Pure Appl. Chem., Vol. 75, Nos. 11–12, pp. 2535–2541, 2003.

Workshop 5.5

Role of the precautionary principle in the EU risk assessment process on industrial chemicals*

Jack de Bruijn‡, Bjorn Hansen, and Sharon Munn

European Chemicals Bureau, Joint Research Centre, 21021 Ispra (VA), Italy

Abstract: This paper discusses the practical implementation of the precautionary principle in the area of management of industrial chemicals in the European Union. An analysis of a number of recent cases where the precautionary principle was invoked shows that the main reason for doing so were the uncertainties in the risk assessment (or the underlying effects or exposure data), which were, according to the scientific experts, so high that the "normal" level of certainty could not be obtained. The challenge for the future is to try to develop general guidance or rules that will support the policymakers in their decision as to whether this uncertainty is so large that action is warranted or whether it is acceptable to wait until further information has become available.

INTRODUCTION

Taking regulatory action on the basis of the precautionary principle (PP) is often presented as an alternative to taking action based on an assessment of risks. In practice, however, many references in international law to the precautionary principle, such as the 1992 Rio Declaration, refer to the use of this approach when there are threats of serious irreversible damage, but there is lack of full scientific evidence. This implies that some sort of identification of the potential hazards and or risks has to be present in order to allow decision-makers to decide on any action to be taken. In February 2000, the European Commission published a Commission Communication on the precautionary principle providing a general framework for its use in EU policy [1]. This paper addresses specifically the practical implementation of the approach in the area of management of industrial chemicals.

COMMISSION COMMUNICATION ON THE PRECAUTIONARY PRINCIPLE

The aim of the Commission Communication was to outline the Commission's approach to using the precautionary principle, to establish guidelines for it, to build a common understanding of how to assess, manage and communicate risks that science is not yet able to evaluate fully, and to avoid unwarranted recourse to the precautionary principle, as a disguised form of protectionism [1]. According to this communication, the implementation of an approach based on the precautionary principle should start with a scientific evaluation, as complete as possible, and where possible, identifying at each stage the degree of scientific uncertainty. Once the scientific evaluation has been performed as best as possible and the conclusions of this evaluation show that the desired level of protection for the environment

*Report from a SCOPE/IUPAC project: Implication of Endocrine Active Substances for Human and Wildlife (J. Miyamoto and J. Burger, editors). Other reports are published in this issue, *Pure Appl. Chem.* **75**, 1617–2615 (2003).

‡Corresponding author: Fax: 0039-0332-785862; E-mail: jack.de-bruijn@jrc.it

or a population group could be jeopardized, this may provide a basis for triggering a decision to invoke the precautionary principle. The conclusions should also include an assessment of the scientific uncertainties and a description of the hypotheses used to compensate for the lack of the scientific or statistical data. An assessment of the potential consequences of inaction should be considered and may be used as a trigger for action by the decision-makers. Clearly, the potential application of the precautionary principle is relevant to the risk management phase.

It is important to recognize that the communication indicates that the application of the precautionary principle should not be confounded with the prudential approach used in the context of assessing the risks. In assessing risks, a wide range of uncertainties have to be dealt with. Examples are the extrapolation of effects seen in laboratory test systems to real world conditions, the extrapolation from single species test results to effects on complex multispecies ecosystems, the extrapolation from effects seen in animal studies to potential effects in humans, and, last but not least, the extrapolation from short or medium-term exposure to lifetime actual exposure conditions. All of these uncertainties are usually taken care of in the risk assessment process, for instance by applying uncertainty or safety factors to the results of single species animal studies. It is the job of the risk assessment experts to provide their ultimate view on the reliability of their assessments, as well as on the remaining uncertainties. The overall level of uncertainty will affect the foundation for protective or preventive action in the risk management phase.

The Commission Communication on the precautionary principle was endorsed both by the European Parliament and the Council of Ministers who in their resolutions on this subject called upon the Commission to actively apply the guidelines and incorporate the principle in drawing up its legislative proposals [2,3].

RISK MANAGEMENT OF INDUSTRIAL CHEMICALS IN THE EUROPEAN UNION

In Europe, the potential risks of industrial chemicals with high-production volumes are assessed under Council Regulation (EEC) No. 793/93 [4]. This regulation introduced a comprehensive framework for the evaluation and control of existing chemicals. It foresees that this evaluation and control of the risks should be carried out in four steps: (1) data collection, (2) priority setting, (3) risk assessment, and (4) risk reduction. In short, the process is as follows: draft risk assessment reports are developed by a Member State, mainly on the basis of information provided by the producing companies. These draft reports are discussed in what is called technical meetings (TMs) of experts from Member States, industry, and NGO's. Once agreed by the TM, the risk assessments are sent to the Scientific Committee for Toxicity, Ecotoxicity and the Environment (CSTEE), which is asked whether it can support the conclusions of the assessments. Subsequently, the conclusions are forwarded to the so-called competent authorities (CAs) of the Member States, which is the policy body responsible for agreeing the conclusions and, where relevant, discussing and proposing the necessary risk reduction strategy. In the implementation, a separation of the risk assessment and risk management processes has been carried through as was also recommended by the Council in their resolution on the precautionary principle [3].

