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**THE FUTURE OF RISK ASSESSMENT IN THE EUROPEAN
UNION**

**THE SECOND REPORT ON THE HARMONISATION OF RISK
ASSESSMENT PROCEDURES**

ADOPTED BY THE SCIENTIFIC STEERING COMMITTEE AT ITS
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Note: This Report may be subject to editorial changes

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1. EXECUTIVE SUMMARY

- i). A risk assessment is required to characterise the risks to human and animal health and to the environment from an ever increasing number of agents (products, contaminants) and processes. Moreover the findings from a risk assessment can result in risk management decisions that have major, sometimes global consequences. It is therefore extremely important that risk assessments are of the highest quality and are viewed by stakeholders as clear, independent and transparent.
- ii). Within the EU there is a wide range of committees and individuals conducting risk assessments as part of the risk analysis process. Although in principle the process is the same, in practice important differences arise in the methodology used, and how it is interpreted and explained. As a consequence the risks from the same agent (stressor) as assessed within the EU may vary substantially. This is the source of much confusion and tends undermine the credibility of the risk assessment process. The addition of more member states and the establishment of an increasing number of agencies that have risk assessment responsibilities could exacerbate this problem further unless firm steps are taken to harmonise the process.
- iii). The SSC identified in its Opinion of 26-27th October 2000 (First report on the harmonisation of risk assessment procedures) that a number of immediate measures could be taken to promote harmonisation. Regrettably very few of these recommendations have been implemented as yet by the Commission services. The SSC also identified a number of areas where further work ought to be conducted before clear recommendations could be made. Many of these are addressed in this Second Report.
- iv). The following issues have been addressed:
 - Procedural matters aimed at ensuring that the process of risk assessment is made more transparent, consistent and clear;
 - use of a common methodology an important element of which is a progressively introduction of a more quantitative approach using probabilistic models;
 - how the extensive amount of data which are consistent for hazard and varying for exposure on individual stressors can be made much more accessible and the benefits of this particularly for the assessment of stressors for which exposure levels are low and the available data is very limited or does not exist;
 - evaluation of the potential impacts of emerging technologies on the risk assessment process;
 - a revision of conceptual methodological approach for assessing the risk for animal populations and ecosystems;
 - an integrated approach to the use of data that has been gathered to assess risks to human health and to the environment from individual stressors;

- how issues such as: allowance for sensitive groups of the population and impacts of exposure to multiple stressors can be addressed in a more structured way;
 - whether additional considerations should be incorporated into the risk assessment process; in particular, quality of life, sustainability and involvement of all stakeholders.
- v). The recommendations set out here should be seen as complementing those of the first report and should be implemented together.
- vi). The principal recommendations are as follows:

a) a comprehensive data bank, microbiological, ecotoxicological and exposure information

It is imperative that genuine progress is made to establish a comprehensive and validated data bank of information relevant to risk assessment e.g. toxicological. This would reduce one of the major barriers to harmonisation namely information seen by one committee is often not accessible to others. Among its other benefits would be: avoidance of unnecessary animal experiments, a substantial improvement in the extrapolation of results between related stressors and a valuable aid to the design of new safer products and technologies.

b) a common framework for the conduct of risk assessments and the ways that the findings are expressed

It is proposed that a more structured approach is adopted to the various considerations that are required for risk characterisation. This includes:

- Methodological:
 - the way that sensitive groups of the population are identified
 - how the impacts of simultaneous exposure to multiple stressors (eg mixtures) are considered;
- Presentation of opinions:
 - how the weighting of evidence that is used can be made transparent
 - a common format for the expression of scientific opinions and the relationship between opinions and reports
 - the way in which uncertainties, of various kinds, in risk assessments are expressed
 - the bench marking of related risks
- Relation to risk managers and risk communicators
 - the need for a dialogue with the appropriate risk managers/ other stakeholders in formulating the questions and avoiding ambiguities in the ways that opinions are expressed

c) A more quantitative approach to risk assessment

Progression to a more probabilistic means of describing exposure and expressing the risks is proposed. Even though the deterministic approach that involves the definition of a threshold has served the needs of risk managers well in the past, it provides an apparent sharp distinction between the level where there is an effect and that where no effect will occur. This may be a poor basis in some cases for risk management decisions and may result in confusion among the public. It is recognised that the introduction of probabilistic approaches also may produce difficulties in understanding. A phased approach to their use for risk assessment purposes is therefore necessary.

d) A more holistic approach

It is recognised that protection against significant biological changes is insufficient to express the total impact that a stressor or stressors may have on humans, other animal species and their environment. More holistic approaches are needed for the future. The introduction of quality of life considerations is suggested to be a key new parameter. Specific research is needed to develop the appropriate concepts and strategies to enable this.

e) Integration of human and animal health and environmental risk assessments

The three domains of risk assessment have many features in common. Ways are identified in which this fact can be realised in practical terms, ranging from harmonisation of methodology for species to species extrapolation.

f) Procedure for the introduction of these recommendations

Although the work of the task force has concentrated on the activities of the Health And Consumer Protection Directorate General (DG SANCO) Scientific Committees the harmonisation issues discussed need to be considered across all activities in the EU that involve risk assessment. Harmonisation across the whole international community concerned with risk assessment is also highly desirable. It is therefore important that the two reports are disseminated widely both in electronic form and in hard copy. It is proposed that one or more workshops are held during 2003 to discuss the key issues and how harmonisation can be progressed in a co-ordinated manner.

2. INTRODUCTION

“The greatest of all virtues is curiosity and the end of all desire wisdom”
J. Stephens 1922 The Crock of Gold

This report is an initiative of the Scientific Steering Committee (SSC) of Health And Consumer Protection Directorate General (DG SANCO), which recognised that:

- the risk assessment procedure varied to a considerable extent not only among the DG SANCO committees but also more widely still within the Commission Directorate Generals and within member states.
- such variations resulted on occasion in conflicting evaluations of the risks posed by individual agents (stressors).

While not wishing to interfere with genuine scientific differences in the interpretation of data the SSC recognised that there were various other causes of differences in risk assessments. These could be ascribed for example to procedural issues, access to relevant information, nature of the expertise available, temporal issues, etc.

The intention of the work described here is to identify aspects where a more harmonised approach would be beneficial and where appropriate to make recommendations as to how this might be achieved. In the main report summaries are provided of the key issues and proposals as to how progress can be made in many aspects more detailed information is provided in the appendices. For details of the risk assessment approach itself the reader is referred to the various guidelines for specific product types eg pesticides, cosmetics, food additives, growth promoters published by the commission services.

2.1. THE ROLE OF RISK ASSESSMENT

Requirements

Risk assessment is a data driven process for determining the likelihood of an event(s) happening. A narrower definition, that sets the framework for the current work of the scientific advisory committees, is: a science led process for establishing the likelihood of adverse effects to human health and to the environment from exposure to risk sources. (Risk sources are specific chemical, physical and biological agents, often termed stressors, or from industrial and other processes). However emerging issues such as animal welfare, quality of life and sustainability are gaining in importance It is appropriate to consider whether this latter definition is too narrow to reflect the future requirements that will be placed on scientific advice relating to both foods and non-foods.

Risk assessments must be objective, but inevitably they involve an element of both scientific and value judgement. It is essential therefore that:

- the process of risk assessment is seen to be thorough and is well understood with a clear identification of all the information sources used;
- very experienced scientists, of high integrity, from each of the requisite fields of science take responsibility for the process;
- each risk assessment should be performed independently of risk management following value based questions provided by risk managers (to achieve this risk

assessments are often conducted through independent scientific advisory committees);

- risk managers state the findings in a form that is clear and unambiguous for all stakeholders and is readily utilisable.

The demand for risk assessments has grown continually over the past forty or so years and this growth is likely to continue (see SSC First Report). Although the overall process of risk assessment has remained broadly similar over this period in the different domains in which risk assessment is conducted, significant differences have developed in the specific of the process.

It is timely to review all aspects of the risk assessment process for a number of reasons:

- (i) the current high importance given to risk assessment as a crucial source of information for the risk management process,
- (ii) the likelihood that risk assessment will be required in additional domains in the future,
- (iii) the increasing demand for the scrutiny of risk assessments by all the stakeholders,
- (iv) the development of new relevant technologies with the potential to strengthen the science base,
- (v) the need to include additional factors in the risk assessment process.

In many cases the risks from particular stressors are changing due to either changing exposure levels and/or differences in the population exposed. For example risks assessments may not consider adequately the fact that people are living longer and therefore their exposure to various drugs, etc is for a longer period of time than was anticipated in the original risk assessments. Such situations require that the risk assessments be revisited.

Triggers for a risk Assessment

The use of new risk sources (stressors) of concern to consumers (e.g. GMO's, new foods, EMF) and the adoption of strategies for sustainable development by the EU and member states expands the requirement for scientific advice. The in depth analysis of current methods is needed to meet these new challenges.

Need for a more Harmonised Approach

A more harmonised approach to risk assessment is highly desirable for a number of reasons:

- To aid the understanding of risk managers and other stakeholders.

- To enable the work done by one scientific body to be utilised without unnecessary duplication of effort by other risk assessors who are concerned with the same stressors or processes.
- To facilitate the comparison of risk from different products or processes that could be used for the same or similar purposes.
- To ensure that the overall risk from multiple sources of exposure to the same stressor can be properly evaluated.
- To enable the training of future risk assessors.
- To assist the integration into the EU addition of new member states with their own practices for conducting risk assessments.

The need for an agreed strategy throughout the EU for harmonisation of risk assessment within the EU is more crucial because of the decision in the EU to separate food and non-food risk assessments from April 2003. Moreover there is a likelihood that in the future further agencies may be established that have risk assessment as an important part of their activities.

2.2. PREVIOUS WORK ON HARMONISATION WITHIN THE EU

In 1999 the Scientific Steering Committee (SSC) of Health And Consumer Protection Directorate General (DG SANCO) set up a working party to identify these differences and the measures that could be taken to establish a more harmonised approach. The SSC recognised that complete harmonisation was unlikely to be achieved because the various scientific committees were required to operate under different regulations. Moreover there could be strong scientific reasons for specific differences in the risk assessment process.

The Working Party produced its first report in summer 2000. This report was adopted by the SSC and issued as an opinion at the SSC meeting on the 26-27 October 2000. The report was subsequently made available both through the SSC web site and in hard copy form. The principal recommendations were as follows:

- (i) Standardise the format for the presentation of risk assessment findings. The Report identifies not only variations in the form of presentation of findings between committees, but also within committees. A format is recommended for future application by all the scientific committees.
- (ii) Ensure that all opinions include an expression of the degree of uncertainty in the risk assessment. This should be in a common style between committees where practicable. It is also recommended that work is conducted to identify possible benchmarks against which a particular risk can be compared (risk comparison).

- (iii) Develop formal means by which issues such as animal welfare, quality of life, socio-economic considerations, and sustainability can be incorporated into the risk assessment process.
- (iv) Give more attention to the environmental effects of products approved for marketing. While the environmental impacts of pesticides are subject to detailed study for other commercial products there is often cursory or no examination of their possible environmental effects (e.g. human medicines). A common framework for dealing with such environmental issues is highly desirable. This development would be assisted by the adoption of an integrated approach to risk assessment (i.e. examination of human and environmental risk assessments alongside one another) thereby facilitating each other assessment (this includes harmonisation of methodologies and models).
- (v) Characterise risk in a more quantitative form where appropriate. Techniques in quantitative risk assessment are developing quite rapidly. The scientific committees should give consideration to the adoption of these techniques, where useful.
- (vi) Standardise, as far as is practicable, the use of terminology. Currently there are no agreed definitions of terms. Moreover, a variety of terms are in use to describe apparently the same phenomenon, e.g. 18 different terms have been identified in the EU to describe de minimis risk. This is unnecessary and a potential source of confusion in risk communication.
- (vii) Enhance commonality in the working procedures of the committees. Among the key issues, which have been identified, are the need to improve the interface with and level of support from Commission officials, while preserving the independence of committee members. Agreed procedures for interaction with other stakeholders is also important.
- (viii) Establish a well resourced common facility for the ready provision of key information required by the committees for their risk assessment activities This should include all the scientific data utilised by committees of the Commission on a particular risk source.
- (ix) Increase the post-marketing monitoring and surveillance of important new products. Consideration should be given to establishing a common “clearing house” in the Commission to co-ordinate this very important activity.
- (x) Develop, or contribute to the development of, databases, which enable structure activity relationships and vulnerable population groups to be identified. It is recognised that currently much of the data received by the Commission is classified as “in confidence” and is therefore not available for access by other committees. However, the achievement of more reliable risk assessments depends on better data bases (see also recommendation IV). It is unacceptable for new animal studies to be required if suitable data already exists. Means have to be found of accessing this confidential information while ensuring the commercial advantage of those producing it.

- (xi) Develop more standard scenarios for use in exposure assessment. At present, for example, there is no agreed “standard European diet” to be used for assessing exposure from contaminants, nor are there any commonly adopted mathematical models for calculating the distribution of substances released into the environment. Co-operation is required with other organisations to achieve this.
- (xii) Ensure that a regular review is carried out of technical developments relevant to risk assessments. For example, new more sensitive methods are likely to identify biological changes occurring below currently recognised threshold levels. It is important that committees have a common approach on which biological changes are deemed “adverse” and which are not.
- (xiii) Establish an induction programme for new committee members and regular workshop programme for all members on key items such as risk communication. Facilitation of advanced training programmes across Member States is also required to ensure the availability of the necessary risk assessment expertise in the future.
- (xiv) Develop a formal link between the Scientific Advisory Committees related to DG SANCO and those other scientific advisory committees concerned with risk assessment and human and environmental health in order that consistency is improved in advice throughout the Commission services.
- (xv) Ensure that there is a clear interface between completion of a risk assessment and the application of the Precautionary Principle.

2.3. BACKGROUND TO THIS REPORT

The Task Force on Harmonisation of Risk Assessment. Terms of Reference

In February 2001 the new SSC decided to establish a Task Force on the Harmonisation of Risk Assessment Procedures to build on the work carried out for the first Report.

The Harmonisation of Risk Assessment Task Force was a working group of the Scientific Steering Committee. It replaced the working party, which produced the First Report on the Harmonisation of Risk Assessment Procedures.

The Task Force comprised members of the Scientific Advisory Committees and external experts. The remit of the Task Force was taken forwards by a number of working groups, each chaired by a member of the Task Force. The working groups were set up so as to cover the different risk sources types (chemicals, micro-organisms, other biological materials, and physical stressors). In addition, since the First Report centred principally on human risk assessment, an environment working group was also needed.

These working groups were required, in respect with their particular domain, to examine how the recommendations regarding risk assessment approaches and procedures set out in the First Report can be introduced across the Scientific Advisory Committees.

The members of the Task Force and its Working groups are listed in the Appendix 1.

The Task Force priorities

The Task Force at its first meeting identified a number of priorities based on:

- recommendations for further work identified in the First Report. The Task Force decided to concentrate on recommendations i)-v). The Task Force endorsed the other recommendations and noted that progress on most of the recommendations depended on action from Commission Services.
- areas that were not addressed in depth in the First Report
- members knowledge of international developments/initiatives in risk assessment
- emerging scientific technologies

2.4. PROGRESS ON THOSE ISSUES NOT FURTHER DEVELOPED IN THE SECOND REPORT

The progress on the implementation of the recommendations set out in the first report has been very disappointing. It is essential if progress is to be made on harmonisation that there is a strong commitment from commission services to implement the recommendations of both the reports and that the resources are made available to enable this.

2.5. THEMES OF THE SECOND REPORT

Risk assessment comprises the following stages:

- hazard identification
- exposure assessment
- hazard characterisation
- risk characterisation

In the First Report each of these stages was considered in turn and the reader is referred to these for further information. In this report chapters are provided on the following topics:

- Quality of life (including animal welfare)
- Quantitative exposure assessment methodology
- Assessment of human health impacts
- Assessment of impacts on the environment
- Developing issues
- Expression of risks
- Interaction between risk assessors, risk managers and other stakeholders.

Many of these chapters are supported by a more detailed report that is provided in the Appendices.

2.6. CONCLUSIONS

Risk assessment plays a major and increasing role in informing the work of risk managers. This is reflected in the rapid growth of EU agencies involved in risk assessment. A co-ordinated approach is needed to avoid conflicting opinions arising from differences in access to data, procedural variations and differences in the quality of the necessary expertise. Recommendations from the First Report are listed to emphasise that for progress to be made implementation by the Commission services is needed. To date this implementation has been very limited.

3. A FRAMEWORK FOR THE RISK ASSESSMENT PROCESS

*“If we cannot end our differences, at least we can make the world safe for
diversity”*

JF Kennedy 1963

In the first report the overall risk assessment process as currently practised was reviewed. In this report we concentrate on specific areas of the process where weaknesses have been identified and/or there are particular opportunities for a more harmonised approach

3.1. DEFINING THE QUESTION(S)

The process of risk assessment is normally triggered through the formulation of a precise question(s) by the Commission services. As noted in the First Report it is essential that such questions are unambiguous and that their purpose is clear to the risk assessors. It is important that the risk managers understand what the risk assessors need in terms of data and what they are able to deliver. Dialogue between risk managers and risk assessors should be encouraged to achieve this objective.

A particular concern of Task Force members is the specification of exposure situations during the framing of the question(s).

Legislation and accompanying guidance documents generally provide the frame for exposure assessment including the approaches to be used and they may include tiered systems according to significance of the risk source.

Exposure assessments are based on information from monitoring programs and usually in parallel on the use of consensus scenarios in appropriate models.

Depending on their design, the interpretation of monitoring programs can be specific or integrated as required. On the other hand scenarios usually do not reflect real local situations, but have the objective to be representative of either mean, typical or most sensitive (worst case) situations in a region throughout the European Community.

Such scenarios should be described clearly as to their representativeness (region/group; which degree of worst case/which probability of exposure they stand for). Ideally, they would be derived from minimal homogeneous data sets and be integrated at higher levels, where appropriate.

Significant issues

Exposure assessment requirements are often particularly sensitive to the exact questions asked.

The level of protection required (taking into consideration the hazard of the risk source) drives the sensitivity, amount, reliability and representativeness of information needed for quantitative exposure assessment. In most cases the information available is insufficient to assess actual exposure with appropriate precision for the specified level of protection. Worst case scenarios may be adopted because of the lack of suitable information. Inevitably the level of protection required has a direct influence on the degree of uncertainty, and this, uncertainty must be expressed in the risk assessment conclusions.

The provision to cope with different degrees of protection given by the characteristics of the adopted scenarios (mean, typical, worst case). These may be applied community wide or specified regions. A similar differentiation is in principle possible for the interpretation of monitoring programs, provided the parent data are available to the assessors. Depending on the framework of the assessment further specifications may be required, e.g. for cultural and dietary habits for human exposure, age groups of the human population, sensitive groups of the human population, predisposed by diseases, ecoregions and highly sensitive ecosystems in the case of environmental exposure.

