National Institute for Public Health
and the Environment
*Ministry of Health, Welfare and Sport*

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A proposed framework: SEATS

RIVM Report 2017-0079
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# Colophon

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# Synopsis

**Estimation of the socio-economic consequences of regulatory measures on toxic substances in food**
A proposed framework: SEATS

There are stringent food safety requirements applicable in Europe. The concentration of any substance which could adversely affect our health in food must be as low as possible. To ensure this, food safety standards are set to enforce a maximum permitted concentration of substances in products. Food safety standards are determined mainly at international level (European and worldwide) and their safety is assessed based on scientific analyses of the hazardous effects of substances in food.

Factors other than hazardous properties can also influence the level of the food safety standards that are set and are, therefore, included in the decision-making process. Currently, there is no standardized and transparent method for doing this. One such example is the societal concern that is created by uncertainties in the scientific assessment. A large economic impact of the established food safety standards can also be expected, for example, in the form of higher prices. RIVM has, therefore, developed a framework (SEATS) to broaden the decision-making process in regard to food safety standards by including criteria other than just the hazardous properties of substances.

SEATS combines a cost benefit analysis with societal concerns like risk perception, uncertainty and trust. SEATS was tested in two case studies (lead and pesticides) in which the impact of lowering the food safety standard was investigated. It was concluded that SEATS works well.

Keywords: socio-economic assessment, chemical food safety, food safety standards

# Publiekssamenvatting

**Het schatten van de economische en maatschappelijke gevolgen van beleidsmaatregelen voor schadelijke stoffen in voedsel**
Een voorgesteld kader : SEATS

In Europa gelden strenge eisen voor de veiligheid van voedsel. Zo mag voedsel zo min mogelijk stoffen bevatten die een gezondheidsrisico vormen. Hiervoor zijn onder andere zogenoemde voedselveiligheidstandaarden ingesteld voor de maximaal toegestane concentraties van stoffen in een product. Voedselveiligheidstandaarden worden voornamelijk op internationaal niveau (EU en wereldwijd) bepaald en zijn getoetst door middel van een wetenschappelijke analyse van de schadelijke effecten van stoffen in voedsel.

Ook andere factoren dan schadelijke effecten van stoffen kunnen van invloed zijn op de hoogte van de voedselveiligheidstandaarden en worden daarom bij de besluitvorming over de standaarden betrokken. Dit gebeurt nu echter niet op een gestandaardiseerde en transparante manier. Een voorbeeld is maatschappelijke bezorgdheid als gevolg van onzekerheid in de wetenschappelijke analyse. Ook kan een grote economische impact van de vastgestelde voedselveiligheidsstandaard worden verwacht, bijvoorbeeld in de vorm van een hogere prijs. Het RIVM heeft daarom een stappenplan (SEATS) ontwikkeld zodat in de besluitvorming over de voedselveiligheidstandaarden breder wordt gekeken dan alleen naar de schadelijke effecten van stoffen.

SEATS combineert een afweging van kosten en baten vanuit een economische invalshoek met maatschappelijke aspecten, zoals risicoperceptie, onzekerheid en vertrouwen. SEATS is voor twee voorbeeldsituaties (lood en pesticiden) uitgewerkt. Er is onderzocht wat de impact is als de voedselveiligheidstandaard wordt verlaagd. Het blijkt dat SEATS goed bruikbaar is.

Kernwoorden: maatschappelijk economische afweging, chemische voedselveiligheid, voedselveiligheidstandaarden

# Contents

# Summary

Although chemical food safety in Europe is, in most cases, more strictly regulated in comparison to other countries, consumers are currently becoming more and more aware and concerned about chemicals in their food. This may eventually lead to precautionary measures being adopted, such as the lowering of food safety standards. At the same time, food safety measures may also be challenged when substantial economic impacts are expected to fall on specific stakeholders, such as farmers who are no longer able to grow their crops in an economically efficient way. Food safety policy measures may be associated with increased costs for food production with the inherent consequences these have on food prices. Consequently, consumer spending and wealth may be influenced. For policymakers to decide what policy measures to take in this frequently complex field of expected impacts where the various actors, all with their own interests, wishes, views, power and resources compete, it is very important to carefully weigh what policy measure would be preferable for society as a whole. A socio-economic assessment of the regulation of toxic substances in food could be very useful and is, therefore, of growing interest to policymakers. To our knowledge there is little or no experience in the European Union (and within RIVM) in assessing the costs and benefits of possible risk management options, e.g. the costs of lowering a legal product limit (e.g. Maximum Residue Limit, MRL), banning a regulated substance from the market or discouraging people from eating foods which contain high levels of environmental contaminants. In short, an inventory of the ways of performing socio-economic assessments of risk management options in the chemical food safety area, to serve policymakers in their decision-making, is urgently needed.