One should realize that this regulation deals with the assessment of the risks of high-production volume chemicals produced in volumes >1000 tonnes per year. The deliberate use of such large volumes implies that human activities almost inevitably lead to pollution.

Risk assessment is then the tool used to evaluate if these inevitable emissions lead to "unacceptable risk". Different judgments on the need to take action can be made by policy makers compared to scientists when there is not sufficient scientific evidence to demonstrate that an "unacceptable risk" exists, though also not enough to demonstrate that the risks are "acceptable". The case studies below will describe some of these situations.

CASE STUDIES

Since the implementation of Regulation 793/93, risk assessment reports have been prepared and discussed for approximately 113 out of 141 priority substances [5]. For approximately 70 of these, the conclusions have been agreed and sent forward to the risk managers to discuss the necessary development and implementation of risk management activities. The four cases described below provide useful information on how the relationship between the risk management process and the actual implementation of the precautionary principle has worked in practice.

Nonylphenol(ethoxylates)

The risk assessment for nonylphenol and nonylphenol(ethoxylates) was finalized in 1999 [6]. The conclusion on the environmental part of the assessment was that there is concern for the aquatic compartment due to the fact that for a range of uses of the substance it was estimated that the predicted environmental concentrations (PECs) would exceed the predicted no-effect concentration (PNEC). This PNEC was calculated using all the aquatic toxicity data present on nonylphenol, including all available data on estrogenic effects. Since these effects generally occurred at higher concentrations, it was concluded that the calculated PNEC should be protective for estrogenic effects in fish as well. The conclusions of the report were supported by the CSTEE [7] and adopted by the CAs. Based on this risk assessment, the Commission is currently discussing the possible implementation of restrictions for marketing and use of a range of uses of these substances in the context of Directive 76/769 on Restrictions on the marketing and use of certain dangerous substances and preparations.

In conclusion the available information allowed the development of science-based conclusions on the risks of the substance that triggered the necessary risk reduction. In this case, there was no need to instigate the precautionary principle.

Pentabromodiphenylether

The risk assessment for pentabromodiphenylether (pentaBDPE) was also finalized in 1999 [8]. The conclusions of the substance were reached after intensive discussions in the TM. The human health section of the assessment concluded that there is a need for further information to clarify the potential risks to infants that are potentially exposed to breast milk or infant formulae prepared from cow's milk. The experts, however, were particularly concerned by the studies that indicated rapidly increasing concentrations of pentaBDPE in women's breast milk in Sweden. The report was reviewed by the CSTEE who agreed that further information is needed to better identify the potential risks of the substance [9].

The conclusions of the risk assessment, including a discussion on the uncertainty around them, were presented to the CAs. The CAs decided that in light of the properties of and available information on pentaBDPE, and in the absence of adequate scientific knowledge, the time it would take to gather the information needed to enable an adequate scientific evaluation, was considered to be unacceptable. Therefore, risk reduction measures should be taken immediately. This conclusion was subsequently forwarded to the relevant bodies within the Commission who developed a ban on the marketing and use of the substance, which has recently been implemented through Directive 2003/11/EC.

Bisphenol A

Both the sections on environment and human health of the risk assessment of bisphenol A have recently been finalized [8]. Interestingly, the conclusions on both parts are very similar in the sense that the TM was of the opinion that further information on the toxicity and ecotoxicity of this substance is needed. On the environment, the discussion focused on the effects to be taken into account in setting the PNEC for water. A preliminary PNEC was derived using the "traditional" endpoint hatchability, but the ex-

perts also recognized the present studies showing potential effects on spermatogenesis in fish and the observations of superfeminization in snails, both occurring at much lower concentrations. However, the TM agreed that regarding these studies there were a number of scientific questions unanswered and that further investigations were needed.

The discussion on the human health aspects of the substance focused on the developmental toxicity. The TM agreed that overall, in standard developmental studies in rodents, there is no convincing evidence that bisphenol A is a developmental toxicant. However, the available and apparently conflicting data from studies conducted using low doses (in the μg/kg range) do raise uncertainties and the majority of the experts felt that these studies could not be disregarded. The data though could also not be used to conclude with sufficient certainty that an *unacceptable* risk exists. It was considered that further testing could reduce the uncertainties. The CSTEE reviewed the report and agreed on the need for more information although they wondered whether in the area of the potential low-dose effects more studies would actually help in resolving the issue since many high-quality studies are already available [10,11].

