for risk managers to implement risk- and uncertainty-based assessments (see also Krayer von Kraus et al. 2005).

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