The aim of this project is to perform a strategic exploration to identify relevant methodologies, information and expertise related to socio-economic assessment (SEA), so that an SEA of the impact of chemical food safety policy can be performed. This exploration should lead to the development of an SEA to evaluate the impact of chemical food safety policies. This methodology should be applicable for all frameworks within the domain of chemical food safety.

The exploration started with a literature search focused on SEAs related to chemical food safety. Several articles described SEAs in relation to exposure to chemicals, however none of the SEAs were specific to the assessment of policy for chemical food safety. To explore ongoing initiatives in more detail a questionnaire was send out to international scientists and scientific agencies dealing with chemical food safety. Although several very enthusiastic responses were received about the project, none of the scientists were currently developing methodology or performing SEAs in the area of chemical food safety. Reference was made to already known adjacent initiatives in, for example, the area of air pollution, endocrine disrupting substances and the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) SEA. During the course of this project, the Organisation for Economic Co-operation and Development (OECD), in collaboration with the European

Chemical Agency (ECHA), hosted a workshop on the Socio-economic Impact Assessment of Chemicals Management aimed at identifying the current status of practice and methodologies for cost-benefit analyses of risk management measures and frameworks addressing the human health and environmental impact of chemicals in OECD Member Countries. The workshop focused on the methods currently used across jurisdictions and intergovernmental organisations, with the longer term goal of developing harmonised OECD methodologies for estimating the societal costs and benefits of managing chemicals. This workshop showed that, at international level, more and more attention is being given to the SEA of chemical legislation. This harmonisation of methodology on societal costs and benefits could be beneficial for the SEA in chemical food safety as well.

Within RIVM there are several different initiatives and experiences in SEA and SEA-like methods for different scientific and policy areas. In this project, the most adjacent types of SEA experiences available at RIVM are evaluated and used to develop a methodology/assessment strategy fit for an SEA within the area of chemical food safety. The Disability Adjusted Life Years (DALY) methodology used in microbiology assessment, the Dutch guidance for Social Cost Benefit Analysis (SCBA), the SEA for Genetically Modified Organisms (GMOs) and the SEA within REACH were selected. The DALY methodology focusses on the cost-utility analysis to compare policy options, where the Dutch SCBA guidance and the GMO guidance have their main focus on the cost-benefit analysis, although other assessment types are evaluated in the Dutch SCBA. Additionally, the Dutch SCBA guidance contains a detailed description of the total assessment strategy which is required independent from the assessment framework (e.g. problem analysis, starting scenario, stakeholder analysis, policy options, etc.). The REACH SEA guidance also contains a detailed description of the different steps of the assessment strategy where several frameworks are proposed in the guidance (e.g. cost-benefit, cost-effectiveness, break-even, etc.).

Experiences with SEA assessments within GMO and REACH indicated that SEAs should also consider risk perception and societal concern when the risk assessment is uncertain or ambiguous and when stakeholders are divided. The currently available SEA guidance focuses mainly on quantifiable impacts (which does not mean that qualitative impacts are ignored). There is a need for more detailed guidance on how to address complex, uncertain, ambiguous risks and societal concern of different stakeholders. The risk governance framework of the International Risk Governance Council (IRGC) provides valuable input that could be applied in current SEA guidance to address ambiguity and uncertainty about risks in/to society. Insights provided by the risk governance framework were used to develop an SEA fit for the area of chemical food safety.

The proposed framework, SEATS, has been developed in an iterative approach using the literature described previously, personal experiences in various SEA projects and applying the framework in the two case studies of this project. Although not worked out in full detail, the case studies show that SEATS can work in the area of chemical food safety and provide a transparent overview of the expected impacts of the

proposed policy measure which can be used as a basis for decision-making. Cases that address complex, uncertain or ambiguous risks are particularly likely to benefit from an SEA that addresses issues like social concern and risk perception, and involves stakeholders in the assessment set up (besides, or instead of, the more quantitative SEAs). SEATS therefore incorporates both the more quantitative SEA methods and the tools available to measure 'softer' aspects like social concern and risk perception by using the concept of risk governance of the IRGC.