A great challenge is the selection of exposure pathways to the risk source. According to the largely sectorial legislation mostly one pathway would be needed to be considered, e.g. by food. In many cases this represents however only part of the total, and consequently from a risk assessment point of view an integrated exposure assessment encompassing all exposures to the risk source is advisable. This can however only be done with harmonised procedures for comparing the contributions of the different pathways to total exposure.

A special issue for exposure assessment are naturally occurring risk sources (radiation, irradiation, heavy metals). Human populations and ecosystems are adapted to significant spatial variations of exposure to the sources and a risk based exposure assessment has to consider this basis. A further issue is the extent to which natural background variation in the levels of a stressor should be taken in evaluating the risk from man-made sources of the same or a closely related stressor.

3.2. A RISK CHARACTERISATION FRAMEWORK

Risk characterisation is the final vital stage in the risk assessment process. Perhaps surprisingly the steps in risk characterisation are by no means universally agreed. Judgement plays a key part in and it is necessary that this is made transparent. Moreover it is important to consider how 'developing issues' could be built in formally into the risk characterisation process. The following framework for the risk characterisation, which is designed to meet these requirements, is proposed. This framework is intended to ensure a systematic approach to consideration of potentially relevant issues. It is recognised that in consideration of the risks from particular stressors/factors some of these issues will not be appropriate.

The proposed framework involves a stepwise process that would address formally each of the key issues in a sequential manner as follows. It should be noted that in the following chapters a number of these stages are considered in more depth:

1. Toxicological/biological/physical stressors

a) Integration of exposure assessment and hazard characterisation

- (i) Check for compatibility and completeness e.g. quality and level of information, exposure routes and matrices.

- (ii) Consideration of particular studies linking exposure and effect e.g. epidemiology findings, toxicokinetics, monitoring results, models and mechanism of action studies.

b) Assessment of whether the data allows a deterministic and /or a probabilistic approach

- (i) Feasibility of practical application
- (ii) Data evaluation including models.
- (iii) Selection of means of risk expression (probabilistic /deterministic /qualitative).
- (iv) Choice of and comparison with norms/potency consideration.

c) Identification of the potential at risk groups in the population/ecosystem.

Data available of likely risk groups identified from mechanisms of action, species sensitivity or other knowledge.

d) Expression of uncertainty

- (i) Identification of assumptions made.
- (ii) Characterisation of real differences in results between different population groups (includes natural variability)
- (iii) Decision on whether numerical and/or description language will be used or both.
- (iv) Scientific basis for uncertainties.
- (v) Sensitivity analysis.

e) Evaluation of potential direct/indirect interactions with other stressors/factors

- (i) Simultaneous exposure.
- (ii) Sequential exposure.

f) Integration of other information sources.

- (i) Risk assessment of the stressor in other domains.
- (ii) Other risk characterisations for the same stressor.
- (iii) Risk characterisation on related stressors.

g) Contribution of societal and other factors to the overall assessment

- (i) Quality of life (general and at risk groups/individuals).
- (ii) Sustainability.

2. Interactions with risk managers and other stakeholders

h) Opinion

- (i) Expression of the general risk and comparison with norms/expression of potency.
- (ii) Discussion of potential/real benefits.
- (iii) A holistic assessment taking into account all of the above.

i) Advice

- (i) Significance of the uncertainties in the context of worst case and "typical" normative exposures.
- (ii) Situations where exceedences/significant adverse impacts could occur and their significance.
- (iii) Possible substitutes/other permanent/temporary measures that might be introduced if significant effects are likely to occur.
- (iv) Recommendations for additional monitoring/surveillance and/or
- (v) Data gaps that might readily be filled and the practical benefits of doing this.

3.3. TRANSPARENCY AND CLARITY ISSUES: INFORMATION SOURCES AND THEIR USE

The increasing pressures for full transparency in the risk assessment process requires the development of a consistent and clear procedure that identifies:

- (i) all the sources of data that have been used,
- (ii) any important limitations of accessibility of potentially significant data ,

- (iii) the weighting given to individual data sets and the rationale for this,
- (iv) whether or not stakeholders have the opportunity to submit additional data.

A rigid approach that defines that one source of data is always more important than another is clearly not appropriate. However it is evident that the identification of the data deemed important for a specific risk assessment is a matter of judgement by the experts. There are certain generally agreed criteria in identifying the quality of individual data sources.

- The availability of suitable information on how the data was derived
- The quality of the experimental work which includes whether the work was conducted included according to GLP, GCP etc
- The scientific standing in the field of the authors and their perceived independence.
- Whether the findings are consistent with the available literature in the field.

Means need to be developed to show how these parameters have been used in the selection of key data and in the rejection of any substantive submissions.

3.4. TRANSPARENCY AND CLARITY ISSUES: TERMINOLOGY

Variations in the terminology was identified in the First Report as a significant barrier to the further harmonisation of the work of the scientific advisory committees. It also is a source of confusion for stakeholders. Major and inter-related concerns here are:

- the variation in terms used to describe apparently the same situation. This is of particular importance for terms that are used to describe the nature and/or the magnitude of a risk. Thus in the first report 18 different terms were found to be in use to describe de minimus risk.
- the difficulties that can be encountered in the translation of committee opinions into the various European languages (see the following table). Again a particular concern relates to those terms that describe the nature and/or the magnitude of the risk.

Risk analysis Terminology used in different languages

English	French	German	Nederlands	Español	Dansk	Suomi	Íslandsk	Norsk	Svensk
Hazard	Danger	Gefähr	Gevaar	Peligro	Fare	Vaara	Hætta	Fare	Fara
Risk	Risque	Risiko	Risico	Riesgo	Risiko	Riski	Áhætta	Risiko	Risk
Risk analysis	Analyse du risque	Risikoanalyse	Risicoanalyse	Análisis de Riesgo	Risiko-analyse	Riski-analyysi	Áhættugreining	Risiko analyse	Riskanalys
Risk assessment	Estimation du risque	Risikobewertung	Risicobeoordeling	Evaluación de Riesgo	Risiko-vurdering	Riskinarviointi	Áhættumat	Risiko vurdering	Riskvärdering
Hazard identification	Identification du danger	Gefährlichkeitsermittlung	Identificatie van gevaar	Identificación de la Peligrosidad	Identificering af sundhedsfare	Vaaran tunnistaminen	Hættukennsl	Identificering af sundhedsfare	Faroidentifisering
Hazard characterization	Caractérisation du danger	Gefährlichkeits-Charakterisierung	Karakterisering van het gevaar	Caracterización de la peligrosidad	Karakteristik af sundhedsfare	Vaaran kuvaaminen	Hættulýsing	Karakteristik af sundhedsfare	Farokarakterisering
Risk assessment policy	Politique d'estimation du risque	Risikobewertungs Grundsätze	Risico(beoordelings)-beleid	Política de la evaluación del riesgo	Risiko-vurderingspolitik	Riskinarviointin toimintaperiaatteet	Áhættumatsstefna	Risiko vurderingspolitik/-retningslinjer	Riskvurderingspolicy
Risk characterization	Caractérisation du risque	Risikokarakterisering	Risicokarakterisering	Caracterización del riesgo	Risiko-karakteristik	Riskin kuvaaminen	Áhættulýsing	Risiko karakterisering	Riskkarakterisering
Risk communication	Communication sur le risque	Risikokommunikation	Risicokommunikatie	Comunicación del riesgo	Risiko-kommunikation	Riskiviestintä	Áhættukynning	Risiko kommunikation	Riskkommunikation
Risk evaluation	Appréciation du risque	Risikobeurteilung	Risicoevaluatie	Valoración del riesgo	Risiko-evaluering	Riskin kokonais-	Áhættuskoðun	Risiko evaluering	Riskevaluering

						arviointi			
Risk management	Gestion du risque	Risikomanagemnt	Risicomanagemen t	Gestión del Riesgo	Risikohånd- tering	Riskinhallinta	Áhættustjórnun	Risiko håndtering	Riskhantering

It is proposed that:

- (i) Categories of risk level that need to be described in non-numerical terms are identified.
- (ii) For each an exercise is conducted similar to that carried out to identify terms that are used to describe de minimise risk.
- (iii) These terms are considered by risk managers experienced in English to select several that would seem to be particularly useful.
- (iv) Translation services are asked to consider how these selected terms translate across each of the languages of the current and new member states identifying those terms whose integrity of meaning is best preserved.
- (v) Scientific advisory committees are asked to use these terms in describing risks.
- (vi) Further terms are selected from the glossary of this report and from endpoint descriptors to identify whether they are appropriate in terms of preservation of meaning as a consequence of translation.

3.5. CONCLUSIONS

1. The Task Force recognises that there have been many new developments in the field of risk assessment. The work of the Task Force has concentrated on those aspects that:
 - are areas where harmonisation appears to be needed for scientific and /or transparency and/or efficiency reasons
 - are new issues that the Task Force consider to be of likely major importance in the future
 - require an overview in order to progress them effectively.
2. A general framework is proposed for risk characterisation that is intended to serve as an aide memoir to ensure that:
 - all the relevant issues are considered in formulating opinions
 - allows for ‘developing issues’ such as quality of life (see chapters 7 and 8) to be included.
3. The need for a dialogue between risk managers and risk assessors has been identified in the framing of questions for which an opinion is requested. The primary purposes of this would be to:

- ensure that the questions are unambiguous, able to be answered in a form that is of practical use to the risk managers
 - agree the data required to answer the questions and how this data is to be obtained
 - identify any linkage to previous or current questions posed to the same or other scientific committees.
4. For reasons of both clarity and transparency the Task Force reiterates the need for:
- a common terminology that incorporates the issues of the translation into the languages of the member states and the need to preserve the integrity of the meaning of terms that describe the nature or seriousness of the risk
 - means of identifying the sources of data used for specific risk assessments, how the data has been used including the rationale for the weighting given to particular elements of the data.

3.6. RECOMMENDATIONS.

1. Discussions are held between officials (DG SANCO and EFSA) and the SSC members of the Task Force on how:
 - the recommendations set out in the first report can be implemented.
 - means of establishing a dialogue on the framing of questions.
2. The proposed framework for risk characterisation is considered by each of the scientific advisory committees in order to :
 - identify aspects where they might have difficulties in using the framework
 - suggest modifications that may be needed in order to achieve compliance.
3. The Scientific Advisory Committees are asked to consider the proposal on improving the transparency of the use of data sources for risk assessment purposes.
4. Translation services are asked to advise on the selection of terms that when translated into the languages of the existing and new member states best reflect the meaning in English (since opinions are normally written in English).

4. QUANTITATIVE EXPOSURE ASSESSMENT FOR HUMAN HEALTH

4.1. INTRODUCTION

Assessment of exposure is typically the weakest component of risk assessments for human and animal health and for populations of ecosystems. One of the particular challenges in exposure assessment is how to utilise data from limited sampling and how to take into consideration the variations in exposure across member states. While this is rather straight forward for human to prescribed drugs for other stressors, for example environmental contaminants, it can be highly problematic. Point estimates are commonly used by risk assessors at present. While these may be efficient as a first step, in order to focus on the most important contaminants and their sources, the use of point estimates for exposure has a number of disadvantages. For example it is impossible to identify where the point estimate is positioned in the range of possibilities. Thus the point estimate can give a false sense of accuracy and ignore important variables. To overcome this problem risk assessors resort frequently to worst case assumptions. However there is a danger of multiply worst case assumptions in an exposure assessment such that the conclusion is unrealistic.

Quantitative uncertainty analysis is a device that may be used to address the propagation of uncertainties in a more scientific manner. The First Report recommended that further work was carried out in order to assess the benefits and risks of progressing towards quantitative exposure assessment in the work of scientific advisory committees. The Task Force has taken up this recommendation and applied it specifically on contaminants (microbiological and chemical) in food.

4.2. QUANTITATIVE ASSESSMENT OF FOOD BORNE BACTERIAL PATHOGENS

The report on quantitative exposure assessment of food borne bacterial pathogens (see Appendix 3) arises from the work of the SSC Task Force on the Harmonisation of Risk Assessment Procedures. It was adopted by the Scientific Steering Committee at its Plenary Meeting the 16-17 January 2003. The main points, the main conclusions and recommendations from the report are covered by the text below, but for the details regarding development of the models and the practical examples the report itself is recommended.

The link between exposure assessment, risk assessment and risk management

The report addresses one of the four basic elements in the risk assessment procedure for micro-organisms in the human food supply. Risk assessment itself is imbedded as one of the 3 interacting elements risk assessment, risk management and risk communication in the overall risk analysis process.

Risk assessment and risk management are inter-linked and iterative in nature, and the successful implementation of both relies heavily on a successful risk communication (“sea of communication”) between all parties involved.

To make the best use of the results of exposure assessments it is important to keep in mind the iterative nature of the overall processes of risk assessment and risk management with the focus on the initial work in the risk evaluation phase of the risk management process where the risk profile is established.

The risk profile

The purpose and objective of an assessment should guide its analysis. In order to clearly define the purpose and scope of the exposure assessment an understanding of the risk management questions is crucial, and a close interaction between managers and assessors is necessary during the initial phases. This work should include the development of risk profiles through initial identification of putative hazards. In some instances it may be necessary to limit the scope to be able to address the questions by making them more specific or, alternatively, to develop more than one assessment. In general, the exposure assessment should be made as simple as possible while still including the important sources of risk.

A risk profile might optimally describe:

- which microbial hazards are causing the problem;
- the difficulty in controlling them (nature and size of the problem, etc.);
- the source(s) of the microbiological hazard considering the entire food chain, including imported food, the environment, travel, animal contact and person to person transmission;
- an evaluation of to which extent the different sources contribute to the health problem;
- the available data on prevalence and numbers of the organism in question from the whole food chain;
- the disease incidence data and the types and severity of the adverse effects;
- which populations may be affected (for example, at risk groups such as the elderly, infants and children, the immuno-compromised, or those whose exposure to the microbial hazard may be increased due to dietary intake; socio-economic status, or other characteristics);
- the consumer perception of the problem;
- what is expected to be at risk (e.g. human health, economic concern);
- the available options;
- the potential consequences of action(s) taken or action(s) which might be taken (including preventive measures);

- the distribution of risks and benefits.

The link from exposure assessment to risk characterisation is established by combining the outcome of the hazard characterisation and the exposure assessment for an identified hazard.

Model development

Exposure assessment is the estimation of how likely it is that an individual or a population will be exposed to a microbial hazard and what numbers of the micro-organisms are likely to be ingested. For exposure assessment the transmission of the hazard involved is modelled through the food pathway, meaning a chain of processes from a source (e.g. the farm) to the moment of consumption. This transmission model follows the prevalence and the concentration of the hazard along the consecutive processes of the food pathway, taking into account the variability and uncertainty attending this transmission. In the model the food pathway is split up into smaller steps. For each step, the input-output relation is described. Essentially, this input-output relationship can be obtained either by observation (surveillance), by laboratory experimentation (simulation in the laboratory of the practical situation concerning certain specific steps) or – increasingly - by mathematical modelling.

The advantage of models is that they force the researcher to arrange and organise all information available in a logical way which helps to define precisely the problem under study and facilitates exchange of knowledge. Models may be used for prediction when verified and validated. The verification and validation processes may require data from both surveillance and experiments. The disadvantage of models may be that the models sometimes may become unrealistic especially in situations where no information for verification and validation is available.

Quantitative risk assessment, in particular the use of stochastic models, is a specialised task that requires skills in mathematics and statistics in addition to microbiological and technological knowledge. As a consequence, risk assessments are usually conducted in large, multidisciplinary projects. Building a comprehensive model may be resource intensive. The output of risk models is relatively complex, and in order to guide risk management and for risk managers to interpret the results of the risk assessment, risk managers need to understand the basic principles of modelling and the concepts behind like uncertainty and variability.

A general framework for doing Quantitative Microbiological Risk Assessment (QMRA), the Modular Process Risk Model (MPRM) was recently proposed. The heart of the proposal is the suggestion that to each of the steps or key activities at the various intermediary stages of the farm-to-fork chain at least one of six basic processes can be assigned: growth, inactivation, partitioning, mixing, removal and cross contamination. These basic processes are the six fundamental events that may affect the transmission of any microbial hazard in any food process. There are two ‘microbial’ processes, growth and inactivation, and four ‘food handling’ processes, mixing and partitioning of the food matrix, removal of a part of the units, and cross contamination. The ‘microbial’ processes strongly depend on the characteristics of the microbial hazard, as the effects of environmental conditions on growth and inactivation differ between species (and even between strains). Essentially, the effects

of the 'food handling processes' are determined by the food handling process characteristics only, assuming a uniform distribution of micro-organisms over the food matrix. The MPRM focussing on the micro-organism has not yet been developed for the primary production, where the animal itself is in focus.

In general, a model is broken down into smaller components (disaggregated) as much as necessary to express significant logic between input variables and to model each uncertain variable as accurately as necessary for the efficient but accurate modelling in relation to the purpose of the assessment. The presently proposed framework can be summarised by the following seven steps, some of which may have to be performed in an iterative process:

1. Define the statement of purpose, the (microbial) hazard and the food product. Consider which are the alternative scenarios (either risk mitigation strategies, or potential changes in the process) that are to be evaluated with the model.
2. Give a description of the food pathway. Processing steps that involve potential alternative scenarios may need a more detailed description than processing steps that will remain unchanged.
3. Build the MPRM model structure, by splitting up the food pathway into small processing steps (modules). In principle, each module refers to one of the six basic processes. If a processing step is too complex or if essential parameters are unknown, and the processing step cannot be assigned to any of the basic processes, it can be considered as a black box process.
4. Collect the available data and expert opinions, according to the model structure developed.
5. Select the model to use for each module, on the basis of the statement of purpose, process knowledge, data availability and the alternative scenario's considered.
6. Implement the available data into the model. For each processing step, select the specific model to use. The use of mechanistic models is preferred, and only use complex models when this is necessary for evaluating alternative scenarios and when the availability of data permits it.
7. Perform an exposure assessment.

The usual modelling of the food chain describes the different processing steps in the food chain as primary production, processing and retails, handling in private households and finally consumption patterns.

Sources of data

The aim of the modelling of each of the basic processes is to describe the change in prevalence and number of micro-organisms per (contaminated) unit for each processing step, and this preferably in quantitative terms. For this, data will be needed on environmental conditions (e.g. temperature, pH) and (handling) practices (e.g.

duration of transport, storage) at the various processing steps. To validate the model, data are needed on total number of cells over all units (N), unit size and the fraction of contaminated units (P) at the start and the end of all steps.