This issue was referred to the CAs who agreed unanimously that further work was required to resolve the uncertainties surrounding the potential for bisphenol A to produce adverse effects on development at low doses. In addition, it was agreed that a provisional NOAEL (no observed adverse effect level) for developmental effects, derived from the rat multigeneration study, should be used in the risk characterization in the interim, while awaiting the outcome of further testing, with the aim of identifying those scenarios which were clearly of concern irrespective of the outcome of the further testing.

In conclusion, on both parts of the risk assessment uncertainties were identified in the data which precluded drawing definitive conclusions regarding the risks of the substance. The experts, however, identified areas for improvement of the database and the risk managers agreed that this route should be followed rather than implementing temporary risk reduction measures. Hence, this is an example where after careful consideration of the results of the risk assessment as well as of the remaining uncertainties, it was decided not to invoke the precautionary principle yet.

Octa- and decabromodiphenylether

The risk assessment reports for these two flame retardants were recently finalized after intensive debate between the risk assessment experts which lasted more than five years and entailed the delivery of substantial information by the producing industry [12,13]. The TM recognized that there are significant uncertainties surrounding the scientific evidence relating to the evaluation of the environmental risks of these substances. These uncertainties are based on their very high persistence, the possible debromination and the uptake of the substance and its debromination products in biota via the food chains. Especially the fact that recent studies indicate that these substances are taken up through the food chain and may end up in eggs of predatory birds caused the TM experts to express their concern about the potential risks for secondary poisoning. The TM agreed that the uncertainties might be reduced if substantial additional information was collected and/or generated but recognized also that it would take considerable time to collect and/or generate this information and that it might not be sufficiently comprehensive to remove all of the uncertainty. Other experts, however, were of the opinion that the information currently provided in the reports and the above-mentioned uncertainties about the actual or potential risks for secondary poisoning should lead to a conclusion that there is a need for risk reduction measures.

The CSTEE also reviewed the results of the assessments and in the case of octaBDPE concluded by using historical evidence from substances with comparable persistence and bioaccumulating properties that there might be a risk to top-predators, including humans [14]. On decaBDPE their conclusion was that long-term effects of this persistent and, at least in some organisms, bioaccumulating substance cannot be excluded. They concluded that further research is needed but also that the uncertainty warrants risk reduction measures directly [15].

The conclusions of the RARs were discussed by the CAs who came to a somewhat similar conclusion as with pentaBDPE that in light of the properties of and available information on the two sub-

stances, the time it would take to gather the information needed to enable an adequate scientific evaluation, was considered to be unacceptable. Therefore, immediate risk reduction measures should be developed.

The Commission has recently implemented risk reduction measures for octabromodiphenylether through Directive 2003/11/EC. For decabromodiphenylether, the discussion is still ongoing. This is another example where, due to the high uncertainties in the outcome of the quantitative risk assessment, it was decided to invoke the precautionary principle.

Dealing with uncertainties

If we closely analyze these examples for the reasons why in certain cases the precautionary principle was invoked whereas in others was not, it basically boils down to situations where the uncertainties in the risk assessment (or the underlying effects or exposure data) are so high that the "normal" level of certainty cannot be obtained. As stated in the Commission communication, this judgment is crucial for the risk managers that face the dilemma of having to act or not to act. Since general rules have until now not been developed the next question is whether we can identify substances or groups of substances for which due to their inherent properties the acceptable risk concept fails due to the high uncertainties is estimating these risks.

The first example of a group of substances for which science cannot provide acceptable risk levels are nonthreshold carcinogenic substances. Since for these substances no safe level can be established the policy reaction is one of risk avoidance by exposure minimization. As a result of that, it is in the EU forbidden to use these substances in consumer products.

A second category for which there can be very high uncertainty in predicting the no-effects level and/or the long-term exposure concentration in the environment and in biota are persistent, bioacummulating and toxic (PBT) substances. For such substances, EU experts have recently concluded that the risks cannot be quantified with the appropriate level of certainty [16]. However, as a result of a benchmarking process using historical evidence from known dangerous substances that have caused long-term effects in the environment, it has been possible to develop criteria for the identification of PBTs and vPvBs.

The question whether endocrine active substances should be treated similarly is less easy to answer. EU experts on reproductive toxicity decided recently that in the context of the risk assessment of chemicals they recognize endocrine disruption more as a mechanism than as an adverse health effect [17]. The Commission in its Community strategy for endocrine disruptors also indicated that the scientific knowledge in this area is limited, with regard to test methods for identification and regarding the actual magnitude of effects that such substances may cause [18]. These substances need not be treated differently from other chemicals, as they will eventually be addressed in the normal assessment, in particular under the reproductive toxicity evaluation, but the Commission urged Member States to give priority to testing, classification and risk assessment of known or suspected endocrine active substances.