It is recognised that SEATS incorporates many steps and that a substantial amount of input data and decisions are required to make a proper assessment. This is typical for an SEA, especially when SCBA is chosen as an assessment tool. However, there is also less data and resource intensive forms of SEA that exist and it is very important to decide what is proportional for the case at hand. Finally, at the moment, SEA has no basis in any chemical food safety legislation. Experiences from other fields show that a legal basis for SEA is very important for getting an SEA implemented in policy practice. It might even be a precondition for implementation and any further development of an SEA. A discussion among scientists, policy makers and other stakeholders in the field of chemical food safety is required if we want to get a better understanding of how and when an SEA could be helpful within this policy context. This is proposed as a potential next step of the project, as is the further testing of SEATS in more extensive case studies.

# Glossary

This glossary briefly defines the various terms used by the authors in this report. In most cases the definitions were adapted from those used in the REACH SEA Guidance documents for authorisation and restrictions.

**Business as usual scenario (BAU)**
Term that describes the 'business as usual' situation that is expected to continue in the foreseeable future in compliance with current legislation and if no additional action is taken. The business as usual scenario should take into account market and demographical trends for the foreseeable future.

**Break-Even Analysis (BEA)**
Type of analysis that identifies the break-even point between costs and benefits in a certain scenario. In impact assessments of chemical policies this type of analysis is sometimes used to calculate the minimal benefits (e.g. number of cancer cases) to offset the costs. This type of analysis is usually performed when the net benefits are unknown and the costs can be predicted.

**Cost Effectiveness Analysis (CEA)**
Type of analysis that relates the cost of a certain (policy) measure to some non-monetary parameter, for instance, the reduction of a certain emission that could be achieved with this measure. This type of analysis is usually performed to evaluate multiple policy measures in order to identify the measure that optimized the cost-effect ratio. It can be used to identify the least cost option among a set of alternative options that all achieve a pre-set target. In more complicated cases, it can be used to identify combinations of measures that will achieve the specified target.

Compared to the CBA, the advantage of the CEA is that there is no need for monetisation of the benefit of achieving the target but is disadvantaged where a specific level of abatement has/cannot been defined.

**Impact Assessment (IA)**
An assessment that evaluates all the possible effects – positive or negative of a (regulatory) change. Can be performed both quantitatively and qualitatively or mixed. The level of detail in which impacts are identified and described is not fixed.

**Multi-Criteria Analysis (MCA)**
A technique that involves assigning weights to criteria, and then scoring options in terms of how well they perform against those weighted criteria. Weighted scores are then added up, and can then be used to rank options.

In MCA, desirable objectives are specified and corresponding attributes or indicators are identified. The actual measurement of indicators is

often based on the quantitative analysis (through scoring, ranking and weighting) of a wide range of qualitative and quantitative impact categories and criteria. This need not be done in monetary terms. Different environmental and social indicators may be developed in parallel with economic costs and benefits and MCA provides techniques for comparing and ranking different outcomes, even though a variety of indictors are used. Explicit recognition is given to the fact that a variety of both monetary and non-monetary objectives may influence policy decisions.

**Policy Scenario (PS)**
Term that describes the situation that is expected to occur in the foreseeable future in compliance with the proposed regulatory measure. Only changes related to the proposed regulatory measure should be accounted for in the Policy Scenario.

**Social Cost-Benefit Analysis (SCBA)**
Analysis which quantifies, in monetary terms where possible, costs and benefits of a possible action, including items for which the market does not provide a satisfactory measure of economic value. The SCBA is based on welfare economics.

The nature of the analysis may range from one which is mainly qualitative to one which is fully quantitative (and monetised). In an SCBA, the trade-offs that society would be willing to make in the allocation of resources amongst competing demands are determined. As a result, a robust CBA can indicate whether or not a particular measure is ‘justified’ in the sense that the benefits to society outweigh the costs to society.

**Socio-Economic Assessment (SEA)**
The socio-economic assessment is a tool in REACH legislation used to evaluate what costs and benefits an action would create for society by comparing what would happen if this action was implemented and comparing this to the situation in which the action was not implemented. For proposed regulatory measures it is common to compare the net benefits to human health and the environment with the net costs to manufacturers, importers, downstream users, distributors, consumers and society as a whole.

**Socio-Economic Assessment of regulatory measures on Toxic Substances in food (SEATS)**
The framework proposed in this project to assess the impact on society of proposed regulatory measures on toxic substances in food.