Another category of data that is needed concerns the description of the food pathway. Although this may seem easy at first glance, experience shows that a description in quantitative terms (the number of animals and their destination or their origin, the number and the weight of carcasses and their destination or their origin, etc) is not easily obtained. Moreover, when the model is to be used also to gain insight into risk factors and risk reduction scenarios, data on alternative food pathways and/or steps will be needed. In case risk may vary between different production systems or is subject of study (e.g. intensive -industrial- versus extensive -ecological- systems), data from various totally different production chains will be needed.

A third category of data is associated with the definition of the population for which the exposure assessment is done. Exposure assessment should provide an estimate with associated uncertainty of the occurrence and level of the pathogen in a specified portion of a certain food at the time of consumption in a specified population. It should therefore identify the food consumption frequencies in a certain time period and the portions consumed in a given population or subpopulation and should combine this information to estimate the population exposure to the pathogen under study through the specified food commodity. Therefore data on amount and frequency of food intake in the given population or subpopulation is needed.

Note should be taken of the dependency of the secondary data meaning data collected for other purposes than the risk assessment. Currently the collection of data for food borne zoonoses is revised within the Community and it would be important if this collection is pulled by the needs for QMRA. One priority could be easing the comparability of data e.g. that sampling is done based on the same amount of foodstuff (1 gram, 25 grams).

Frequently the risk assessors and managers have to deal with missing, incomplete, incomparable information sources, biased data or not representative results. While these situations are annoying, it is possible to deal with them in two ways to overcome data limitations and improving data collection. These options are model simplifications and predictive microbiology including use of surrogate data handled through an expert opinion. An expert opinion will complement other data sources in particular in building realistic scenarios. In addition the methodology of meta-analyses can be used for collating and analysing data from different sources.

Nevertheless it is crucial that risk assessors carefully communicate their data needs to both risk managers and scientists involved in observational or experimental studies, and that the latter promote incorporation of the necessary data collection efforts within current budgets.

Choosing a modelling strategy

The process of model development is an iterative process, where initial choices are refined and modified as the insight in the underlying process grows and the availability of data is explored in greater depth. Since the exposure model itself is a

tool to understand the problem under study and to identify knowledge gaps it is desirable that it is developed independently from the consideration of the availability of data. However, this may be difficult in practice, since the choice of model may be very dependent on the data that is available. A fundamental choice is between mechanistic (explanatory) models and empirical (statistical, associative) models. In general, mechanistic models capture the details of the process under consideration in greater details than empirical models.

Current risk assessment models generally are of a static nature, i.e. they do not explicitly consider the effect of time. The typical static model considers the events that take place during a fixed period of time, such as one year, and treats differences between or within time periods (e.g. seasonal variation) as variability. Embedded in these static models one may find dynamic modules for microbial growth or death. However, the output of these dynamic modules is usually of a static nature, e.g. the relative increase or decrease in microbial numbers.

Another important distinction is that between deterministic and stochastic models. In a deterministic model, the effects of chance are ignored and all parameters have a fixed value. The end result of a deterministic model is a one point estimate. In a stochastic model, all events are considered as variable and are represented by probability distributions. It is also possible to express the uncertainty in the model parameters with a probability distribution. In exposure assessment, deterministic models are particularly useful in the first stages of a project, when the events that have a major impact on risk must be identified. Subsequently, stochastic models are usually constructed to fully account for variability and uncertainty in the most critical stages.

Only in the most simple cases is it possible to solve such stochastic models analytically but in general numerical simulation methods are necessary. Monte Carlo simulation is a particularly useful tool for simulation of risk assessment models and is frequently applied. Other possibilities are Bayesian belief network and fuzzy methods.

Variability and uncertainty

The probability distributions used in stochastic risk models may represent variability as well as uncertainty. In this context, uncertainty represents the lack of perfect knowledge of a parameter value, which can be reduced by further measurements. Variability, on the other hand, represents a true heterogeneity of the population that is a consequence of the physical system and irreducible by further measurements.

Sensitivity analysis

The assessment of the response of a model to the effects of different methods is often referred to as sensitivity analysis. There are different methods for sensitivity analysis such as correlation analysis, spider plots, factorial designs, and gradient estimation. Each method gives insight in another aspect of this relation.

Reporting the results of exposure assessment

The results of an exposure assessment usually consist of a set of output values from a Monte Carlo simulation. It is important to carefully consider the presentation of such results. They must be meaningful to specialists who read and review the risk assessment, but also to readers who are less specialised in statistics and modelling. As a general starting point, the following presentation of results is recommended as a minimum:

- A listing of all input parameters and their distribution. It is advisable to also give some characteristic values such as mean or median and some percentiles (e.g. 5th percentile and 95th percentile). The added value of graphical representations (histograms, cumulative frequency plots) should be evaluated on a case-by-case basis.
- Mean, median, some percentiles and variance or standard deviation of all relevant output statistics.
- Typically, exposure models result in the prediction of the prevalence of contaminated food items, and the concentration of pathogens in a contaminated item. These outputs should be extensively characterised.
- It is usually instructive to also summarise the results of several intermediate steps in the food chain. Particular attention can be given to those steps where the risk manager plans interventions.
- A graphical presentation of all relevant output statistics. A histogram is easily understandable by most readers, but a cumulative frequency plot may be more informative for specialised readers.
- A graphical representation of the results of sensitivity analysis. It is advisable to also report these results in a tabular form. Apart from providing insight in the uncertainty of the model results, these scenario analyses are also critical in providing insight in the most critical data gaps, and thus to formulate key research recommendations.

Model validation

Model validation can be defined as demonstrating the accuracy of the model for a specified use. Within this context, accuracy is the absence of systematic and random error, in metrology commonly known as trueness and precision. All models are, by their nature, incomplete representations of the system they are intended to model, but, in spite of this limitation, models can be useful. Major aspects of model validation are conceptual validation, validation of algorithms, validation of software code and functional validation.

Peer and public review

The process used to develop the results can improve credibility of risk assessment results. Peer and public review of results is an essential part of the process. Interdisciplinary interaction is essential to the process of risk assessment and should be extended to the review process. Experts in the biological processes involved should

review the basic concepts and underlying assumptions used in an exposure model. Furthermore, statistical experts should review the data analysis and model construction. Critical evaluation of an exposure assessment is a demanding task that requires highly specialised experts. Therefore, adequate resources for the peer review process should be made available as an integral part of the project plan. The results of the peer review process should be accessible to all interested parties, including a statement on how comments are incorporated in the final version of the document and if relevant reasons why specific comments are not accepted.

Conclusions

1. Quantitative risk assessment is a specialised task that requires skills in mathematics and statistics in addition to microbiological and technological knowledge. As a consequence, risk assessments are usually conducted in large, multidisciplinary projects. Building a comprehensive model may be resource intensive. The output of risk models is relatively complex, and in order to guide the risk assessment and interpret the results, risk managers need to understand the basic principles of modelling and concepts.
2. The pivotal step in the whole risk analysis process is the risk evaluation step, where one identifies hazards, develops risk profiles, sets priorities and allocates resources; commissions risk assessments (including exposure assessments) and evaluate their results.
3. Exposure assessment provides an estimate of how likely it is that an individual or a population will be exposed to a microbial hazard and what numbers of organisms are likely to be ingested.
4. One should look upon the exposure assessment as an iterative and continuous process.
5. Food pathways are very complex and any model is by necessity simplification of the real world. The exposure assessment should be as simple as possible while still including the important sources of and steps leading to, the risks of concern.
6. A framework, the modular process risk model, MPRM, where the steps in the exposure assessment can be identified as one of six basic processes: growth, inactivation, partitioning, mixing, removal and cross-contamination, is suggested for the processing stages of the food chain.
7. The MPRM approach appears to be appropriate in the processing stage. It would be desirable to explore the possibilities for using the MPRM approach also in the primary production and consumption stages.
8. The black-box approach could be useful when dealing with processes where the outcome is not critical for the results of the exposure assessment, where one is dealing with emerging issues not completely understood and where interpretation is in the observed intervals.

9. Large progress is required for predictive microbiology to be adapted to the needs of quantitative risk assessment. Limitations include that the temperature variations over time are not taken into account, since primary models are not yet fully validated under non-isothermal conditions. Variability and uncertainty of model parameters are not separated. Moreover, secondary models do not enable a realistic prediction of lag times, especially after stressing conditions (such as those encountered by the bacterial population during the processing steps).
10. Preference should be given to biologically plausible models or models with biologically interpretable parameters.
11. The explicit separation of variability and uncertainty in exposure assessments should be a goal of risk assessors, and such a separation would allow decision-makers to understand how model outputs might improve if uncertainty is reduced. It also provides the risk manager more insight than working with default or worst-case assumptions.
12. There is often no good match between the data available and the data needed for the exposure assessment.
13. The evolution of the methodology of quantitative risk assessment is highly desirable.
14. Despite available documents there is still confusion on definitions and concepts in risk assessment.
15. Peer and public review of results is an essential part of the exposure assessment process. Interdisciplinary interaction is essential to the process of risk assessment, and should be extended to the review process.

Recommendations

1. Risk managers should clearly define the scope and purpose of the risk assessment, including the exposure assessment, before it is commissioned. That should take place during the risk evaluation step.
2. Data collection strategies for exposure assessments should be changed with a view to produce the information required. Risk assessors should communicate their data needs to risk managers and risk managers should prioritise current surveillance programs to meet that need.
3. Data gaps and priority of requirements should be clearly communicated to the risk managers.
4. The strategy for dealing with data gaps should be clarified during the risk evaluation step.
5. In the meantime risk assessors will have to do their best to work with the available data and communicate the uncertainties and limitations associated with exposure assessments based upon these data.

6. One should at least for large exposure assessments always include an expert opinion step to obtain useful scenarios and reasonable estimates for likely exposures.
7. In data collection the use of meta-analyses techniques should be considered, as well as the use of Bayesian methods. It is important to keep the risk assessment methodology open to many different scientific paradigms at the present state-of-the-art and therefore a quick harmonisation should be avoided.
8. The resources when doing exposure assessments should be directed towards the most critical stages in the assessment in the relation to the risk management questions.
9. Adequate resources for the peer review process should be made available as an integral part of the exposure assessment.
10. The results of the peer review process should be accessible to all interested parties, including a statement on how comments were incorporated in the final version of the document and if relevant reasons why specific comments were not accepted.
11. The limitations in the predictive microbiology models should be addressed.
12. Traceability in the food system needs to be developed to make trust worth exposure assessments.
13. The possibilities of using the modular processes approach for exposure assessment in primary production and consumption should be explored.
14. Definitions and concepts in the risk assessment paradigm should be harmonised as soon as possible at all levels e.g. OIE and Codex.

4.3. QUANTITATIVE ASSESSMENT OF CHEMICALS IN FOOD

Exposure assessment is one of the keyparts of the risk assessment process. Only intake of toxicologically significant amounts can lead to adverse health effects even for a relatively toxic substance. In the case of chemicals in foods this is based on three major aspects:

- (i) how to determine quantitatively the presence of a chemical in individual foods and diets, including its fate during the processes within the food production chain;
- (ii) how to determine the consumption patterns of the individual foods containing the relevant chemicals;

- (iii) how to integrate both the likelihood of consumers eating large amounts of the given foods and of the relevant chemical being present in these foods at high levels.

The techniques used for the evaluation of these three aspects have been critically reviewed to determine those areas where the current approaches provide a solid basis for assessments and those areas where improvements are needed or desirable (Kroes et al. 2002). For those latter areas, options for improvements are being suggested, including, for example, the development of a pan-European food composition database, activities to understand better effects of processing on individual food chemicals, harmonisation of food consumption survey methods with the option of a regular pan-European survey, evaluation of probabilistic models and the development of models to assess exposure to food allergens. In all three areas, the limitations of the approaches currently used lead to uncertainties which can either cause an over- or underestimation of real intakes and thus risks. Given these imprecisions, risk assessors tend to build in additional uncertainty factors to avoid health-relevant underestimates. This is partly done by using screening methods designed to look for “worst case” situations. Such worst case assumptions may lead to intake estimates that are higher than reality. These screening methods are used to screen all those chemicals with a safe intake distribution. For chemicals with a potential risk, more information is needed to allow more refined screening or even the most accurate estimation. More information and more refined methods however, require more resources.

The ultimate aims are:

- (1).to obtain appropriate estimations for the presence and quantity of a given chemical in a food and in the diet in general;
- (2).to assess the consumption patterns for the foods containing these substances, including especially those parts of the population with high consumption and thus potentially high intakes; and
- (3).to develop and apply tools to predict reliably the likelihood of high end consumption with the presence of high levels of the relevant substances (see also figure 1).

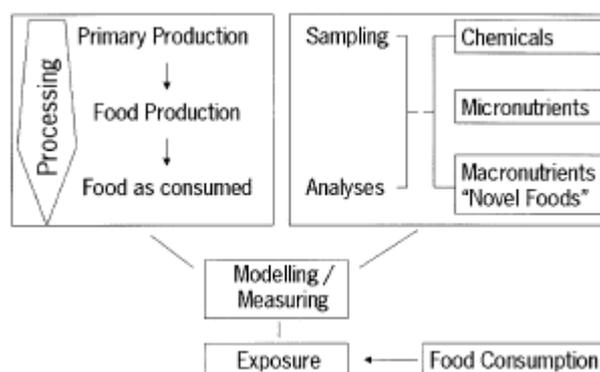


Fig. 1. Considerations for levels/qualities of chemicals in foods.

5. ASSESSMENT OF HUMAN HEALTH IMPACT

“When you can measure what you are speaking about and express it in numbers you know something about it; but when you cannot measure it, when you cannot express it in numbers your knowledge is of a meagre and unsatisfactory kind.”

JC Maxwell 1883

5.1. INTRODUCTION

Across the EU only a few member states are already using probabilistic risk assessment extensively to assess human and animal health and environmental risks from particular stressors. Among the DG SANCO scientific advisory committees, however, a deterministic methodology is currently favoured. In part this reflects the legislative objectives of these risk assessments. In contrast in the USA probabilistic risk assessment is widely used. It is important for the EU to consider the extent to which, if at all, it wishes to adopt a more quantitative approach to risk assessment.

5.2. DETERMINISTIC RISK ASSESSMENT

Deterministic risk assessment has been widely discussed in the first report and will therefore be only briefly mentioned here.

Much of the EU legislation is based on the use of standards. There is a common misunderstanding that such standards mark a sharp distinction between no adverse effect and an adverse effect. This is of course incorrect. Nonetheless such standards are very valuable tools for risk management. The deterministic approach has been used almost exclusively to set these standards and in this respect has served the community well. However the uncertainties involved in the assessment are not always clear because the output of quantitative risk assessment is a yes/no answer. It is important to review whether or not deterministic risk assessment should continue to be the principle approach to risk assessment within the European community.

5.3. PROBABILISTIC RISK ASSESSMENT CHARACTERISING UNCERTAINTIES

Principles

The essence of probabilistic risk assessment is that it aims at ranges of plausible values, rather than single values or point estimates. The aim of

In probabilistic risk assessment one tries to quantify uncertainties associated with any of the steps involved in the risk assessment process, be it data or assumptions. These uncertainties are then combined using statistical techniques, in order to quantify the uncertainty in the end result of interest. A common technique for combining uncertainties is The Monte Carlo method.

For more complicated assessments, the Monte Carlo approach is in principle easy to understand and implement. Making a probabilistic assessment meaningful is mostly a matter of a proper conceptual understanding of the various uncertainties involved, and how they relate to each other.

It is important to distinguish between uncertainties that reflect imperfect scientific knowledge from uncertainties that reflect variability in a population (sometimes denoted as type I and type II uncertainties, respectively). The imprecision in any point estimate as reflected by its standard error or confidence interval is an example of type I uncertainty. The uncertainty that the human being could be more, or maybe less sensitive than a factor of ten compared to the test animal, is another example. The variation in sensitivity among individuals exemplifies type II uncertainty, but the question how large this variation exactly is constitutes type I uncertainty.

It is not meaningful to combine these two types of uncertainty into a single uncertainty distribution. It should always be clear how a derived uncertainty distribution must be interpreted. For example, a 5th percentile may reflect either a 5% probability of being wrong (type I uncertainty), or a fraction of 5% of the population considered (type II uncertainty). By maintaining the distinction between these two types of uncertainty in the Monte Carlo analysis, one may end up with statements such as: There is a 95% probability (level of confidence) that at most 10% of the population exceeds the acceptable daily intake (ADI). Uncertainty distributions that result from mixing type I and type II uncertainties are difficult to interpret, and can only be used as a sort of worst case approach to see if there might be a potential problem.

A second crucial aspect is the quantification of the magnitude of the uncertainties involved. In the case of uncertainties of estimates resulting from (experimental) data, common statistical techniques can be used. It is more difficult to quantify uncertainties in assumptions that have to be made in situations of lacking data, such as in extrapolating from no adverse effect levels observed in animals to humans. In those situations one may base an estimate of the uncertainty associated with the extrapolation factor on relevant data for other compounds, for which both human and animal data are available, and consider the statistical characteristics of such data.

Illustration of potential use -Probabilistic assessment of ADI, TDI, RfD

The procedure for deriving a probabilistic ADI is as follows:

- (i) A certain Critical Effect Size (CES) is determined, i.e., a certain percent change relative to the level of the endpoint observed in the controls, assuming that this particular percent change is non-adverse for the endpoint considered.
- (ii) The associated Critical Effect Dose (CED_{animal}) is derived from the fitted dose-response model, together with its uncertainty distribution.
- (iii) This distribution is then “divided” by the distributions for the relevant EFs, usually inter- and intraspecies, and, if necessary, for other EFs, e.g. for subchronic to chronic extrapolation.
- (iv) The resulting distribution for the NAEL_{sens. human} has to be analysed to derive an ADI (or TDI, RfD), for example by selecting a low percentile of the uncertainty distribution. An obvious choice for this lower percentile is 5%, since this is generally considered in science as an acceptable error in

significance testing (including significance testing in the classical approach aimed at deriving NOAELs).

Interpretation of findings from probabilistic risk assessment

Thus, the interpretation of a probabilistically derived ADI (or TDI, RfD) is that it is unlikely (with quantitative information on how unlikely) and that the true NAEL in the sensitive human is lower than the derived value. It should be noted however that the interpretation of probabilistic model results relies on the uncertainties that have been allowed for. It is therefore important that the assumptions adopted are made clear to risk managers and to other stakeholders. Uncertainties that were considered initially but not incorporated into the actual assessment also need to be identified clearly. Unless this is done different probabilistic risk assessments on the same stressor could yield apparently different results (Sources of uncertainty are dealt with in several parts of this report for example chapter 9). It is important to ensure that both risk assessors and risk managers become well versed in the concepts and interpretation of probabilistic models including the form of presentation of results.