CONCLUSION

The Commission in its Communication on the precautionary principle clearly argues for a separation between the scientific assessment of risks and the subsequent application, if necessary, of the precautionary principle based, among others, on the results of this assessment. This separation has worked well in the context of the implementation of the existing substances regulation. The key question to be answered is when and under what conditions the uncertainties in the risk assessment are so high that the "normal" level of certainty is not obtained. The challenge for the future is to try to develop general guidance or rules that will support the policymakers in their decision whether this uncertainty is so large that action is warranted or whether it is acceptable to wait until further information has become available.

REFERENCES

1. CEC 2000. Communication from the Commission on the precautionary principle, COM/2000/0001/final.
2. EP (European Commission). European Parliament resolution on the Commission communication on the precautionary principle (COM(2000)1-C5-0143/2000 – 2000/2086 (COS) (2000).
3. EC (European Commission). Council Resolution on the Precautionary principle. Annex III to the Presidency Conclusions of the Nice European Council Meeting, 7–9 December 2000, SN 400/00 ADD 1 (2000).
4. CEC 1993. Council Regulation (EEC) n° 793/93 of 23 March 1993 on the evaluation and control of the risks of existing substances.
5. European Chemical Bureau. Existing chemicals, <http://ecb.jrc.it/existing-chemicals/>.
6. EC (European Commission). 4-nonylphenol (branched) and nonylphenol. European Union Risk Assessment Report, Vol. 10, Publication No. EUR 20837 (2002). Internet publication at <http://ecb.jrc.it>.
7. Opinion of the CSTEE on the results of the Environmental Risk Assessment of Nonylphenol, straight chain (CAS N° 84852-15-3) and branched chain (CAS N° 25154-52-3), 4 February 2000, <http://europa.eu.int/comm/food/fs/sc/sct/outcome_en.html>.
8. EC (European Commission). Diphenyl ether, pentabromo derivative. European Union Risk Assessment Report, Vol. 5. Publication No. EUR 19730. Office for Official Publications of the EC, Luxembourg (2001). Internet publication at <http://ecb.jrc.it>.
9. Opinion of the CSTEE on the results of the Human Risk Assessment of Pentabromodiphenyl ether (CAS N° 32534-81-9), Adopted on 19 June 2000, <http://europa.eu.int/comm/food/fs/sc/sct/outcome_en.html>.
10. EC (European Commission) (2002). Bisphenol-A. Draft European Union Risk Assessment Report, Internet publication at <http://ecb.jrc.it>.
11. Opinion of the CSTEE on the risk assessment of Bisphenol A - Human Health part (Cas no: 80-05-7). Adopted on 22 May 2002, <http://europa.eu.int/comm/food/fs/sc/sct/outcome_en.html>.
12. Opinion of the CSTEE on the results of the risk assessment of Bisphenol A - Environmental part (CAS no: 80-05-7). Adopted on 27 June 2002, <http://europa.eu.int/comm/food/fs/sc/sct/outcome_en.html>.
13. EC (European Commission). Diphenyl ether, octatabromo derivative. European Union Risk Assessment Report, Vol. 16, Publication No. EUR 20403 (2002). Internet publication at <http://ecb.jrc.it>.
14. EC (European Commission). Bis(pentabromophenyl) ether. European Union Risk Assessment Report, Vol. 17, Publication No. EUR 20402 (2002). Internet publication at <http://ecb.jrc.it>.
15. Opinion of the CSTEE on the results of the Risk Assessment of: Diphenyl ether, octabromo derivative - Environmental and Human Health Part (CAS No.: 32536-52-0). Adopted on 31 October 2002, <http://europa.eu.int/comm/food/fs/sc/sct/outcome_en.html>.
16. Opinion of the CSTEE on the results of the Risk Assessment of: Bis(pentabromophenyl)ether - Environmental and Human Health Part (CAS No.: 1163-19-5). Adopted on 31 October 2002 <http://europa.eu.int/comm/food/fs/sc/sct/outcome_en.html>.
17. EC (European Commission). Technical Guidance Document on Risk Assessment in support of Commission Directive 93/67/EEC on Risk Assessment for new notified substances and Commission Regulation (EC) No 1488/94 on Risk Assessment for existing substances, and Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market, Parts 1–4, 2nd ed. Publication No. EUR 20418/EN/1, EUR 20418/EN/2, EUR 20418/EN/3, EUR 20418/4. Office for Official Publications of the EC, Luxembourg (2002). Internet publication at <http://ecb.jrc.it/>.

18. CEC 1999. Communication from the Commission to the Council and the European Parliament - Community strategy for endocrine disrupters - A range of substances suspected of interfering with the hormone systems of humans and wildlife, COM/1999/0706 final.