# 1 Introduction

## 1.1 Introduction

The history of modern food safety legislation starts with the first Food Adulteration Act in Victorian England, in 1860 (Rowlinson 1982). Since then, food law has evolved into the sophisticated framework of legislation that now exists in most parts of the world to protect consumers. Loosely speaking, the legislation can be divided into regulations that address 1) food hygiene, aimed at reducing the number of foodborne pathogens, 2) substances that are present in food unintentionally e.g. by environmental contamination such as heavy metals, dioxins, or natural toxins like aflatoxin and 3) substances that are intentionally added to the food chain like food and feed additives, flavourings, veterinary drugs (as residues), pesticides (as residues).

Key to the set of regulations referring to 2 and 3 is the development of food safety standards which indicate the level of an unwanted substance that may be present in the food without raising concerns about safety. The magnitude of a food safety standard is determined by a comprehensive evaluation that is specific to the particular legal framework. Besides protecting the health of consumers, food standards serve a second goal. Over the last century, the amount of food traded internationally has grown exponentially. Internationally harmonised food standards ensure fair practices in the food trade.

Food safety standards are based on a quantitative risk assessment considering both hazard and exposure (in the EU usually prepared by the European Food Safety Authority EFSA). European regulations can be divided into two types; pre-market authorisation and no pre-market authorisation. If substances are deliberately added to a product, or are used in a way that raises suspicion about food contact, then the legislation requires a pre-market authorisation to be supplied by the producer or applicant. Examples are the residues of pesticides on food, substances in food contact materials or residues of veterinary medicines which can be expected in food. For such pre-market authorisation, the applicant should provide both toxicological hazard information and expected exposure information based on the intended use. Subsequently, a competent authority in an EU member state will evaluate this information and perform a risk assessment to identify whether there are any risks associated with the intended use. Only when no risk is expected may a pre-market authorisation be granted. For substances that occur naturally in food or that are included/formed during the processing of food, an authorisation process is not applicable. Food safety standards are set based on the ‘as low as reasonable achievable’ (ALARA) principle, where the exposure or usage (depending on the type of legislation) is kept as low as possible. Additionally, the toxicity of the food safety standard is assessed using the tolerable daily intake (TDI) indices which are based on the toxicological hazard profile of the substance and the consumption of the food item.

In Europe, most of the legislation in the food safety area is harmonised in the European Union (EU), which requires intense debate on the magnitude of food safety standards among 28 EU Member States. On top of that, the Codex Alimentarius Commission (CAC), established by the Food and Agricultural Organization (FAO) and the World Health Organization (WHO) in 1963 develops harmonised international (global) food standards, guidelines and codes of practice. The CAC does this in cooperation with 186 Codex Members – 185 Member Countries and 1 Member Organisation, the EU. Most, if not all, EU Member States are Codex Members. This means that national policymakers have to take part in a complicated network of decision-making committees. The final decision on food safety standards is a policy-decision in most cases driven by risk, however, other factors may also play a role, such as economic considerations (e.g. impact on production of food, availability of substances for food production) or societal concern (e.g. impact on food availability and costs for populations). CAC, The European Commission and EU Member States do not explicitly mention these other factors in the final decision. It should be noted that, although food standards are fixed values in legislation, there is always uncertainty around the chosen magnitude due to data gaps, limitations of current risk assessment methodologies and, on some occasions, ambiguity of the toxicity of substances.

On the other side, consumers are more and more aware and concerned about chemicals in their food. Although food in Europe is, in general, safe, there are a lot of organisations claiming possible adverse health effects for consumers caused by certain chemicals in food (e.g. PAN Europe). Scientific conclusions are sometimes contradictory or ambiguous, this results in contradictory advice being provided by different EU member states or governmental organisations (See Textbox 1).

*Textbox 1: Contradictory advice from different EU governmental organisations. The example of glyphosate*

Glyphosate: Recently, the herbicide glyphosate was evaluated for its potential human carcinogenicity by two agencies: the *International Agency for Research of Cancer* (IARC), associated with the World Health Organisation (WHO) and the *European Food Safety Authority* (EFSA) of the European Union.

While IARC classified glyphosate in class 2A “probably carcinogenic to humans”, EFSA did not consider it as representing a carcinogenic risk.

This difference in classification initiated a public debate among scientists and between the agencies.

Media attention amplifies these differences and consumer organisations demand stricter regulation on chemicals in food products, in many cases with reference to the ‘precautionary principle’. This may lead to precautionary measures being adopted, or to a withdrawal of the substances by industry which may be associated with high costs for food producers and other involved stakeholders, with inherent consequences for food prices. One might ask whether the risk perspective is still

realistic, for example, as described in detail in ‘Our food, our health’ (van Kreijl, Knaap et al. 2006).