Conclusions

The procedures for probabilistic risk are sufficiently developed that they provide a practical alternative to the application of deterministic risk assessment.

There are good scientific reasons to justify their adoption since they have a number of potential advantages. However it is important that the methodology and its legitimate interpretation are thoroughly understood prior to its take up.

Recommendations

A progressive introduction of probabilistic risk assessment is recommended with a view to it becoming standard practice in the assessment of risks from stressors to human and animal health and to populations in the environment (where the database is adequate for the purpose).

An evaluation of whether changes in the way hazard data and exposure data is collected and recorded should be embarked on.

Early consideration is needed as to how risk managers and risk assessors can become familiar with the concepts and interpretation of the findings from such studies.

6. ASSESSMENT OF IMPACTS ON THE ENVIRONMENT

6.1. INTRODUCTION

The initial scope of the First Report was limited to ecological/environmental risk assessments. However, the scientific knowledge developed in other areas, such as animal health and animal welfare, suggested the expansion of the scope of this document to all non-human health related risk assessments. Considering the specific expertise and the time restrictions, the in depth analysis of current systems and available information has been limited to two main areas, the ecological risk assessment of chemicals, and the risk assessment of animal populations mostly restricted to non-GMO biological stressors and chemicals.

However, some general conclusions on the possibilities for a better use of the knowledge for assessing non-human health risks, and the prospective integration on human and environmental risks are also presented.

6.2. RISK ASSESSMENT IN THE ENVIRONMENTAL ARENA

The risk assessment fundamentals and paradigms initially focused exclusively on human health protection. In the late 80s and during the 90s, the possibilities for extrapolating the scientific basis of risk assessment to the environmental protection concentrated the efforts of ecotoxicologists and environmental fate experts. The activities of the US EPA, EU, OECD, SETAC and other organisations are considered among the main drivers in this process. The publication in 1998 of the US EPA Guideline on Ecological Risk Assessment is assumed as the inflexion point leading to a new paradigm for ecological risk assessment.

Within Europe, this period also represents the starting point for the development of environmental risk assessment protocols as scientifically based tools for supporting regulatory needs. The first drafts of the Technical Guidance Document describing the risk assessment of industrial chemicals (1993-1994), and the first Guidance Documents on the environmental risk assessment of pesticides including the publication of the technical annex of Directive 91/414/EC (1996) represent some European milestones. In the UE, the risk assessments are designed as environmental risk assessment, not purely ecological, and therefore, in addition to the ecosystem goals, other related hazards such as the environmental exposure of humans or the effects on abiotic compartments including global warming or ozone layer, are also covered.

This chapter presents a general overview of the current situation of the environmental/ecological risk assessment, the possibilities for harmonisation, and the contribution of Health And Consumer Protection Directorate General (DG SANCO) Scientific Committees. To offer a broader perspective and harmonisation possibilities, other non-human-related risk assessment protocols and strategies have been considering, in particular, the assessment of animal-health risk. Two basic documents (Appendices 5 and 6) have been produced to substantiate the opinions presented here.

The first document offers a critical comparison of the ecological risk assessment of chemicals in the European Union. Due to legal and administrative designs the assessment of some chemical groups is handled differently from what is called the “General Chemical Strategy”. These particular groups include plant protection products (pesticides), biocides, feed additives, veterinary and human pharmaceuticals and cosmetics. The application of “vertical legislation principles” with well-defined responsibilities, has conducted to parallel developments of the risk assessment protocols, where exchange of views among groups, even at the scientific and technical level, has not always been as broad as expected.

This task distribution is also observed in the arena of the DG SANCO Scientific Committees. The Scientific Committee on Toxicity, Ecotoxicity and the Environment (CSTEE) is responsible for giving scientific advise on general chemicals and biocides, the Scientific Committee on Plants (SCP) covers pesticides, and the Scientific Committee on Animal Nutrition (SCAN) has been responsible for developing the strategy for feed additives. Pharmaceuticals are outside the scope of DG SANCO Committees, and currently the environmental risk assessment does not cover other chemicals such as cosmetics or food additives and therefore the activity of other DG SANCO Scientific Committees in this area has been quite limited.

The second document also offers a comparative assessment, but focussing on the risk assessment for animal populations. Two main objectives are covered with this approach. First, the comparison of risk protocols developed for assessing animal health and the endpoints of ecological risk assessments settled at the population level. Second, to offer a broader spectrum of potential stressors, covering infectious agents, non-infectious micro-organisms and chemicals. Other stressors, such as Genetically Modified Organisms, species introduction, or physical stressors such as heat or radiation have been explicitly excluded from this evaluation due to time constrains.

The outcome clearly indicates large differences in the degree of development of the different risk protocols and strategies. Differences are not just related to the regulatory use of these approaches, but include the level of development currently available on the scientific basis supporting these assessments.

In the ecological arena, the larger amount of scientific knowledge is concentrated on the risk assessment for chemicals. Most EU protocols focus specifically on the assessment of individual chemicals as this is the basis for management, while the scientific community shows a greater interest in multistressors assessments as a more realistic approach, with a tendency for moving from chemical mixtures to a broader evaluation covering chemical, physical and biological stressors simultaneously.

In the animal health/ population risk arena, the risk related to infectious agents, and particularly the risk for introducing infections diseases in geographical areas, offers well-developed and sound schemes, conceptual models and analysis plans, while the evaluation of other stressors is mostly considered as a parallel “minor” activity of the human health risk assessment, being dominated by expert judgement analysis on a case-by-case basis, or by the extrapolation of the ecological risk assessment principles in the case of chemical stressors.

Large possibilities for harmonisation and common development have been observed within ecological risk protocols, but also, among protocols for ecological, animal health and human health evaluation. Several outcomes and proposals are discussed in this chapter.

6.3. FUNDAMENTAL SIMILARITIES BETWEEN RISK ASSESSMENTS THAT APPLY TO ECOLOGICAL SYSTEMS

Ecological risk assessment is concerned with estimating the probability of harm to an ecological target from human-derived agents. This is done to derive a sound basis for managing the sources of the agents to reduce risk.

For ecology, the targets rarely involve individuals only (cf. human health risk assessment). They involve collective groups: populations (single species), communities (mixed species) and ecosystems (mixed species in interaction with their abiotic surrounds).

Hence risks ought to be considered and expressed in terms of probabilities that agents lead to: reductions in population sizes (extinctions of populations/species); reductions in species diversity; reductions in ecosystem processes leading to loss of services to humanity.

The agents might be anthropogenic chemicals, physical disturbances (e.g. changes in temperature, habitat destruction), disease organisms that are spread as a result of human activities, and a combination of these. They may be present continuously or in association with episodic events.

Hence, the probability of ecological harm =
 $f(\text{exposure to agent(s)})$ and $f(\text{potential of the agent(s) to cause harm})$

where,

exposure = $f(\text{likelihood of event})$ and $f(\text{intensity of event})$

potential harm [hazard] = $f(\text{interaction between agent and target})$

Sometimes risk assessments are expressed solely in terms of the likelihood of exposure; e.g. p. of an accidental spillage, likelihood of import or export of disease organism. But generally the assessment considers the consequences as well.

The exposure can be assessed from monitoring programs when addressing existing activities, from ad-hoc scenarios based on a set of assumptions, or from predictive models. Models can predict exposure taking into account the properties of the agents, their levels of production and likely releases (at least for chemicals), and the properties of the environments into which they are released. These can either be deterministic leading to a specific exposure prediction, or stochastic, taking into account uncertainties and inherent variabilities and leading to a predicted exposure plus/minus limits.

Effects ought to be expressed in terms of dose/concentration responses for population dynamics, or biodiversity, or ecosystem processes. But risk assessors rarely have laboratory assays that incorporate this complexity. Instead ecotoxicology focuses on observations on the ways individuals respond to agents in terms of survival, development and reproduction. Sometimes models that relate these variables to population dynamics are available, and (rarely) to biodiversity and ecosystem processes. More commonly the available data is used to estimate dose/concentration thresholds below which ecological effects are unlikely. These are often expressed deterministically, but can be expressed as ranges and sensitivity distributions to capture uncertainty and inherent variability.

With full information on exposure and effects, it would be possible to compute a likelihood of harm from a particular exposure scenario and the sources/circumstances leading to it. Ignorance generally means that the risk assessment can only approximate to this by comparing predicted exposure with predicted threshold dose/concentration. This can be done on the basis of deterministic information (eg leading to a risk quotient – PEC/PNEC) or on the basis of stochastic information where resampling of a distribution of exposure and effect/no effect predictions might lead to a statement about the probability that a threshold dose/concentration might be breached and the likelihood of ecological consequences (eg in spp extinctions).

6.4. BASIC PRINCIPLES FOR ECOLOGICAL RISK ASSESSMENT

Theoretically, ecological risk assessment aims to quantify the probability for effects on the structure and function of ecosystems associated to human activities. Reality is still far beyond the possibility for direct assessment of ecosystem effects.

In general, the basic concepts for ecological risk assessment follows similar approaches than those linked to human health evaluations, the different steps are covered in the risk assessment paradigm and include the exposure and effect assessments and the final risk characterisation.

However, the information required for this assessment, and the tools required for obtaining it, are largely different from those used for human health evaluations.

Protocols for ecological risk assessment have been mostly developed for chemicals. The exposure assessment focuses on the possibilities for environmental emissions and the environmental fate and behaviour of the chemical in the environment once it has reached the initially contaminated compartment. The effect assessment uses the results of ecotoxicity tests, which vary in complexity, possibilities for standardisation and ecological relevance. Risk characterisation is obviously based on the comparison of the expected environmental concentration and the toxicity of the chemical. The complexity required for this comparison depends on the capability of the assessment for covering the lack of homogeneity of the environment. Simple risk characterisation protocols are based on worst-case assumptions and deterministic approaches and do not consider variability in the space and time scales. Higher tier comparisons can be obtained using two basic procedures, covering variability using probabilistic assumptions, or increasing realism using more complex exposure and/or effect tools.

Development of conceptual models.

The conceptual model constitute the link between the specific risks intended to be assessed, those defined in the problem definition, and analysis plan that presents the way exposure and effect assessments are done.

Most EU regulations do not present a clear conceptual model for environmental risk assessment, and during the scientific review of the assessment, the basis of these conceptual models must be extracted from a set of definitions, not always clear enough, of the scenarios employed for the assessment.

As a basic rule for harmonisation, it should be recommended that the opinions of the Scientific Committees include a clear mention to the appropriateness of the conceptual model employed for the ecological risk assessment, potential discrepancies between the applied model and the assessment goals which could invalidate or reduce the value of the results, and non justifiable differences between the conceptual model for ecological risk assessment and the conceptual model for assessing the risk of humans exposed through the environment.

The identification of the protection goals and the level of protection expected to be achieved in the assessment constitute a major problem for setting the scientific basis of regulatory assessments. Basically, ecological risk assessment focuses on effects on the structure and function of the ecosystems. Those effects on lower levels of biological organisations, such as individuals or populations are assumed to be not relevant if no changes on communities and ecosystems are expected. However, this statement is not always followed in the regulatory risk assessments.

In same cases, protection aims are extended to cover population or even individual effects, due to economic or ethical reasons. For example, bird or fish kills following the application of a pesticide will be regarded as unacceptable incidents even if these kills do not affect the population dynamics of the affected species.

The opposite can also be observed in other cases. For example, pesticides and biocides will obviously affect the target species, producing significant changes at the population, community and ecosystem level. The risk assessment in these cases is restricted to direct effects on non-target populations and functions. Direct effects on the target species, and the indirect effects on non-target organisms related to the desired effects on the target (e.g. due to reduction in food or habitat losses) are considered as acceptable and excluded from the assessment, even at the higher tier level.

In this sense, it should be scientifically proper to establish distinctions between truly ecological risk assessment, focusing on community/ecosystem effects including biodiversity; an other environmental risk assessment which protection aims are subordinated to specific concerns.

Tools for exposure assessment.

The environmental exposure assessment constitutes probably the first opportunity for moving towards a more Integrated Risk Assessment, not only because it is used for

both, ecological and human (exposed through the environment) assessment, but also because it must define a set of properties which will be used for both in-doors and out-doors evaluations.

Exposure tools are basically a set of assays, models, and the possibilities for using measured data when the assessment covers an on-going activity.

Assays are designed for assessing under controlled conditions specific aspects related to the environmental fate and behaviour of the stressor. Typical examples are the degradation tests for chemicals, the assays conducted for assessing the persistence of biological agents in inorganic matrix such as soil or water, or those designed for quantifying the losses in intensity and energy of radiations with the distance to the emission source.

Models for assessing chemical and physical agents mostly cover physical-chemical interactions defining abiotic processes such as distribution, dilution, dispersion, etc. Two main exceptions to this rule must be considered for chemicals, biodegradation and bioaccumulation, where living organisms constitute the essential element. Modelling exposure in the case of biological agents require a different approach because the agent may increase in number, and also in potency, after emission. Changes in the virulence of an infectious agent or in the population reproduction rate of an introduced species can dramatically affect exposure predictions.

Measured data on emissions under current situations and on the real presence and intensity of the stressor in environmental compartment are of great value when properly used. Comparison of model predictions and real measurements is a key element for setting the uncertainty of the exposure assessment.

These tools are combined in the exposure assessment. Most risk assessments follows tiered protocols for a better use of the available information and minimising the need of further information to those cases in which it is really essential.

Therefore, the exposure assessment can be conducted following certain levels.

Level 1. Generic deterministic worst-case scenarios.

This level constitutes an initial screening evaluation using as less information as possible. The behaviour is determined in standardised laboratory assays.

Non realistic worst-case scenarios are developed using for example the most conservative data and the 90th or 95th percentile for each individual parameter, as default value in the models.

Exposure is basically considered constant in time and homogenous in space, using equilibrium partitioning and/or the highest predicted level.

Level 2. Generic scenarios using probabilistic estimations.

The single data are replaced in the models by the probabilistic estimations. Then tools such as Monte Carlo analysis may be used for setting the final probability distribution of the exposure.

Level 3. Realistic scenarios covering when required changes in time and space.

Default values are replaced by realistic estimations. The time and/or space changes in the exposure level are included in the models, which are not longer defined on the basis of homogeneity. More realistic assumptions, considering for example that organism will move between contaminated and non-contaminated areas.

Level 4. Semi-field and field studies.

Controlled emissions in field situations allow realistic estimations.

Level 5. Exposure assessment based on real measurement.

Large scale monitoring programmes allow a direct assessment of exposure using direct measurements instead of model predictions. Obviously this level can only be applied to on-going activities.

This classification represents just a descriptive method for shortening the different possibilities for exposure assessments. In general, the initial assessment of tiered risk assessment methods will start with methods corresponding to level 1, and exposure will be refined, if required by methods from levels 2 to 5. However, the methods should not necessarily be applied in sequence, in each case, the available information and the scope of the assessment must be considered to decide which refinement tool is more appropriate. Levels 4 and 5 are more realistic but also include very specific local conditions, therefore their suitability for generic assessments will depend on the relevance of those conditions.

Tools for effect assessment.

Bioassays with different organisms are the basic tools for the evaluation. Five different levels for effect assessment can be identified:

Level 1. Deterministic approaches on single-species tests.

For chemicals, the assumption is that if the exposure is lower than the concentration producing relevant effects (applying a margin of safety for covering extrapolations related to the endpoint, exposure conditions, and species sensitivity) no effects on populations are expected.

For infectious diseases, a similar approach is employed. If the exposure dose is lower than the infective dose (applying appropriate margins of safety), no effects on populations are expected.

It is assumed that if populations are not affected, communities and ecosystems will also remain unaffected. The basic use of this approach is to determine thresholds or safe concentrations. No further estimations (i.e., the risk for community effects for concentrations expected to affect sensitive populations) can be conducted.

Level 2. Probabilistic approaches on single-species tests.

For chemicals, the assessment is based on the species sensitivity distribution. The sensitivity function is used to establish the percentage of species that will be affected at a certain exposure level. If the percentage of affected species is low enough, no effects on communities and ecosystems are expected.

The rationale for this assessment can be presented under two basic forms:

- Ecological perspective: Considering ecosystem redundancy it is assumed that a small percentage of the species can be affected without changes in the structure and function of the ecosystem. In most cases it is not possible to determine which species will be affected or their ecological role. Acceptability will also depend on the species potentially affected.
- Pragmatic approach: These protocols are basically presented as a scientific valid option for using the whole toxicological profile instead of the most sensitive species alone. Basically, the approach justifies that use of statistical methods (SSD) with or without additional margins of safety is a better procedure for estimating the concentrations which is expected to be safe for non-tested organisms than the use of a margin of safety on the most sensitive organisms.

A lot of efforts are presently on going for the further development and validation of these models. Currently the use focuses basically on a similar approach that Tier I, setting thresholds or maximum acceptable exposure limits. The value of the SSD for quantifying probabilities for community/ecosystem effect at levels above the threshold requires further development.

Level 3. Refined single species laboratory tests

This level includes tests with an ad-hoc design for addressing the real population effects of the endpoints affected in the standardised toxicity assays. Aspects such as recovery after exposure, acclimatisation, or direct measurements of effects on populations using large vessels containing a steady-state population are used for refining the risk. Additionally, the design can also include more realistic exposure conditions (i.e. moving from the laboratory tests on non-target arthropods exposed to sprayed glass surfaces to the extended laboratory tests where the organisms are exposed to sprayed plants or soil).

The information is still related to a single species and therefore the approach is equivalent to that for tier 1.

Level 4. Laboratory multi-species tests

Artificial assemblages are constructed reproducing simplified food chains. The basic idea is to detect indirect effects.

Level 5. Mesocosms and field studies.

Mesocosms tries to reproduce a real ecosystem, while field studies expose natural systems under controlled conditions.

The ecological relevance is clear but our limited understanding of ecological effects and the poor reproducibility are clear limitations for the extrapolation of results.

6.5. POSSIBILITIES FOR INTEGRATED RISK ASSESSMENT

Human health, animal health and ecological risk assessment offer both significant commonalities and large differences. For truly ecological risk assessment, the level of protection (communities/ecosystems instead of individuals/populations) represents the main conceptual difference.

It is however possible, as well as current practice, to use common tools in both the exposure and the effect assessment.

The exposure of humans through the environment can be perfectly integrated in the environmental exposure models, where concentrations in water, soil, air and different food items must be estimated. Obviously, integration can also work in the opposite direction, and models developed for setting the exposure of operators and bystanders to pesticides have been suggested as useful tools for addressing the inhalation and dermal exposure of mammals and birds.