Finally, taking food safety measures is a policy decision, policy makers, therefore, need to carefully weigh the arguments for setting food safety standards. Socioeconomic analysis of regulating chemicals in food is of growing interest to policymakers. There is currently little or no experience within policy makers in the EU (and within RIVM) in assessing the costs of possible risk management options e.g. lowering a legal product limit (such as the Maximum Residue Limit (MRL)), banning a regulated substance from the market or discouraging people from eating foods containing high levels of environmental contaminants. However, before implementing such measures, it would be wise to understand the associated social-economic costs and benefits associated with potential policy measures and incorporate this information into the decision-making process on the proposed measure. In short, an inventory of the ways of performing a socio-economic assessment (SEA) of risk management options in the (chemical) food safety area is urgently needed. A framework for socio-economic assessment in food safety management can help to transparently incorporate a wider knowledge base into decision-making.

A new development that might benefit from a socio-economic assessment framework for food safety is the current interest on ‘cumulative risk assessment’ or ‘mixture toxicity’, and ‘aggregate exposure’ to chemicals. The underlying idea is that as humans are exposed to more than one chemical within the same timeframe, or to one chemical via different exposure routes, the effects may accumulate. The risk assessment methodology is currently being developed to address this issue (EFSA and the EUROMIX project) particularly in the area of exposure to pesticides. Once implemented, this cumulative risk methodology could require risk managers to decide which substance from a group of chemicals needs to be banned. This is a new aspect to the current decision-making process. Developing new decision support frameworks, such as a socio-economic assessment, to assist decision-making of this type is, therefore, of importance.

At present, there is no framework available to perform a socio-economic assessment in the field of food safety standards and/or measures. Meanwhile, the need to develop such an assessment increases. At RIVM, there is expertise on developing socio-economic frameworks within the chemicals legislation for industrial chemicals REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) and in the area of microbiological food safety (Quantitative Microbiological Risk Assessment QMRA). In addition, work relevant to the current proposal was done in research projects which attempted to balance food safety risks against nutritional benefits (e.g. risk benefits from nitrate in vegetables (EFSA 2008)) and extensive expertise on health economics is available in the context of health care. Integrating and building upon existing knowledge will provide an initial approach to developing a socio-economic assessment in the food safety area.

## 1.2 Aim

The aim of the project is to make a strategic exploration of relevant frameworks/methodologies and functionalities for socio-economic assessment (SEA), and information and expertise to perform an SEA for food safety standards. This exploration should finally lead to the development of an approach for an SEA to evaluate the impacts of food safety standard policies. This SEA assessment framework should be applicable to all legislative frameworks within the chemical foods safety domain and could be used by food risk assessors and SEA experts to inform the decisions of policy makers.

# 2 Project approach and methodology

The project consisted of five phases, each one with the objective of contributing to the overall aim. In phase one, the general components for an SEA are explored and set for the context of this project. In phase two, SEA assessment frameworks, methodologies and experiences currently available which are specific to chemical food safety are collated from literature and international experts. Experiences currently available in adjacent regulatory fields within RIVM are collected. In phase three, an assessment framework is developed based on the defined criteria and methodologies available. In phase four, the approach is applied in two case studies, one on a pesticide (representing a substance intentionally added to the food chain), and a second on lead (representing an environmental contaminant). The intention of these case studies is not to perform an SEA that can be used for actual policy decisions, but to briefly test the proposed assessment framework. In the last phase, the assessment framework is evaluated and conclusions are drawn.

# 3 General requirements for an SEA applicable to the food safety domain

The European General Food Law (Regulation EC 178/2002) states that our food should be safe. The safety of our food is, among other factors, determined by the chemical content. Some substances are natural or occur in food unintentionally (for example, natural toxins or heavy metals), other substances are deliberately added to the food(chain) or are the result of human processing or human activity (for example, pesticides or contaminants which form during processing of the food). Based on the above difference, the European regulations can be divided into two types: pre-market authorisation and no pre-market authorisation requirement (see Table 1). In none of the Regulations is reference made to socio-economic assessments forming any part of the regulatory underpinning.

*Table 1: European food safety regulations subdivided by pre-market requirement.*

| **Regulation name** | **Number** |
|---|---|
| *Pre-market authorisation required* | |
| Food additive Regulation | EC 1332/2008, EC 1333/2008 and EC 1334/2008, for food additives, flavours and food enzymes. |
| Food contact materials | EC 1935/2004 and EC 10/2011 |
| Veterinary medicines | EC 37/2010 and EC 470/2009 |
| Feed additives | EC 1831/2003 |
| Plant protection products | EC 1107/2009 and EC 396/2005 |
| Biocides | EC 528/2012 |
| *No pre-market authorisation required* | |
| Contaminant Regulation for natural toxins and contaminants | EEC 315/93, EC 1881/2006 and EC 853/2004 |
| Feed contaminant Regulation | 2002/32/EC |

The main aim of this project is to develop an approach for socio-economic assessment to be used to underpin policy decision-making within the area of chemical food safety. The assessment framework should be applicable to the whole spectrum of food safety regulation. Socio-economic evaluations are particularly helpful in cases where policy decisions based on the standard toxicological risk assessment are not sufficient, and other arguments like social concern and economic impact play an important role.

Currently, decisions on food safety standards (e.g. MRLs) are based on the ‘as low as reasonable achievable’ (ALARA) principle, where the exposure or usage (depending on the type of legislation) is kept as low as possible. The toxicity of the food safety standard is tested by quantitative toxicological risk assessment. However, in some cases the final food safety measure is questioned. This can be the case when there is a (large) economic impact on specific stakeholders within Europe. The food safety measure can also be questioned when there is concern by actors in society about the proposed limit value. Known issues in

toxicology like combination toxicology, endocrine disruption and the applicability of animal toxicity studies to humans can create ambiguity among the stakeholders about the appropriateness of the limit value. Finally, there are situations in which there is no safe limit (non-threshold effects) value for a chemical present in food products. In these cases, socio-economic assessments (besides risk assessments) can be useful to provide the information needed to assess the various impacts on the stakeholders and make well-informed policy decisions.

The purpose of an SEA is to describe the impacts of a policy measure in various domains, e.g. society, health, environment and the economy. These impacts may be positive or negative for society as a whole. Usually, an SEA is constructed in such way that the net effect (positive or negative) of a policy measure, considering the impact it has in all domains, for society as a whole is estimated. Another purpose of an SEA might be to provide insight into the distribution of the impacts within society.

The exact content of the SEA framework is explored later during the project phases, although it can be stated, at this point, that the socio-economic assessment might include the following parts in general:

- Impacts of a granted or refused/lowered food safety standard on the benefits for human health and the environment. Including the distribution of these benefits (for example, geographically among specific subpopulations).
- Impact of a granted or refused/lowered food safety standard on the applicant(s)/industry.
- The impact on all other actors in the supply chain, downstream users and associated businesses in terms of commercial consequences such as impact on investment, research and development, innovation, one-off and operating costs (e.g. compliance, transitional arrangements, changes to existing processes, reporting and monitoring systems, installation of new technology, etc.) taking into account general trends in the market and technology.
- Impacts of a granted or refused/lowered food safety standard on consumers. For example, product prices, changes in composition or quality or performance of products, availability of products, consumer choice.
- Social implications of a granted or refused/lowered food safety standard. For example, food availability, job security and employment.
- Wider implications on trade, competition and economic development of a granted or refused/lowered food safety standard. This may include consideration of local, regional, national or international aspects.
- Changes in societal perception of food safety (worries of consumers, risk perception by consumers, retailers and NGOs) Availability, suitability and technical feasibility of alternative substances and/or technologies. Information on the rates of, and potential for, technological change in the affected sector(s).

# 4 Literature review, questionnaire and workshop

As a starting point of the project, a literature search of published literature was performed, a questionnaire was distributed to obtain information on useful assessment frameworks/methodologies, experiences and good practices from (inter)national scientists, and a workshop was attended on socio-economic assessments for chemicals management organised by the OECD.

## 4.1 Literature review

### 4.1.1 *Search strategy*

A literature review was performed using the databases Medline and Scopus. Because SEAs can be used for a variety of different subjects, the scope of the search strategy was limited to assessments that relate to chemical food safety.

*Table 2: Search words in the literature search strategy:*

| | |
|---|---|
| 1 | Pesticides, herbicide, insecticide, fungicide, rodenticide, biocide, plant protection products, insect repellents, pesticide residues, food contact materials, additives, food additives, food preservatives, feed additives, flavours, food enzymes, stabilizers, food packaging materials, veterinary medicines, veterinary drugs, drug residues, antimicrobial residues, natural toxins, feed contaminants, food contaminants |
| 2 | Policy standards, limits, measures, valuation and risk, food safety standards, residue limit, migration limit, allowable concentration |
| 3 | Cost benefit, benefit-cost, cost beneficial, cost effect, cost utility, cost efficiency, pharmacoeconomic, economic evaluation, economical evaluation, economic analysis, socio-economic, societal costs, multicriteria, health impact, impact assessment, public health evaluation, risk benefit |

The search was limited to 1950 to the present (18 January 2016), and to the languages English and Dutch, duplicates were removed. Details of the search strategy are available in Appendix 1.