In the effect assessment the commonalities mostly focus on the use of the same mammalian toxicity test battery. Tests, initially designed for addressing human health effects, are also used in the ecological risk assessment as source of mammalian data. The relevance of these domestic/laboratory animals for addressing effects on wild populations has been frequently discussed, and basically, the use of the results of these bioassays in ecological risk assessment has been supported by relevant fora on the basis of the following arguments:

- Although differences between laboratory and wild populations have been observed, these differences falls within intraspecies and interspecies variability, and there are not scientific arguments suggesting that laboratory species animals has a clear tendency to be either more or less sensitive than wild animals.
- Current guidance on standardisation as well as ethical concerns require the use of animals reared in the lab and under fixed conditions. Therefore the use of truly wild organisms is neither possible nor desirable.

It is, however, current practice to reconsider the test outcome on the basis of the ecological relevance of the measured endpoints. For example, some biochemical or histological effects which are considered relevant in the human health assessment, and therefore constitute the basis for setting the NOAEL, can be regarded as not ecologically relevant if the test demonstrate that these effects have no consequences on survival, growth or reproduction. In this way, the same test is used for both human health and ecological effects, but different assessment endpoints are employed.

The tendency for moving to a more integrated risk assessment process does not only covers human health and ecosystem effects, but also other assessment such as animal health or economic risk.

As previously mentioned, the effect assessment for vertebrates, and particularly for birds and mammals, is often deviated from a truly ecosystem assessment, considering as unacceptable some effects on individuals (e.g. lethality) even if these effects have no consequences on populations and communities. Therefore, this assessment moves through protection goals typically considered in the human health (individual level) and animal health (population level) assessment, offering plenty opportunities for harmonisation.

6.6. CONCLUSIONS

Risk assessment protocols are frequently classified in two major components, Human Health Risk Assessment and Environmental (Ecological) Risk Assessment. The analysis of the different European protocols and guidelines for assessing Non-Human risk assessment demonstrates, however, a much more complex, and rich, reality. At least four parallel assessments can be identified in most EU proposals through an in-depth revision:

- Human Health Assessment
- Animal (Plant) Health Assessment
- Abiotic Compartments Assessment
- Ecological Risk Assessment

Obviously, each assessment has specific goals, methods and requirements, however, there are a large list of commonalities with not always are recognised and fully utilised for getting an optimum use of the available information and scientific knowledge.

All risk assessment could get significant benefits from a better exchange of information and techniques among the scientific basis and conceptual models developed for assessing different kinds of risk.

Ecological risk covers the wider spectrum of species (in principle all species including those not yet identified, with the only exception of those covered by other risk assessment) and all levels of biological complexity, ecosystem/communities (as the generic protection goal), populations (covering the assessment of certain species that require additional protection goals due to socio/economic or ecological reasons) and even individuals (due to ethical reasons, like for birds or mammals in some assessments, or to ecological implications, such as for severely endanger species where individual protection is required for maintain biodiversity). Therefore, the scientific advances in risk assessment concepts and methods developed in other areas (human health, animal health) can be easily analysed under the ecological angle and useful aspects incorporated in the assessment.

But also other assessments can get benefits from developments initially oriented to the environmental arena, and for example, the extrapolation of the effects observed on individuals to the expected consequences for the population, a basic need in ecological risk assessment, also constitute a key element in animal health assessment.

However, all these possibilities are not fully considered, either by the scientific community or in the regulatory processes. The analysis of the available protocols for animal population risk assessment and environmental risk assessment of chemical indicates that exchange and harmonisation among the different assessment methodologies and regulatory needs is very limited.

- In current practice, animal health assessments are covered (or just assumed to be covered) by the human health assessment, the exchange of information, is in most cases, a purely exchange of the mammalian toxicity, and the expertise on assessing effects at the population level is rarely assembled for getting a more solid scientific basis.
- In the “General assessment schemes”, i.e. those designed for a general authorisation or re-evaluation of an specific agent (either chemical or biological in nature) which cover Human Health, Animal Health and Environmental Health, the guidelines and protocols covering effects on animal populations are very generic, and frequently vague, declarations summarising the potential hazards but without well defined methods for covering the expected risk associated to those hazards.
- There are, however, some specific cases where the risk assessment focuses on animal populations and well defined tiered methods have been developed. The risk assessment conducted for the introduction of infectious diseases associated to animal movements presents a perfect example.
- Within the EU system, the Environmental Risk Assessment protocols include in reality several parallel assessments with different aims and goals:
- A pure Ecological Risk Assessment, based on the risk estimations at the community/ecosystem level.
- Additional specific assessments, with protection goals focusing on risk estimations for hazards related to non-biotic effects (e.g. global warming, stratospheric ozone, groundwater contamination), or on biotic effects other than ecosystems’ structure and functioning (e.g. individuals or populations of specific relevance).
- In the Ecological Risk Assessment arena, most efforts have focused on chemicals. These efforts have produced a solid scientific basis and conceptual frame. The possibilities for expanding this knowledge to the assessment of other stressors (e.g. physical and biological agents) has not been sufficiently investigated.
- A clear lack of harmonisation among the assessment procedures, either within the “chemicals” arena, or between different stressor types, has been identified. Similarly, the revision of the available information suggests several possibilities for harmonisation, at the short and medium time levels.

- The analysis indicates large possibilities for exchanging basic scientific knowledge among the risk assessment schemes, both between human and non-human evaluations and among the non-human assessment. These possibilities have been rarely considered.
- Independently of the regulatory needs, which may require independent assessment for human health, animal health and environmental protection, the scientific evaluation of information and knowledge in the risk assessment framework would clearly benefit for a closer Cupertino and even integration of the protocols. The advantages, inconveniences and difficulties of Integrated Risk Assessments, covering all requirements under a common framework with independent but interactive evaluations of the different hazards should be investigated.

6.7. RECOMMENDATIONS

General recommendations

It is strongly recommended to consider the viability of a common, harmonised and integrated risk assessment framework, allowing the required special features of each assessment but guaranteeing the best use of the common scientific knowledge.

The commonalities of those assessments based on population risk, should be further explored. They can offer a very good alternative for bridging together the risk assessments for humans and the environment, which in most current assessment are not fully linked.

Then, a wide framework, from human to ecological risk applicable to all stressor types should be presented.

Additional issues, such as animal welfare or quality of life, should also be incorporated covering simultaneously human health and non-human health concerns.

In this process, it is critical to consider that these assessments assume different levels of protection and may require different methodological approaches, particularly at the higher tier level, these differences should be clearly identified in the regulations and guidance documents.

Possibilities for Harmonisation

Harmonisation of the Ecological/Environmental Risk Assessment Protocols is not only a desirable target but also an urgent need. The WG considers that this need should be stated at two different levels, short and medium terms, considering priorities and realistic possibilities. As a long-term goal, the development of a common framework for Integrated Risk Assessment, accounting for the specificities of the different stressors, regulatory needs, and protection aims, is desirable.

The Scientific Committees must play a role within this harmonisation process, but additional efforts outside these committees are also required. The following proposals are presented:

A) Harmonisation at the Short Term Level.

a) General needs

- (i) Harmonisation of the terminology employed in the risk assessment and particularly in the risk characterisation and risk communication aspects.
- (ii) Definition of common generic scenarios (e.g. scenarios for agricultural soils, pasture/forest land, generic river basins, etc.) based on similar assumptions, parameters and default values.
- (iii) Harmonisation on the possibilities for data extrapolation (e.g. use of QSAR, extrapolation between taxonomic groups).
- (iv) Cross-reading of the approaches employed for the analysis of different stressors (both, between different chemical types and among different stressor agents).

b) Possible contributions from the Scientific Committees

- (i) Considering the conceptual models inherent to each specific assessment and developing of harmonised proposals for presenting the scientific relevance and appropriateness of these models in each particular assessment.
- (ii) Include in their opinions the equivalence for the risk assessment terms employed in the evaluation, in particular, those typically used in closer guidance and recommendations
- (iii) Development of an harmonised proposal for presenting the uncertainty and variability of each assessment
- (iv) Cross-reading of the opinions adopted by the different committees on different stressor types, and particularly between physical, chemical and biological agents, in order to identify both, commonalties and specificities.

B) Harmonisation at the Medium Term Level

a) General needs

- (i) Revision and identification of the conceptual models employed in the different risk assessment protocols and identification of the possibilities for harmonisation.

- (ii) Development of specific guidance for addressing the Animal (Plant) Health Assessment; Wild Species (individuals or population level) Assessment and Abiotic Compartments Assessment as intermediate assessment between human health and ecosystem analysis, combining the conceptual frame for both.
 - (iii) Addressing the possibilities for moving through a real Integrated Risk Assessment
 - (iv) Give priority to the research needs, particularly those focusing in the development of a conceptual frame applicable to all stressor types.
- b) Possible contributions from the Scientific Committees
- (i) Revision of a set of selected risk assessment, covering different stressor types, and the opinions adopted by the relevant SCs.
 - (ii) Present a set of research needs and their priorities.
 - (iii) Harmonisation of the procedures for expressing both, the identified levels of risk and the remaining uncertainty.

7. DEVELOPING ISSUES

7.1. INTRODUCTION

For the purposes of this report a developing issue is defined as an issue of increasing importance for the risk assessment process. As a consequence there may be a need for its formal consideration during the risk assessment process.

The issues can be grouped under headings:

- new uses of existing data
- factors not commonly evaluated in risk assessments
- application of methodological advances
- new areas of concern.

Those addressed by the task force have been: *In Silico* toxicology, thresholds of toxicological concern, mixtures, susceptible groups and individuals, uses of genomics and sustainability. (Quality of life and related concerns are dealt with in chapter 8.). Inevitably this list is not an exhaustive one.

7.2. NEW USES OF EXISTING DATA

a) Integrated risk assessment.

The potential benefits of utilising the data base developed for human risk assessment purposes to support the environmental risk assessment and visa versa has already been addressed in chapter 5 and will not be pursued further here.

b) *In Silico* Toxicology

Computer modelling offers good prospects for further advances in both hazard characterisation and exposure assessment. However, such advances depend on the availability of quality input information. A very large amount of data on the hazards from chemicals has been generated over the past 30-40 years. The majority of this data has not been published in the scientific literature and is not ready available for risk assessment purposes. Means must be found to make this data available in order to achieve the following objectives:

- avoid duplication of in vivo studies and thereby minimise the use of animals for testing purposes;
- develop a robust programme for extrapolation of data between chemicals based on structure activity information;
- ensure that all relevant data on a particular chemical is available to the risk assessors;
- aid the identification of vulnerable groups/populations;
- facilitate the determination of priorities for toxicological research;

- help in identifying likely suitable substitutes for those chemicals for which a clear risk has been determined.

The establishment of such a database has become an urgent requirement for the proper implementation of the Commissions white paper on its chemicals policy. This requires the risk assessment of many thousands of chemicals by 2012.

Establishment of such a database will need the active collaboration of industry which owns much of the necessary data. Expert advice will need to be sought on: its format, criteria for acceptance of data, potential uses, compatibility with other toxicological data bases and search engines, rules for accessibility etc.

Such a database will not be cheap either to establish nor to maintain and develop. However this and the difficulties of data ownership must not be used as an excuse for the continuing the lack of real progress in achieving of the above objectives.

c) Low dose effects and thresholds of toxicological concern

The conventional approach used in hazard characterisation is that stressors fall neatly into one of two classes:

- threshold stressors ie those for which a no observable effect level can be identified or assumed.
- non threshold stressors for which it is appropriate to assume, as a worst case, a linear response with dose down to infinitely small exposure levels.

Recent research has called into question the universality of this assumption. Work on endocrine disruptors for example has raised the possibility that at exposure levels well below the identified threshold, as determined in conventional toxicity tests, effects may occur. Others have found that on a population basis for well known non carcinogenic substances such as small particles and NO₂ a threshold cannot be identified. On the other hand research on some genotoxic carcinogen would appear to indicate a thresholded effect. J and U shaped dose response curves are being demonstrated for an increasing number of stressors and the phenomenon of ‘hormesis’ is attracting growing attention. it is important to establish how common such phenomena are, the types of stressor for which they are most likely to arise, the most likely types of effects involved, and how they should be evaluated in risk assessments for both human health and for the environment.

A very interesting approach to the use of dose response information is the attempt to establish a ‘threshold of toxicological concern’ (TTC) that is applicable to the great majority if not all chemicals. This is an exposure level below which all/the great majority of chemicals can be considered to be without any adverse effects. In principle an appropriate level for the threshold of toxicological concern can be defined based on published NOAEL values for all chemical classes (ILSI, 2003)

The potential practical benefits of the adoption of such a concept in the field of risk assessment are very substantial for those many chemicals where only low level exposure of consumers is likely. In principle a threshold value could also be set for

environmental effects however identifying the appropriate value will be more challenging than the selection of the TTC for human protection.

For chemicals where exposure levels are likely to be consistently low a staged approach to their risk assessment could be adopted:

Stage 1 → Examination of the chemical and physical properties to ensure that there are no structural alerts that could indicate a particularly high potency and therefore a need to treat the chemical differently.

Stage 2 → Evaluation of the likely worst case, total exposure when the chemical is in use. This should take into account exposure to other closely related chemicals (see ‘mixtures’ section of this chapter). If the exposure levels are below the threshold of toxicological concern, no new toxicological studies would be required.

Stage 3 → If the exposure levels are only just below or within an order of magnitude above the TTC value limited toxicity testing would be required concentrating on the potential to cause specific effects eg genotoxicity. At this stage in principle in vitro tests could have a major role.

Stage 4 → Full hazard characterisation. This would only be needed for those chemicals that raised important concerns during stages 1-3.

It should be noted that both the selection of an appropriate TTC value and the reliability of the structural alert scheme are dependent on a very robust and comprehensive database (see above).

Adoption of a TTC approach would be in keeping with the aim of the Commission of reducing animal use for testing purposes and avoiding unnecessary costs to industry. It would however place much more reliance on the development of reliable means of exposure assessment and provide great assistance in priority setting of stressors for risk assessment.

7.3. FACTORS OFTEN NOT FORMALLY CONSIDERED IN THE RISK ASSESSMENT PROCESS

In chapter 2 a framework has been set out for the consideration of various factors during risk characterisation. Key considerations are how to address the issues of mixed exposure and susceptible groups in the population.

a) MIXTURES

Man and other species are exposed daily to many chemical, biological and physical agents through their food supply, water, ambient air and a variety of other sources. Taking the simplest situation of simultaneous exposure to two stressors one of four consequences may arise:

- the effects of the two stressors are independent of one another;
- the effects are additive;
- the effects of the two stressors antagonist one another;
- the effects are synergistic (ie greater than would have been anticipated from the knowledge of their individual effects).

Clearly the situation is much more complex where an individual is exposed to a number of stressors either simultaneously or within a relatively short period of time.

In most risk assessments only the effects of individual stressors are considered and no account is taken of the prospect of simultaneous exposure to other stressors. From time to time over the past twenty or so years the issue has been raised within the scientific community and by the public on how to address the changes in risk that might arise from exposure to combinations of stressors. However because of the relative lack of good data on the subject no general strategy has evolved to tackle this issue.

Nonetheless for a few specific groups of chemicals guidelines have been agreed internationally. An important example is the group of structurally related chemicals known as the dioxins. A number of chemicals in this class (but by no means all) have been shown to have a common mechanism of toxic action (ability to bind to the Ah receptor). It is accepted that under such circumstances the effects of exposure to combinations of these chemicals should be regarded as additive. Each chemical is assigned a potency score and the combined effect is estimated from their levels of exposure.

Proposed strategy for addressing the question of exposure to mixtures.

In terms of confidence in the likelihood that an interaction between two or more stressors will be additive it is suggested that the following approach is adopted in which category 1 indicates a high likelihood of interactions.

Category 1: there is direct, reliable scientific evidence to demonstrate that interactions can occur.

The key issues in this case is whether the studies are conducted in a model(s) where there is confidence that interspecies extrapolation is appropriate.

Category 2: Stressors are known to have a common mode of toxicodynamic/toxicokinetic action

From a scientific point of view it is reasonable to assume that where stressors have a common mode of action in producing their adverse effects, for example because they involve the formation of a common metabolite or affect the same receptor, the impact of exposure to a combination of these should be considered additive for risk assessment purposes. Inevitably to arrive at a conclusion that two or more stressors

have a common mode of action demands that such substances have been the subject of rather extensive research studies.

Category 3: stressors can be assumed to have a common mode of action

However some degree of extrapolation may be acceptable. For example if two stressors have a very similar toxicological profile and bear a close structural resemblance it may be considered appropriate to assume that additive effects will occur if there is simultaneous exposure.

Category 4 stressors have a common target cell type in an organ

To be placed in this category it is assumed that no data exists on possible modes of action.

The evolving technologies of genomics and proteomics (see below) can be expected to make a substantial contribution, in the future, to the identification of interactions between stressors. For example a good match between DNA array profiles for particular stressors might indicate that interactions between them were probable.

Use of this categorisation system.

The issue of mixtures should be addressed during the process of risk characterisation (See chapter 1, Introduction). It is recommended that in each risk assessment of a stressor the potential for significant co-exposure to stressors in categories 1-4 is considered. Priorities for consideration of possible interactions should be based on:

- the seriousness of the nature of the effect for which interactions are being considered;
- the frequency with which simultaneous exposure to the stressors of interest is likely to occur in practice;
- the exposure levels in relation to their threshold effect levels;
- other information such as structural alerts for possible synergism.

Once the criteria are agreed computer modelling could contribute greatly to this prioritisation process.

b) SENSITIVE GROUPS IN THE POPULATIONS

In human and animal populations, there is a wide range in susceptibility (vulnerability) to chemical, physical and biological agents. Hence, there are groups and individuals at higher and lower risk. This influences strongly the shape of the dose-response relationship curves for populations whether they linear to very low exposure or have a threshold.

Both toxicodynamic and toxicokinetic factors must be considered in the risk assessment.

Furthermore, there is usually a wide variation between population subgroups in exposure to the agents.

Factors affecting susceptibility

Sex is a major determinant of susceptibility to many chemical agents. This is obvious as regards agents affecting the primary and secondary sex characteristics. For example, the toxicity of agents damaging the gonads may vary between females and males. Also, risks associated with agents affecting breast tissues varies between the sexes.

But the sex/gender may be associated with differences in risk in many other ways: The most obvious one is the risk of effects in the offspring in fertile women, either through transplacental transport, or through lactation. However, the sex/gender is also important in other ways, e.g. through differences in nutritional status or life style (see below).

Age is a major determinant of the risk associated with many agents. The most obvious one is the high risk of the fetus, e.g. at exposure to ionising radiation or some of the heavy metals, as methylmercury and lead. But the newborn infant and small child is also particularly susceptible to some agents, e.g. because of differences in metabolism (absorption and distribution), or a particular sensitivity of maturing organs, such as the central nervous system. Another well-known aspect of age is differences in risk by some agents in females before and after menopause, a situation that might be bind to endocrine disruption.