### 4.1.2 *Results of search*

Twenty- three relevant articles came up from the Medline search, and 20 from the Scopus search. Based on the title and abstract of the Medline search, ten articles were deemed relevant and were downloaded and further investigated (Zilberman, Schmitz et al. 1991; Vasanthi and Bhat 1998; Wu 2006; Khlangwiset and Wu 2010; Anonymous 2012; Osteen and Fernandez-Cornejo 2013; Te Beest, Paveley et al. 2013; Ackerman, Whited et al. 2014; Tago, Andersson et al. 2014; van Eerdt, Spruijt et al. 2014). From the Scopus search, seven articles were deemed relevant and further investigated (Gren 1994; Zilberman and Millock 1997; Archer and Shogren 2001; Templeton and Jamora 2010; Jacquet, Butault et al. 2011; Wu, Bui-Klimke et al. 2014; Xiong and Beghin 2014).

#### 4.1.3 *Useful elements in information from literature*

The relevant articles provided some information about the economic implications of general pesticide bans, or the economic implications of mycotoxin contamination. One article described the health effect of pesticides for users, relatives of users and consumers (Tago, Andersson et al. 2014). None of the articles found in Medline or Scopus specifically described a methodology or a case in which a socio-economic, risk-benefit or equivalent assessment was performed in relation to chemical food safety. Therefore, the found literature was not used for the development of proposed SEA methodology in the area of food safety. Some elements in the found literature were used in the case studies.

## 4.2 Questionnaire

A questionnaire was sent to scientists working in the area of chemical food safety in order to obtain information on methodologies, experiences and good practices of SEA in the field of chemical food safety. The questionnaire was send to 41 (inter)national scientists from 21 different organisations all over the world (Europe, USA, Canada, Australia, WHO, OECD, FAO, etc.) and was focussed on acquiring information about possible initiatives in this area in their country. Details about the questionnaire can be found in Appendix 2.

None of the responses described an applicable assessment framework or any initiatives in which socio-economic assessment was performed in the area of policy measures for toxic substances on food. The literature and responses to the questionnaire described initiatives in the area of microbiology, social sciences, air pollution, environmental pollution without a connection to food production, endocrine disrupting substances, and REACH related initiatives.

*Email received from US EPA*

One email contained details of an initiative from the US EPA who were planning to include non-chemical stressors in the risk assessment process and, in this way, preclude the need to modify or change the risk assessment process. In this initiative, the risk assessment is considered to be the analytical – and quantified, evaluation of dose response and exposure to the stressors of concern. The idea that a socio-economic stressors can be a dose-response modifier to a regulated stressor is the approach that is considered to be most constructive. However, this still presents one with the problem of gathering sufficient data to quantify the dose-response. This is thought to be a better fit for risk assessment than to consider the non-chemical stressors as totally separate stressors – since these are not regulated. If the stressor (e.g. poor diet or poor access to health care) cannot be demonstrated to have a common mechanism of toxicological action as that of regulated chemical stressors (pollutants, etc.), then it is not considered in the risk assessment.

Following this line of thinking, the non-chemical stressors could be considered in the context of a different sort of assessment, such as, for example, Cumulative Impact Assessments or Health Impact Assessments. The results of such a study could then be included in the risk management phase.

The basic idea is to protect the quantitative rigour of the risk assessment, but provide an alternative means of introducing qualitative (or non-toxicological) information into the risk management decision-making process. Unfortunately, this concept has not yet been worked out thoroughly and publications are not available. This concept, therefore, will not be discussed further.

4.2.1 *Useful elements in information received from questionnaire*

Based on the responses from the questionnaire, it can be concluded that no specific methodology or attempts to perform a socio-economic assessment for regulatory measures for toxic substances in food is currently available. Literature was suggested in the area of microbiology, social sciences, air pollution, environmental pollution without a connection to food production, endocrine disrupting substances and REACH related initiatives. Most of the suggested literature and experiences were already available from experts within RIVM. The provided information which was not already available within RIVM was not directly used to develop the proposed assessment framework for an SEA in the area of toxic substances in food, since it was concluded that this literature was not directly relevant to the project. An overview of the provided information is available in Appendix 2.