Genetic traits may also affect the risk. A classical case is the sensitivity to cancer induced by ultraviolet radiation in subjects with *xeroderma pigmentosus*, induced by a genetically-based deficiency in DNA-repair. Genetic polymorphisms in several other genes have been demonstrated to influence risks: Varying human leukocyte antigen (HLA) genotypes differ as to liability to develop respiratory sensibilisation at exposure to some low molecular weight chemicals. The genetic differences in enzymes related to metabolism should be considered. Also, the risks of cancer at exposure are assumed to vary between genotypes in the cytochrome P450 and glutathion transferase enzymes. The prevalences of different such genotypes may vary between populations in different parts of the world. However, the interaction between genotypic traits and risk factors is often complicated and yet not fully understood.

Diseases/disorders may also affect the sensitivity. For example, subjects with diabetes run an increased risk of kidney damage, which will induce high sensitivity to nephrotoxic agents like cadmium, and subjects with osteoporosis, e.g. because of physical inactivity, would be expected to be particularly sensitive to the (kidney-damage mediated) effect of cadmium on the skeleton. Individuals with bronchial hyper-responsiveness, due to allergy or other reasons, have a much higher susceptibility to respiratory irritants than other subjects; due to the rising prevalence of respiratory allergens in European populations, such susceptibility is present in a large fraction of the young population. Further, resistance to virus and bacterial infections is affected by inborn or acquired immune deficiency conditions. The long

lasting drug treatments and preventions may change the response to chemicals and other drugs.

Nutritional status affects the response to infectious agents. Thus, the protein status is one of the determinants of the resistance to infections by mycobacteria. Also, the toxicity of some chemical agents is influenced by nutrition. For example, a low iron status causes an increase of the absorption of cadmium, which will make the iron-deficient part of the population, mainly some of the menstruating women, a particular high-risk group as at cadmium exposure. Also, at exposure to agents producing free radicals, as ionising radiation or chemical agents, the status as regards antioxidants, or other nutrients involved in the protection against free radicals, e.g. selenium, will be of importance.

Life style factors are important in some cases. The most well studied factor is smoking. For example, smokers run a much higher risk of lung cancer than non-smokers at exposure to asbestos and inorganic arsenic. Beside the enhancement of the risk at a certain exposure, the tobacco is a source of several agents, e.g. some heavy metals, which will add to exposures from other sources. As another example, since ethanol interacts with the biotransformation of many chemicals, alcohol habits will affect their associated risks. Alcoholic beverages is also a source of some agents, e.g. lead.

The exposures through tobacco smoke and alcoholic beverages are examples of mixed exposures.

Present risk analysis procedures

For a particular stressor the variation in the dose-response relationships may be known from studies in experimental animal models or from human studies.

From this information the presence of susceptible groups should be considered in the risk assessment. Thus, the dose-response relationships, established from epidemiological studies in expected high-risk populations are the basis for the definition of lowest or no observed adverse effect levels. This has been employed for, e.g. lead and methylmercury, where the risk of the foetus has been the major concern, and thus fertile or pregnant women constitute a critical susceptible group to consider in population.

However, in most cases, identification of susceptible groups is not attempted in any systematic way. Instead, a standard safety or uncertainty factor is employed, which intended to cover, together with other reasons for uncertainty, the variation in sensitivity. Where dose-response information is available only for non-human species, the factor has been made large enough to cover assumed inter-species differences.

Further, sometimes, in the risk management and communication, as a complement to the steps taken as a direct consequence of the risk assessment, the risk associated with exposure of certain high-risk groups has been the subject of additional actions. For example, because exposure to methylmercury and polychlorinated organic pollutants, women who are pregnant or lactating, or who are planning to become so, have been advised not to restrict their intake of some species of fish from certain areas.

Proposed approach for addressing the issue of sensitive populations

In the future, as a step towards a more systematic and harmonised procedure, it is proposed that identification of susceptible groups should be a part of any risk analysis of chemical, physical and biological stressors.

- a) Groups likely to have an atypically high exposure should first be identified using conservative (worst case) assumptions.
- b) Consideration should then be given as to how the following factors could change substantially the effects of the stressor at a given exposure level

- Sex/gender
- Age
- Genetic traits
- Diseases/disorders
- Nutrition
- Life style
- Other factors.

A priority approach along the lines discussed above for mixtures could be appropriate. Thus where the mechanism of action is known this will assist in focussing on the key variables. Other important considerations are; persistence in the body, the exposure levels in comparison with the level at which significant effects are likely, the number of the population affected and whether either of these factors is likely to increase in the future.

The more exact the information on variations in susceptibility, the more reliable risk analyses may be made. Whenever possible, dose-response consideration should be made separately for any particularly susceptible groups that have been identified. Their prevalence in different populations should be assessed.

This will reduce the necessity for risk managers to cover uncertainty by large uncertainty/safety factors, without sound scientific basis, and increase the reliability of probabilistic risk assessment.

There is a great need to strengthen the scientific basis for anticipating the likely susceptible groups for important stressors.

An increasing number of publications refer to individuals who appear to be exquisitely sensitive to stressors (eg multiple chemical sensitivity). Some have attempted to explain this as purely psychological based on the fact that these extreme sensitivities are difficult to explain using a conventional toxicology paradigm. It is necessary to revisit this very important issue. In some cases immunological mechanisms may have an important role to play however this is evidently not always the case. There are claims that these sensitive individuals may have higher total body burdens of chemicals than the average member of the population and/or that their tissue repair mechanisms are less effective. Despite the uncertainties regarding the aetiology it is important from a risk assessment/risk management view point to try to characterise

why such extreme sensitivity arises and may be exacerbated in order to identify situations in which it is most likely to occur.

A more holistic approach

It is becoming increasingly apparent that for many human diseases a variety of genetic and environmental factors (often termed risk factors) can contribute to their initiation and /or their progression. For risk management purposes it is becoming increasingly important to judge the relative contributions of individual risk factors and groups of risk factors to a particular chronic adverse effect eg colon cancer. This has for example been manifest in trying to understand the 'gulf war syndrome'.

In the field of cardiovascular disease (CVD) some interesting strategies have been developed to evaluate the overall risk from the various identified risk factors. This is based on a very extensive epidemiological database. The conclusions of this work include:

- a number of the risk factors are interactive
- some at least of these have a common mechanism of action.

Risk equations have been developed to take into account these interactions. A project named SCORE (systematic coronary risk evaluation) is underway to develop and compare European risk factors for CVD in different countries. Whether such risk equations can be extended to other human diseases needs to be examined.

7.4. DEVELOPMENTS IN MOLECULAR BIOLOGY.

It is important that risk assessments utilise up to date technology both in the garnering the relevant data and in interpreting the results. However too rapid an introduction of new technology may result in it being applied inappropriately. Thus although a number of new developments have the potential to be applied for risk assessment purposes each needs to be examined critically first to identify how it might be applied and the advantages and disadvantages of doing this. A harmonised process should be put in place (preferably in collaboration with OECD and WHO) to ensure this occurs as too rapid an introduction of a new method can lead to it becoming discredited.

Genomics and proteomics

The successful sequencing of the human and other genomes was a major breakthrough in the understanding of biological processes and how they are controlled. The use of genomics and proteomics could transform the risk assessment process in the future. Already the USA environmental genome project which was begun in 1997 has identified over 500 environmentally responsive human genes. The findings are already beginning to contribute to our understanding of key factors in human genetic variability in response to environmental agents but the potential ramifications of these techniques go much wider. Among possible applications are:

- uncovering the mechanisms by which individual stressors cause their (adverse) effects however by passing bioavailability.
- distinguishing between true physiological effects and adverse ones. This would provide a much sounder basis for identifying whether or not a true threshold exists for individual stressors.
- Impacts from simultaneous exposure to several stressors.
- Intraspecies variability in response to stressor exposure.
- Characterisation of factors influencing defence mechanisms against stressors. This information should be of benefit in identifying individuals who are likely to be particularly susceptible to specific types of stressor and could thus aid the design of drugs and other chemicals for which significant levels of human exposure are anticipated.
- species to species extrapolation of data
- development of a new generation of much more predictive in vitro tests.

The adoption of these techniques for risk assessment purposes will need to be incremental based on a good understanding of the relationship between genome differences and their biological consequences. Initially the application should concentrate on hazard identification focussing perhaps on specific endpoints such as endocrine disruption.

A co-ordinated approach to the adoption of findings from these methodologies for risk assessment purposes will be needed within the EU. Too hasty an introduction may result in inappropriate applications and a loss of credibility of such methodologies.

7.5. NEW CONSIDERATIONS IN RISK ASSESSMENT

Traditionally the risk assessment process has been very largely restricted to the identification of truly adverse effects on human health (from cradle to grave) and on the environment and to establishing the exposure levels below which such effects will not occur or can be viewed as insignificant. However it is now necessary to consider whether this paradigm of the role of risk assessment is entirely adequate for the following reasons:

- the public's expectations of 'safety' and 'acceptability' have broadened
- there is an increasing appreciation that man has a duty to 'preserve' the planet for future generations

Two aspects where a major change in the coverage of risk assessment are seen as very important are sustainability (see below) and quality of life (see chapter 8).

Sustainability

Sustainability is increasingly becoming regarded as an objective that ought to be taken account of in judging the acceptability of a product or process. Strategies for Sustainable Development have been adopted or are under the process, at the EU and

Member States levels. Sustainability represents a balance for economic development, social benefits and environmental protection, with the basic goal of protecting future generations.

Risk assessment should play a critical role in defining sustainable conditions, but we must recognise that until now the integration of risk assessment in sustainable definitions has been scarce. Three main challenges are essential for allowing a further integration of risk assessment and sustainable development strategies.

- **Estimation of long term risks.** Significant discussions are currently on going regarding the real capacity of the scientific community for estimating long term risks. The debates on POPs (Persistent Organic Pollutants) and PBTs (Persistent, Bioaccumulable and Toxic chemicals) represent a good example. There is a clear consensus that these chemicals require a special assessment that cannot follow the “standard” scenarios, defaults and parameters selected for “normal” chemicals. However, there is a clear disagreement on the use of scientific based decisions or the application of the Precautionary Principle. In general, the scientific community considers that the real risk of these chemicals can be assessed if proper data are produced. By contrast some risk managers assume that as a sound risk assessment cannot be conducted on the basis of the “standard” information, these chemicals should be regulated on the basis of the Precautionary Principle, reducing emissions and uses as much as possible. Independently of the management decision for minimising the risk as much as feasible, risk assessors should face up if the remaining long-term risk is compatible with sustainable development.
- **Evaluation of the expected consequences for the identified risk.** Most risk assessment protocols are conducted due to specific regulatory requirement. The risk is therefore presented in a form adapted to that particular legal framework. In some cases the regulation address specifically the level of risk considered acceptable, and therefore risk assessors just conclude if the product or process fulfil with the acceptability criteria. In other cases the acceptability triggers are not clearly identified, and the risk characterisation is basically oriented to establish if the risk is or not expected to be low. However, the consequences of the identified risk, expressed as the likelihood for effects, are normally not addressed, while those consequences are the key for defining sustainability. The consequences of an industrial effluent representing the same level of risk for aquatic populations (based on the generic scenarios) will largely differ depending on the ecological value of the exposed ecosystem. The presence of endangered species in the area could represent an unsustainable risk for biodiversity, while if the risk focuses on widely distributed species, were recovery and recolonisation are guaranteed, the discharge could be classified as sustainable if medium-term plants for emission reductions and ecosystem recovery are implemented.
- **Development of a multistressor framework for risk assessment.** Current risk assessment protocols focus on specific products or processes. For example the different fertilizers and pesticides used by a farmer are addressed independently, but what is the real risk of the sum of agricultural practices conducted in the farm? Sustainability cannot be addressed at a single point, but as a combination of all practices, including land management, soil conservation, use of fertilizers and pesticides, water management, residues valorisation, etc. in the previous farm

example. The combination of Risk Assessment and Life-Cycle Analysis is increasing our capability for addressing the combined risk of a product or process, but our current conceptual models cannot be easily applied in a multi-activity scheme, and a general framework is urgently required.

It can be concluded that, actually, we are still far for extracting “sustainability” criteria from the current risk assessment methodology. Both conceptual and methodological gaps should be covered. In this report on several occasions integration of risk assessment and combinations of procedures have been addressed. This concept in a wider perspective, needs to be adopted into the sustainability assessment concept. This is a great challenge, but also a clear possibility for enhancing the capability of risk analysis as a scientifically based tool for supporting decision makers.

An open debate between stakeholders on the integration of risk assessment processes within the implementation of the European and National strategies for sustainable development is proposed.

8. SETTING THE SCIENTIFIC FRAME FOR THE INCLUSION OF NEW QUALITY OF LIFE CONCERNS IN THE RISK ASSESSMENT PROCESS

8.1. BACKGROUND

The main recommendation vii in Chapter 10 of the First Report on the harmonisation of risk assessment procedures was to “develop formal means by which issues such as animal welfare, quality of life, socio-economic considerations, and sustainability can be incorporated into the risk assessment process (see Chapter 10)”.

Within the Task Force on Harmonisation of Risk assessment Procedures a working group including outside expertise on quality of life issues, such as the impact of risk perception and communication, was established. The report of the working group was made publicly available for comments. The comments received were considered prior to adoption of the report by the Scientific Steering Committee.

8.2. FRAMEWORK

The quality of life concept is multidimensional and covers such aspects as human functional and psychological health. It can also include concerns about animal welfare, environmental impacts, aesthetics, ethics and community identity. In addition to the biological risk assessment, risk perception, communication, benefit estimates, and value identification play an important role in the process of dealing with quality of life aspects.

Within public health policy, quantitative indicators such as physical health and life expectancy play a dominant role in risk assessment. In many cases public crises arose probably because of not considering enough the human quality of life in a broader sense at an early stage in risk assessment and risk management. Two factors trigger the interest of such an enlargement. Most of the innovations have an endogenous character where humans are causing the benefit and the risk and that ambivalence depending on interest and transparency can lower the confidence in assessment and management. Actions are either performed by individuals or by decision makers for whole populations.

8.3. CONCLUSIONS

Consequently there seems to be a need to enlarge the standard biological risk assessment by introducing several new components in the analysis, in particular psychological and social traits. The ultimate goal is to trigger amongst the decision makers a reflection on a change in paradigm, namely to maximise the health or the quality of life instead of merely minimising the risks. One criterion to be considered particularly in the process is the perception that an individual has of the situation. It means that the communication of the scientific analysis changes the way the subject can perceive the risk and then change his or her quality of life. The analysis of the communication and interactions between the relevant groups of the society is thus an important part of the whole strategy.

Such an enlargement of the analysis in principle includes addressing societal and ethical issues. The ones sustaining the questions asked to the risk assessors are of particular importance. Others are found when defining the recommendations. Many parameters can be used for assessing the quality of life. The weights to give to each of them for reaching recommendations are mainly taken on ethical, cultural and political grounds and are under the manager's responsibility. They can be presented as absolute values for example by stating that a parameter should not be above or below a threshold value. Those weights can also be relative between different parameters. One major difficulty is that the weights given to those parameters can differ between individuals and between groups of the population depending on their cultural attitudes and preferences. A framework needs to be developed to allow risks and non-economic, societal benefits to be compared in an understandable and transparent manner. Progress in this area is essential. One key point when reviewing a risk assessment document is to distinguish between the different kinds of data sets, facts and figures, models and theoretical assumptions, values and beliefs. Further research is needed to characterise the different types of information and arguments in terms of importance and strength of evidence.

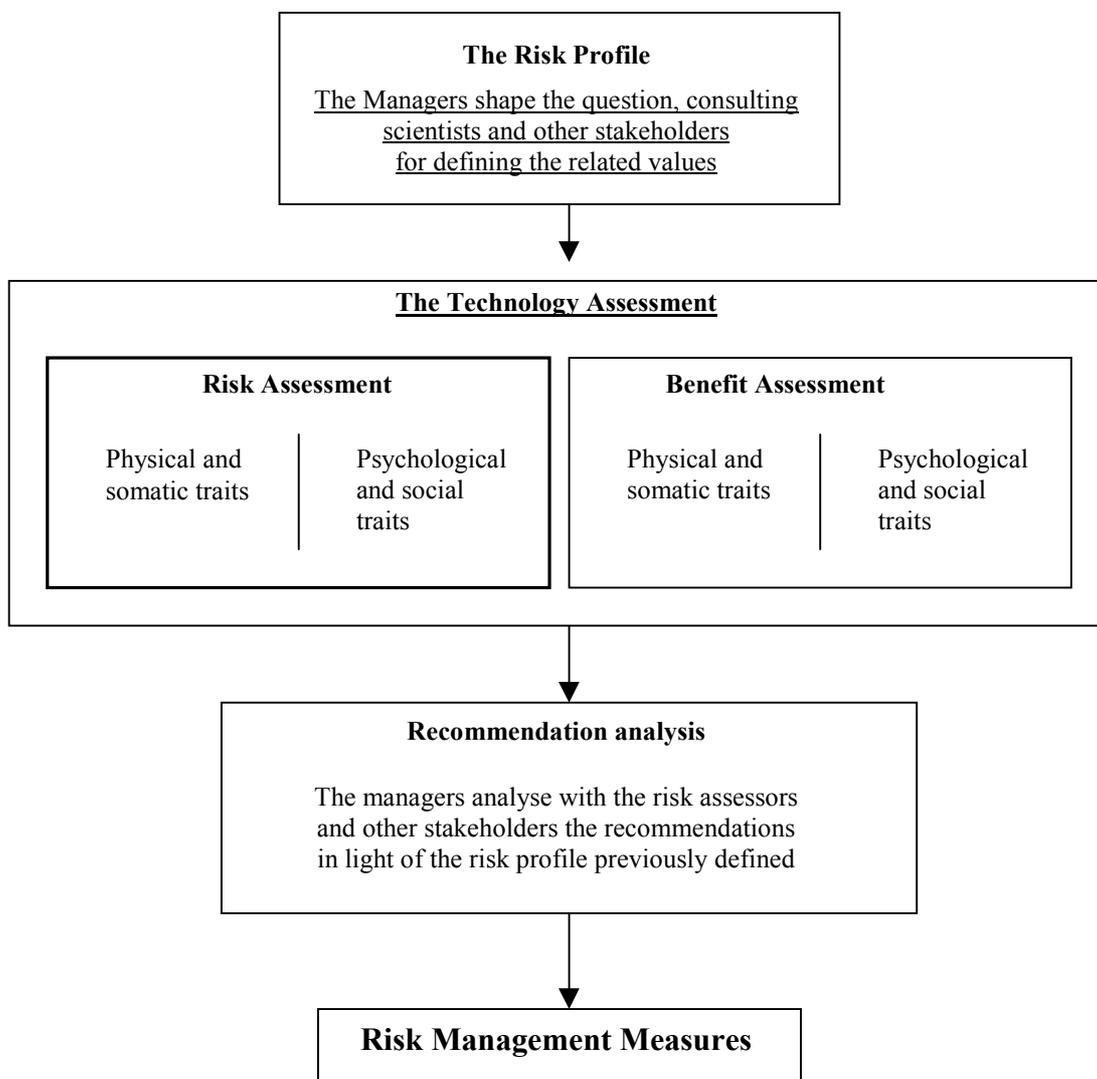
Considering quality of life aspects requires special emphasis on communication of risks and also consumer benefits, transparency, clarity and reasonableness. Bad or poor communication can easily lead to largely irreversible non-facts perception and public crisis. Professional risk communication tools are essential in all cases and must in particular facilitate the individual decisions. Despite recognising this need, they are still not well developed and implemented. They also show that the generally accepted strict and absolute separation between scientific assessment and management does not fully work in reality due to societal prerequisites for scientific assessments as well as uncertainties and biases in the expert judgement processes.

Although these managerial issues are outside the mandate of scientific committees, they influence the work of the assessors when the managers frame the questions. They have also an influence on the way managers use the recommendations proposed by the assessors. One objective of the proposed actions is to elaborate on these links and to develop transparent tools for a systematic strategy. Furthermore it is well understood, that more and different arguments than those expressed here have to be included when developing such a strategy. Nevertheless it is considered legitimate to express the thoughts of the scientists involved in preparing this opinion.

Therefore, it is – as one element in the process - proposed to complement the standard risk assessment by including new quality of life parameters from the beginning and particularly psychological and social traits. It needs to be considered whether the assessment of those traits should constitute an additional dimension to the assessment as it is performed today or if it should be conducted in a separate, regular and interactive process.

The following simplified scheme, which does not include interactions and feedback, is to summarise the broader issues to be addressed and show the position of scientific assessment within the process (Figure 1).

Figure 1: Possible framing of the quality of life traits in the Risk Analysis Process



8.4. RECOMMENDATIONS

Scientific Risk Assessment

The scientific part of quality of life parameters, and in particular psychological and social traits, should be considered as elements of the scientific risk assessment.

The links between that assessment and other criteria (e.g. ethical and political) need to be transparently addressed.

The quality of life assessment should cover the physical impact of the risk factors as well as the perceived impact wherever it is possible. It could also include the foreseen perceived impacts of managerial decisions.

It will need to be decided where the psychological and social trait analysis fits on the overall risk analysis: in parallel, prior or possibly after the classical risk assessment. In any case the scientific panels should meet to interact and prepare a comparative report at the end of the assessment process. Experts from disciplines not involved today, and in particular those from human and social sciences, should be involved in the risk assessment process. It is recommended to invite a group of experts from those disciplines to analyse further the questions elaborated in the report and to prepare a targeted guidance providing the details for the introduction of the identified quality of life criteria and tools in the risk assessments of the scientific committees.

Framework for the Risk Assessment

It is proposed to consider a consistent and transparent approach, which could include three steps (see Figure 1 also):

1. Risk assessors, risk managers and other stakeholders would jointly elaborate the risk profile, identify the criteria to be used, the specific issues to be addressed and the major concerns stated. This will give the opportunity to the risk managers to define the different criteria that will be used for taking their decisions (societal, economical, ethical, political...). In light of those criteria, the risk assessors will be able to decide the objective tools and models that will be the more appropriate to help the decisions to be taken afterwards.
2. The assessments of risks should be performed to answer on the ground of the set of criteria elaborated in the first step. It should be clear that some other aspects could also be assessed, and in particular the social and economic benefits, but they are probably not to be included at least in the short term in the framework of the risk assessment.
3. The strength, limits and uncertainties of the assessment could be analysed jointly by the managers, the other stakeholders, and the assessors, in order to discuss with transparency the selection of management tools of societal and economic consequences.

Such a process will be particularly important at the beginning of the evaluation for defining a comprehensive risk profile and at the end to help to better characterise the risk and to propose measures to the community to handle the risk cycle with utmost acceptability to all groups concerned.

8.5. RESEARCH

Quality of life is part of the ongoing program of research launched by the Commission Research Directorate General. Its results are expected to be of capital importance for this development of risk analysis. Specific research is needed to improve required tools and further develop the concepts and strategies to optimise operation and get experience for the social and biological scientists to work in interaction. Research to minimise uncertainties on risk related questions needs to be continued to improve risk assessment and in particular to provide a basis for facts-based risk perception.

A substantial new research effort is recommended at the interface between risk assessment, management, communication and perception. This approach needs to be elaborated using a transdisciplinary network, regarding the scientific issues including the disciplines involved in risk assessment and the medical and social sciences involved in quality of life assessment as well as those societal groups, which are responsible for the non scientific (democratic, ethical) criteria. The workshop on the interface between the risk assessors and the risk managers that will be held in 2003 should be very important for clearing those questions.

Specific research topics should include:

- Elaboration of a quality of life terminology by harmonising needs and approaches,
- Development of improved tools for uncertainty communication,
- Tools to analyse variability in the parameters discussed, their causes and how to improve them,
- Development of deterministic and stochastic systems for balanced societal cost and benefit evaluation in the risk analysis,
- Benefit of the introduction of the Quality of Life concept for health care, potential economic constraints in other sectors,
- Development of education programmes for scientists and journalists in risk communication

9. EXPRESSION OF RISKS

9.1. INTRODUCTION

A systematic, comprehensive, transparent and generally accepted approach for expression of risks is urgently needed. The objective is an unequivocal interpretation of the outcome of risk assessments by all users, not only by the experts in a detailed field. Although such an approach needs time to be completed and adopted, there are areas within the issue where harmonisation is possible.

Risk assessments are increasingly becoming more specific with regard to differentiation in local human populations or regarding regions or different types of differentiation in ecosystems with different sensitivities. These are needed for risk management in addition to the more generic, averaging assessments and requires in the expression of risks at least a precise mentioning of the targets, information used with its uncertainties and identification of the weights with their uncertainties given to the different pieces of information.

9.2. FRAMEWORK OF RISK EXPRESSIONS

Normative risk assessments have to follow legislatively fixed procedures on the basis of adopted methodologies and data sets. They usually results in yes/no decisions, whether the data set is complete and valid and whether the risk source meets the requirements for pre-set acceptable risk. These assessments are only changed when required by new scientific information, improved methods becoming available or upon additional societal requirements.

The other area of risk assessments especially on emerging issues on which norms have not been set requires a case by case in depth analysis attempting to achieve a quantitative assessment. These assessments may include further data requirements and need to be updated upon provision of that information.

9.3. UNCERTAINTIES AND THEIR EXPRESSION

For the purpose of risk assessment “uncertainty” is defined as the gap between scientific valid knowledge and the complete ultimate scientific evidence.

Following this use of the term uncertainty, it includes data gaps and measurement errors as well as conceptional/modelling missing aspects or unknowns

There are, in addition, two areas of concern summarised under the term uncertainty, which are not related to each other from a risk assessment point of view and which play a largely different role in risk assessments. These are

Data gaps and measurement errors of single data points reflecting the degree and precision of information needed for assessments

True variations of environmental data and biological responses reflecting the ranges of reality and upon proper statistical and modelling evaluation provide important information for a specified risk assessment. From a risk assessment point of view these variations consequently are not uncertainties but facts.

In analytical and statistical practise these two areas are mixed possibly for historical reasons, when it was the ultimate objective of measurements and data interpretation to provide best averages or means. Standardised and largely accepted error and uncertainty terminology (ISO/NIST) so far is measurement driven and does not sufficiently consider the needs of risk assessment. In the measurement and statistics areas this terminology should be consistently used. It is however not only a matter of terminology but also on the methodology to provide information on biological, chemical and physical variables. To provide the dispersion of values (preferably adjusted for systematic error before further use) upon proper stochastic treatment (xx percentile at yy probability and the type of distribution) including overall confidence intervals is a progress for assessors as compared to the still predominant deterministic delivery of results.

The so-called type B uncertainties (expert judgement) involving the interpretation and integration of measurement, of statistical evaluation and modelling information with their uncertainties is much more difficult to express consistently. Considering that a full set of information for valid quantitative risk assessment is rarely available, information with different degrees of validity has to be used in risk assessments. Provided models would be available to deal with this problem, their scientifically sound use, including error propagation would not lead to useful results. As one consequence at least for complicated risk assessments the wording for expression uncertainties involved is adopted to the issue. Furthermore, for such complex situations it is not possible to impose a mandatory wording to the expert groups for the result of a difficult consensus finding regarding all areas of uncertainties included.

It needs to be re-emphasised, that the uncertainties in a weight of evidence for a risk to be assessed including all levels of information from hypothesis/theory via different levels of experiments and possibly field observations can not be treated mathematically - e. g. as a “uncertainty propagation” like error propagation. The results would be of no use – and not reflecting the true total uncertainty.

Consequently the requested **common format for expressing uncertainties** under the harmonisation point of view can not be a set of terms for the range of “quantitative “ uncertainties but should include nomination of the types of uncertainties considered with their weights (where possible also values) and contributions to the final judgement.

9.4. SCIENTIFIC EVIDENCE

Scientific evidence and overall uncertainty are directly related and expression of the degree of scientific evidence thus is equivalent to expressing uncertainty.

Precautionary principle and weight of evidence (with merely being cautious) are approaches in regulatory regimes. They may be considered complementary or alternative, but both rely on the scientific evidence of a risk, and its expression in transparent, unequivocal terms becomes more important, when risk assessment points to high severity, irreversibility, and high uncertainty (especially when time for collecting adequate data is long).

9.5. USE OF RISK COMPARISONS

The results of comparative risk assessments play an important role in risk management. For the purpose of expression of risks they are of limited use only within the scientific assessment, since principally only risks for identical biological and health related endpoints should be subject for comparative assessment regarding their sources. This prerequisite avoids to deal with otherwise needed value judgements within the assessments. At a first glance, risk comparisons are easier to be given than full individual risk assessments, since uncertainties within the sequence of evidence may be similar. This assumption is valid whenever the available, whole body of information is similar. In addition, risk comparisons are helpful for a preliminary assessment, when information providing evidence is not available, but the physical and chemical factors governing exposure are similar.

Disregarding the above prerequisite for comparative risk assessments they are inevitable for substitutes replacing a risk source. This has not consistently and comprehensively been done in the past (e.g. fire retardants). The risk comparison of the original source with the substitutes should be available prior to management actions on the original source in order to provide information on the consequences of actions to risk managers. Special emphasis should be given in comparative risk assessments on comparing the uncertainties.

9.6. INTEGRATED RISK ASSESSMENT

There are essentially two areas including their combination for integration

- in the assessment of risks for biological endpoints (human health and environment)
- in the assessment of exposure pathways to a risk source.

In the first area, despite using a common methodology (WHO-report), the final expression of risks needs to be kept separate, in order to avoid value judgement within the scientific assessment. Severity, irreversibility and associated uncertainties should be expressed as usual.

In the second area, when addressing one biological endpoint, the objective of integration is to express one total risk resulting from a source. In this area, where the different exposure pathways may also include different exposure regimes, with

different true variability and uncertainty, the integration requires high transparency of the assessment process and careful expert judgement to achieve a final expression of the total risk

9.7. OPINION FORMATS

The advice given to the European Commission by its scientific committees can have a great influence on both consumers and the industry in member and non-member states. In its statement of 26 May 2000 on Advice to the Commission from its scientific committees, the Scientific Steering Committee (which includes among its membership, the chairman of the eight scientific committees) considered it important that the organisation and working procedures behind the scientific advice are transparent. These are briefly presented in the statement.

To enhance the transparency of the scientific advice, it is important that the various Scientific Committees as much as possible adopt harmonised working procedures. The purpose of the current document is to recommend how opinions should be set out and the relationship between opinions and reports. As the guidance proposed here extends beyond the current frame of scientific advice at the level of Commission Services, the remainder of the text refers to “scientific advisory committees (SACs)” rather than to scientific committees.

Key issues in the conduct of a risk assessment by the scientific advisory committees are:

- The increasing need for transparency throughout the process;
- Ensuring a very high and consistent scientific standard;
- Clarity both for scientists and other stakeholders about the outcomes of the risk assessment, both at the time of issuing an opinion and subsequently;
- A harmonised approach between different scientific advisory committees to avoid apparent ambiguities in assessments and to facilitate joint working between committees where practicable;
- Reducing unnecessary duplication of work both between EU scientific committees and with other national and international scientific committees;
- Enabling RAs carried out by one scientific committee to be readily utilisable by others.

The Scientific Steering Committee realises that these recommendations, when implemented, may have a greater impact on some Scientific Advisory Committees (SAC's) than others. However, harmonisation can only be achieved by modifications in the details of the way the SAC's currently function. The recommendations should be seen as a framework for a harmonised approach, rather than a set of rules. It is

recognised that some aspects of the work of the committees are not amenable to this framework.

It is appreciated that adoption of these proposals would change to some extent the relationship between a committee and its working groups responsible for generating reports.

The principal proposed changes from current practice are as follows:

The roles of Scientific Advisory Committee and Working Groups

SAC's should continue to have the responsibility for establishing, where necessary, a Working Group (WG) to address a specific issue. The SAC should set the WG's terms of reference and the chairman of the WG should be appointed from among the SAC members. The terms of reference for a working group may not necessarily be identical to the questions asked of the SAC. It is recognised that some WGs comprise only members of the main Committees, whereas others comprise mainly external experts. Inevitably the balance of internal to external members will influence the interactions between the WG and the SAC.

To ensure that the scientific report meets the needs of the SAC it is important that agreement is reached at an early stage between the committee and the particular WG responsible for developing the report on:

- Source data to be utilised
- Structure of report
- Time Scale.

Relationship between the Opinion and the Report

The Opinion and the Scientific Report, although closely related, should be produced on the assumption that for some purposes they may be used as stand alone documents. SAC's may draw on information not covered in the report in reaching their Opinion. Opinions should, however, be based on the Scientific Report. In drafting both documents it should be assumed that, for various purposes, the Opinion and the Report might be utilised separately. Opinions should typically be quite short (1-5 pages). It is recommended that where possible the opinion and the report be published simultaneously. However, this may not be practicable, particularly if publication of the Opinion is deemed to be urgent. It is essential that scientific reports be of high quality, based on the best available scientific data. Risk assessment is becoming a recognised academic discipline in its own right. High quality reports, in addition to being valuable for a specific purpose, also serve to raise the status of the discipline.

Recommendations should not normally be included in the final Scientific Report. They should, however, be a specific sub-heading of the Opinion.

It is proposed that SACs should not alter the content of these reports, (and would therefore not have the responsibility for editing them) although as part of the peer review process they should be encouraged to propose improvements to the authors of any report. In making this proposal the Scientific Steering Committee notes that it is expected to be an increasingly common practice for these Reports to be commissioned (and paid for) by Commission Services / European Agencies which require specific risk assessments.

The Scientific Report should, wherever it could be of value to those outside the relevant committee, be prepared on the assumption that it will be published in an appropriate form. Reports published on the Internet following review and acceptance by an SAC may be considered to be peer reviewed. However, it is acknowledged that in many cases the format may differ from the procedure used by existing scientific journals. It is recommended that the principal authors names are included in the Report. This measure is consistent with encouraging a high scientific standard and making participation in working groups more attractive to non-members of the SAC's in that it would provide much more tangible professional recognition of the authors for the work they carry out. It will also aid transparency and help to reduce duplication of effort by different committees. A crucial element of the Opinion is that it should be written in a form that is unambiguous and can be understood readily by the appropriate stakeholders.

Sources and confidentiality of information

Whether a full literature search was conducted or whether the working group only used the literature provided by Commission Services should be identified. In future this identification should include whether or not individual stakeholders were invited to submit information. All sources of information that are used must be cited along with the rationale for excluding from consideration particular data sources.

Individual committees draw, to a variable extent, on information provided by manufacturers 'in confidence'. This situation has a substantial impact on the detail that can be cited in the Scientific Report and the Opinion and the transparency of the process. The committee/working group should identify the way that confidential material has been used to reach its conclusions/opinion. It should be made clear in the report what weight has been given to any unpublished data that is used and the basis for this.

Expression of alternative opinions

From time-to-time genuine significant differences arise in committees on the interpretation of scientific data. Where these differences cannot be resolved by extensive discussion they should be expressed in an alternative opinion to ensure transparency. It is also important for risk managers to appreciate that on a particular risk assessment there are differences of view.

The alternative opinion should be noted in the text of the opinion and the detailed scientific argument attached as an appendix. Normally it is recommended that the authors of the alternative opinions are not identified specifically unless they require

so. In instances of serious disagreement it may be appropriate to hold a formal vote of the SAC and to publish the results of this.

The revised recommended structure is as follows:

For the Opinion (ie: Committee's position)

- a) Title
- b) Terms of Reference and statement on sources of information available
- c) Brief background
- d) Summary of key issues
- e) Conclusions and recommendations
- f) Key words
- g) References including cross references to other relevant opinions by SACs
- h) Appendix (to include declarations of interest if relevant, alternative opinions, statement on sources of information available, etc.)

For the Scientific Report

- a) Title
- b) Table of Contents
- c) Summary abstract
- d) Purpose of the report and background to the issue(s)
- e) Scientific discussion of the issue(s) following, where appropriate: a statement of sources of information available, hazard identification, hazard characterisation, exposure assessment, risk characterisation, other scientific considerations. (It is recognised that some aspects of the work of the SACs cannot be fitted into this framework).
- f) Scientific interpretation (but not recommendations)
- g) Key words
- h) References
- i) Appendix (to include declarations of interest if relevant, alternative opinions).

The Task Force recognises that these recommendations, when implemented, may have a greater impact on some Scientific Advisory Committees than others. However, it wishes to point out that harmonisation can only be achieved by modifications in the details of the way the Committees currently function.

9.8. CONCLUSIONS

The expression of risks, even for risk sources and effects where a fully quantitative risk assessment is possible is a continuing issue. Despite significant advances in stochastic modelling including their validation for modelling uncertainty, there remain basic uncertainties – in the best cases in quantitative terms only. Since it is difficult to

express these with a consistent terminology, the description at least needs to be transparent as regards all the parameters and information used .

9.9. RECOMMENDATIONS

1. Consider the above issues when phrasing questions.
2. Ask wherever possible for an integrated exposure (all pathways) assessment for the risk source.
3. The common development of further scenarios and expansion of models should be adequately supported.
4. The increasing use of stochastic risk modelling is inevitable. It should be developed in an integrated approach to assess a risk source, but also individually for each variable, which may be changed by risk management. Results need to be translated into common consistent language.
5. Additional precisely targeted, comprehensive monitoring/surveillance should be implemented.
6. Provide original, non integrated data sets to the assessors and eliminate data gaps that might readily be filled.

10.INTERACTION BETWEEN RISK ASSESSORS, RISK MANAGERS AND OTHER STAKEHOLDERS

10.1. INTRODUCTION.

An important aspect of the risk assessment process is to demonstrate independence of the risk assessors while ensuring that the work they conduct is clear, appropriate and timely from a risk management point of view. To achieve this, dialogue must take place between risk assessors and risk managers at particular stages in the risk assessment process. These need to be transparent in order to satisfy possible concerns of other stakeholders. There is also a need to establish 'good practice' in the risk assessment process.

10.2. INTERACTIONS BETWEEN RISK ASSESSORS AND RISK MANAGERS

The risk cycle is quite complex and the Figure 1 already presented in the report of the quality of life illustrates that complexity. It is not complex because it needs a lot of information but also because it makes several different partners to interact to reach an agreement and to decide on actions. Among the partners it is possible to differentiate the scientists, the different stakeholders (consumers, patients, producers, environmentalists, animal protection societies) and eventually the political and notifier bodies. They all have to be involved at some stage of the risk analysis. Even if the most common question is the way to deal with the interface between the risk assessors and the risk managers, the implications of the other stakeholders are also very important and can probably not be solve only by the risk communication. It is sometime not clear however how all those different groups interfere and at what stage of the process.

The first report on the harmonisation of the risk assessment stressed the importance of a clear involvement of them: "Among the key issue which have been identified are the need to improve the interface with and the level of support from Commission officials, while preserving the independence of committee members. Agreed procedures for interactions with other stakeholders is also important". That question was also dealt with during two meetings of the steering committee. On the 25-26 a draft was presented on an "SSC contribution to the reflection on procedures for enhancing the effectiveness of the interface between scientific committees and Commission officials". It was suggested to establish a "working group comprising representative of the SSC and officials from the appropriate Directorate Generals". On the 21-21 February 2002 that question was also put on the floor when discussing the access to documents request. In that last text it was stressed that the independence of the scientific assessors should be preserved during the elaboration of the reports. Several authors have described the background of the scientific process: Conclusions are issuing from observation, they are accepted by the scientific peers and they can be falsified. In the minutes from the SSC on the 21 and 22 of February 2002 the importance and the difficulties of the building up of an opinion is described. It is proposed to maintain the independence of the assessors during their work. The question of the disciplines to involve in the process is still opened. In the report on the quality of life for example it has been proposed to introduce in the assessment social scientists even if it is not clear if those scientists should be mixed with the biological scientists or if they should be working as independent and parallel bodies.

However, some authors have challenged that general scheme of the risk analysis involving the separation between the risk assessors and the risk managers. In particular they proposed a much higher involvement of the other stakeholders. Forum meetings with citizens or hybrid forums where all the stakeholders are part of the exercise are proposed. They propose such structures in particular in case of high uncertainties. They argue that it is a way to bring up knowledge which is not described in an academic way but which are important and also better reflect the “real world”.

To be able to solve that question one main goal is to clear all the values that are at stake, the legitimacy and independence of the participants so to have the process as transparent as possible. It is necessary also to stress that the risk questions can be tackled by using scientific, ethical or societal approaches and that merging those approaches is not so simple. Mixing all those questions is probably not a good alternative to the existing framework.

The working group thinks that the best way to carry on that exercise and in particular involving the stakeholders is to invite them during two of three steps of the risk analysis:

The first step should be handled by the managers and would be devoted to define the term of reference. It is during that work that the values at stake should be defined with all the stakeholders. From that work, the term of references could be given to the risk assessors making clear what are the important items. It will be then to establish a risk profile. From that profile it will be possible to address a question to a scientific committee or to several committees depending of the scope of that question. In the past that procedure has already been used. For example, the consequences of the use of BST for dairy cows have been analysed by two different committees. The difficulty will be to have a clear procedure to define the values at stake and to be sure that they can be analysed by the scientific committee which will receive the request. It is then probably necessary to have a clear mandate and the possibility for the scientific committee to ask for clarification.

The second step should be the risk evaluation. It seems necessary to maintain the autonomy of the committee during that exercise for the different reasons that have already been given. The output should be a report which will be given to the public in a transparent way.

The managers should then involve the stakeholders to comment on the report, and in particular on the recommendations. It should be possible to ask for another report or to implement another step as it can be done in multi-tier procedure. One possibility is also to put the report for comments on the net to have the reactions of the people having an interest in the question.

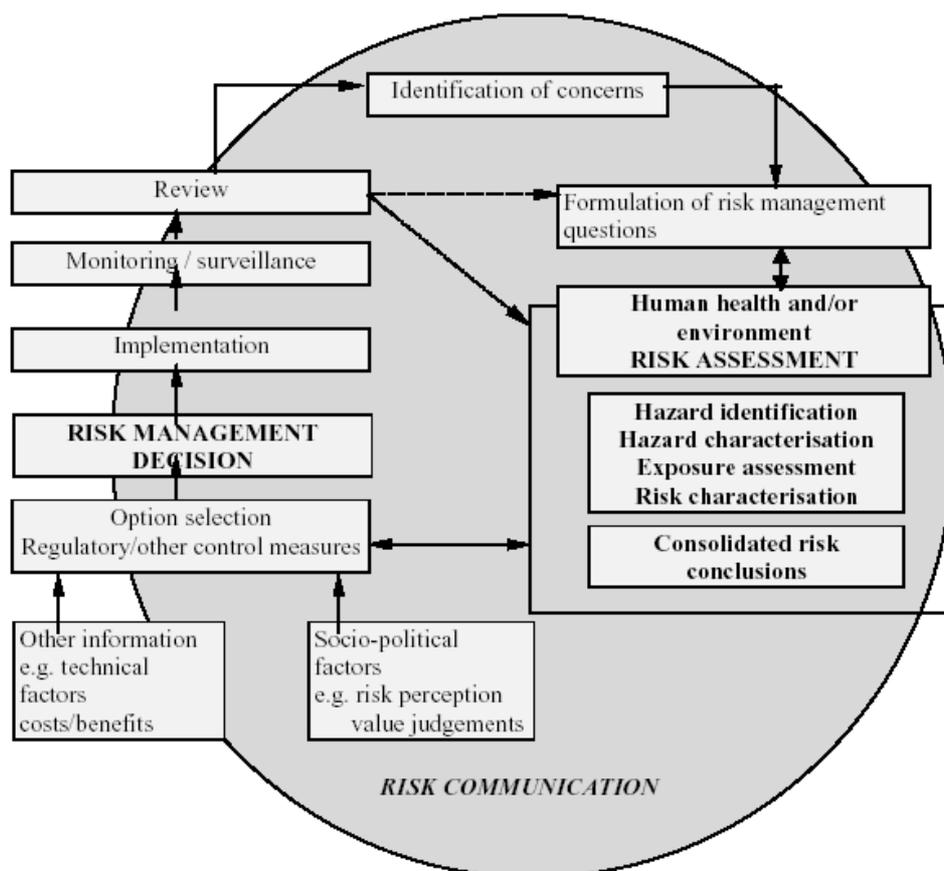


Figure: General Schedule of Risk Analysis Cycle

10.3. GOOD EVALUATION PRACTICE.

Criteria to demonstrate good practice are commonly applied to the collection and use of data (good laboratory practice, good clinical practice) and to the management of organisations (eg ILO 9001).

Although the findings from risk assessments from the scientific advisory committees of Health And Consumer Protection Directorate General are widely available how specific risk assessments were conducted may be less clear to those who are not members of the committee. Committees should aim to provide sufficient detail that their work could be amenable to external auditing. It is appropriate therefore to try to establish criteria of good evaluation practice. These could include the following:

- evidence that all the accessible relevant data has been considered and transparent ranking of the weight of evidence has been applied (see Chapter 2).
- details of any calculations used provided.

- follows agreed format or where not reasons for the differences are presented. Deviations from practice eg late acceptance of unpublished data for example should be defined (see Chapter 9).
- suitable independent external expertise drawn on where there is insufficient expertise on a particular important issue in the committee itself
- all possible conflicts of interest of committee members are identified
- any communication of members of the committee with stakeholders during the risk assessment is logged and explained
- timeliness against pre-agreed targets
- Due consideration to controversial views including minority opinions
- clarity of expression of the opinion along with the clear identification of uncertainties in the opinion (see Chapter 9)
- utilisability by risk managers
- evidence of significant contributions from a number of committee members
- all key statements appropriately referenced
- consistency with other opinions of the same committee and of other committees. where its is not the case reasons should be given

Further work is needed to examine how these criteria might be weighted and/or others introduced. A pilot study should be embarked on to examine the practicality of using each criterion.

10.4. OTHER CONSIDERATIONS

The system of expert advice is dependant on the availability of experts from many fields and their willingness to work for the commission. The primary motivation appears to be a belief that the work that they carry out for the commission is important and that their contribution can make a difference. It is anticipated that for a number of reasons it will become increasingly difficult to recruit suitable members unless positive steps are taken by the commission to change current trends and practices viz.

- (i) the increasing demand to demonstrate total independence is reducing progressively the number of individuals who qualify. Ruling out members from industry would cause increasing difficulties as industry seeks to recruit more of its own experts/consultants in order to fulfil the requirements of the new chemicals policy and other new regulations. Moreover University and research institute staff are having to rely increasingly on industrial support for their research due an increasing short fall in government support and a need to find levels of funding that reflect the real costs of the research. It is important that is not viewed as a serious impediment to participation in scientific advisory committees as long as scientific integrity prevails.
- (ii) the shortage of experts in various fields which is a reflection of the lack of any co-ordinated assessment of manpower needs. This was illustrated in the first report by the dwindling number of toxicologists and pathologists but the problem is not confined to these areas. It is exacerbated by the narrowing of areas in which scientists are likely to gain experience of during their careers.

- (iii) the relatively poor level of scientific and administrative support for the work of the scientific advisory committees. This compares unfavourably for example with that given to many national scientific advisory committees.
- (iv) an inflexible, often very slow and financial unattractive reimbursement system. Thus no payment is made for the many hours members spend working on committee papers outside of committee meetings. It should be borne in mind that in order to be a member of a committee, members may have to reject more remunerative consultancy work.
- (v) lack of flexibility in the venue for meetings, the use of teleconferencing etc

The commission should consider how these problems can be mitigated. This analysis should include:

- How expertise in industry can be utilised in the risk assessment process
- provision of induction programmes for new members and potential new members
- the need for dialogue with Universities etc on how the growing need for training of risk assessors can be met
- how the work of its committee members can be optimised and the members and their employers feel that their involvement is worthwhile.
- a review of the reimbursement system particularly in respect of 'homework'.
- Means by which scientific advisory committees work can be attractive to the leading scientists
- It is important that the managers are seen to value the risk assessment process and the work of the risk assessors.

A further issue is the means by which this report is made available to all those involved in the risk assessment process and its use. It is recommended that the report is published in both electronic form and in hard copy. It is also suggested that a series of workshops is held for risk assessors and risk managers to establish an action plan for the implementation of the findings.

In conclusion, we recommend keeping the scientific risk assessment as a separate procedure of the risk analysis. We however recommend to have a better understanding of the values and items of importance to make the best analysis as possible. To do that it is probably useful to involve the stakeholders from the very beginning and to have clear feedback with them.

11. CONCLUSIONS

(NOTE THAT MORE DETAILED CONCLUSIONS CAN BE FOUND AT THE END OF EACH CHAPTER)

- (i) Risk assessments are having a growing impact on the process of risk management. It is vital, for the purposes of stakeholder confidence in particular, that risk assessments are seen to be of the highest scientific quality, independent, transparent, consistent, clear, appropriate to the practical needs and within an agreed time frame.
- (ii) Apparent inconsistencies continue to arise from time to time between the different scientific committees of the EU in:
 - * the methodologies used
 - * the hazard characterisation conclusions reached on the same stressors
 - * the ways that opinions are expressed (including the use of terminology)
 - * the nature of the communications with stakeholders
 - * the involvement of external experts
 - * consideration of uncertainties
 - * allowance of the background/other sources of exposure to the stressor
- (iii) there is a rather poor and uneven system for communication between the various agencies in the commission involved in risk assessment and a prospect that this situation will worsen with the separation of food and non-food risk assessments and the likely establishment of further independent agencies. It is concluded that prompt action must be taken across the Commission and other national and international bodies to facilitate harmonisation
- (iv) The purpose of the present work is to identify some areas where a more harmonised approach is both desirable and achievable. The report complements largely that of the first report on the harmonisation of risk assessment procedures, which was published in April 2000. Regrettably the implementation of the recommendations of the first report by commission services has been very limited to date.
- (v) Over the next decade it is estimated that many thousands of additional risk assessments will need to be conducted within the EU to meet additional regulatory requirements. For ethical, consumer perception, economic and scientific resource reasons this will require new strategies for risk assessment. Key components of this strategy should include: better use of existing data, a co-ordinated approach to the introduction of new technologies in the risk assessment (eg genomics) and a better use of the scientific expertise by the Commission.

- (vi) in particular cases a better quantification of the risks involved and a greater breadth of assessment is a necessity. Evaluation of impacts on the quality of life and on sustainability are considered to be particularly important in this context.
- (vii) it is concluded therefore that formal consideration is given in all risk assessments to factors such as the possible contributions from co-exposure to several stressors as well as assessment of the effects on particularly sensitive sub groups of the human and animal populations or ecosystems.
- (viii) several possibilities for short and immediate harmonisation of non-human risk assessment are proposed. Animal health appears as a promising bridge for integrating human and environmental risk assessments.
- (ix) effective and widespread dissemination of the findings of this report are essential if progress towards genuine harmonisation is to be achieved. It is concluded therefore that the report is published both in electronic form and in hard copy and that a workshop(s) is held for risk assessors and risk managers and other appropriate stakeholders to establish a clear agreed action plan for implementation of the recommendations of the report.

12.RECOMMENDATIONS AND PROPOSALS FOR IMPLEMENTATION

(NOTE THAT MORE DETAILED RECOMMENDATIONS ARE TO BE FOUND AT THE END OF EACH CHAPTER)

The key recommendations are summarised under four headings:

- Measures that can be implemented immediately
- Further work but probable implementation within in the short term
- Measures for the long Term
- Multidisciplinary research priorities to facilitate harmonisation

For convenience the key recommendations of the first and second reports have been merged.

12.1. MEASURES THAT CAN BE IMPLEMENTED IMMEDIATELY

- a) Develop the co-operation between the scientific committees and Commission services and EU Agencies, particularly the European Food Safety Authority and Research Directorate General. Other bodies involved with risk assessment are listed in the appendix to the Second Report. Harmonisation between these bodies is highly desirable. As a first step, put in place a co-ordination procedure for situations where the same stressors is dealt with by more than one committee/panel.
- b) Adopt an agreed glossary of terms involved (identified in the First Report).
- c) Request that each of the scientific advisory bodies test the risk characterisation framework in pilot studies and report back with any suggestions for improvements etc.
- d) Adopt the common format for the presentation of opinions (as set out in chapter 9 of the Second Report)
- e) Introduce a familiarisation programme for new committee members (see First Report). Hold annual seminars/workshops for committee members and risk managers to discuss strategies, methodology and other aspects of the risk assessment process (see First Report)

12.2. FURTHER WORK BUT PROBABLE IMPLEMENTATION WITHIN IN THE SHORT TERM

- f) Establish a procedure to ensure dialogue between risk assessors, risk managers and other appropriate stakeholders.

- g) The Scientific Assessment process:
- Introduce probabilistic risk assessments initially as a pilot scheme,
 - Establish a strategy for the adoption of integrated risk assessment (see chapter 6 of the Second Report)
 - Develop a common EU database of risk assessments of chemical, biological and physical stressors. This database should include risk assessment conducted on human and animal health and the environment across Commission services and EU Agencies as well as those carried out for national and other international bodies.
- h) Formalisation of approaches for dealing with key variables:
- Adopt a strategy for the identification of sensitive groups of the human, and animal and plant population and allowance to the ecosystems (see chapter 6 of the second report)
 - Introduce a stepwise process in the assessment of exposures which includes consideration of multiple stressors (chemical, biological and physical). This requires in terms of environmental contaminants particularly the establishment of a set of generic European scenarios for instance in terms of environmental contaminants (industrial and municipal discharges, waste disposal, soil.)
- i) Development and communication of opinions:
- Selection of a short list of descriptive terms for the expression of levels and likelihood of risk. Request translation services to identify the most robust of these other translated (see First Report).
 - Agree a format for the presentation of uncertainties in each risk assessment (see chapter 9 of the Second Report).
 - Establish a framework for risk comparisons/bench marking (see chapter 9 of the Second Report).
- j) Additional criteria that should be considered:
- Set up a co-ordination group to explore and prepare the introduction of quality of life parameters into the risk assessment process.
 - Decide whether or not to adopt thresholds of toxicological and ecotoxicological concerns in a stepwise scheme of risk assessment.
- k) Review:
- Develop a strategy for situations in which monitoring/surveillance should be implemented (see first Report)
 - The parameters for good evaluation should be agreed and implemented (see chapter 9 of the Second Report)
 - A transparent process for the periodic review of the risk assessment of stressors should be established.

12.3. MEASURES FOR THE LONG TERM

- l) Introduction of quality of life parameters into the risk assessment process (see chapter 8 in the Second Report)
- m) Introduction of sustainability criteria into the risk assessment process (see chapter 7 in the Second Report)
- n) A systematic approach to involve the appropriate stakeholders in the risk profiling stage (see chapter 8 and 10 in the Second Report)
- o) Develop a methodology for a harmonised risk benefit analysis.
- p) Revision of the conceptual models for non-human and ecosystem risk assessment (see chapter 6 the Second Report)

12.4. MULTIDISCIPLINARY RESEARCH PRIORITIES TO FACILITATE HARMONISATION

A number of research priorities in specific areas are identified in the individual chapters and appendices of the Second Report.

12.5. IMPLEMENTATION

In view of the importance of harmonisation the SSC strongly recommends that Health And Consumer Protection Directorate General takes the initiative and co-ordinates the actions set out in these recommendations. It recognises that this will require active discussions with a number of other DG's and independent Agencies (such as The European Food Safety Authority) in the EU and other international and national bodies.

13.LIST OF APPENDICES

- APPENDIX 1: Members Of The Task Force
- APPENDIX 2: Glossary of Terms
- APPENDIX 3: Report On Food Borne Pathogens: A Quantitative Assessment Exposure
- APPENDIX 4: Report On Probabilistic Risk Assessment
- APPENDIX 5: Report On Ecological Risk Assessment On Chemicals
- APPENDIX 6: Report On The Risk Assessment In Animal Populations With Emphasis In Wild Life.
- APPENDIX 7: Report On Setting A Scientific Frame For The Inclusion Of Quality Of Life Concerns In The Process Of Risk Analysis