## 4.3 OECD workshop – Socio-economic Impact Assessment of Chemicals Management

The OECD (Organisation for Economic Co-operation and Development) and ECHA (European Chemicals Agency) hosted a workshop on the socio-economic impact assessment of chemicals management on 6, 7 and 8 of July 2016 (OECD 2016). The workshop aimed to identify the current status of practice and methodologies for cost-benefit analysis of risk management measures and frameworks addressing human health and the environmental impacts of chemicals. Some points were raised during the workshop about how cost-benefit analysis could be improved more generally, namely, that there needs to be clear legislative requirements in place and clear and uniform rules governing decision-making.

Furthermore it was concluded that lack of information and methodological gaps could create asymmetry in the obtained results. The limitations and uncertainties should, therefore, be carefully considered. There is also a need to improve approaches to dealing with unknown costs and for a consideration of other components of socio-economic analysis that could improve the equity of the distribution of benefits and costs. Finally further work on the valuation of health and environmental impacts was recommended.

# 5 SEA assessments which could be used as basis for the assessment framework

In this chapter, an overview and evaluation was made of the SEA assessments from adjacent risk assessment areas that are currently used within RIVM. The strengths and weaknesses of the described assessment are defined and whether the described assessments are useful for the socio-economic assessment of regulatory measures on toxic substances in food is evaluated.

## 5.1 Assessments used within RIVM working practices

### 5.1.1 *Microbiology Disability Adjusted Life Years (DALY) assessment*

The aim of this assessment is to select the measure which is most cost-effective in terms of costs per unit of reduced human disease burden. It is occasionally used in the field of microbiological food safety.

*General description of the assessment method*

In the field of microbiological food safety, the changes are ideally made in the food chain to reduce exposure, the reduced exposure is then modelled. The output of the model is the frequency with which a consumer is exposed to a pathogen dose and the size of the dose (which is variable). The food chain consists of the production farm, the slaughterhouse, retail and the consumer phase. Exposure assessment is followed by dose response modelling, where output is the number of cases of illness. This biological part is usually the only part considered. In exceptional cases, the analysis is carried out further to include social and economic aspects. One such case is the CARMA project (Risk assessment of Campylobacter in the Netherlands via broiler meat and other routes) whose main results were published around 2007 (Havelaar, Mangen et al. 2007). This project focused on chicken meat and the pathogen Campylobacter. The structure of the CARMA project is illustrated below in Figure 1.

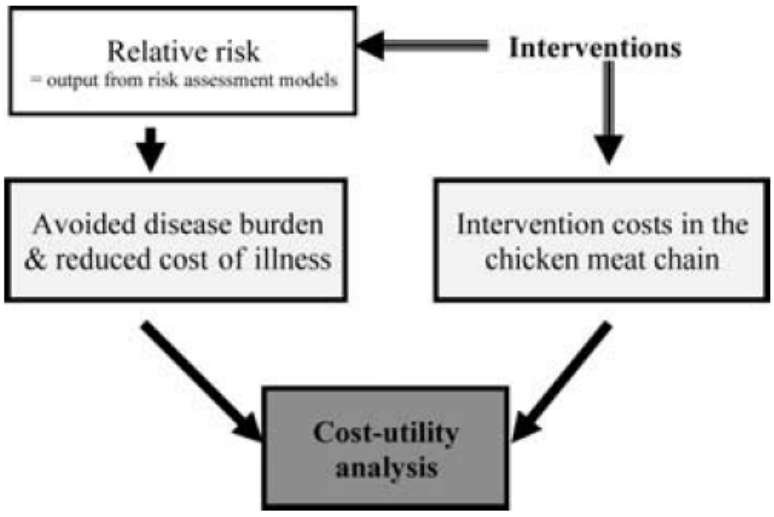



*Figure 1: The different steps within the economic evaluation.*

The idea was to perform a cost-utility analysis of potential interventions. An intervention leads to a reduction of the relative risk, the output of the microbiological risk assessment model. This is directly related to a reduced human disease burden in disability adjusted life years (DALYs) (Z) and reduced cost of human illness (W), while direct intervention costs (investments and variable costs) (K) are necessary for the intervention. The cost-utility ratio (CUR) is shown in Equation 1.

*Equation 1:* $$CUR = \frac{K - W}{Z}$$

The DALY calculations include the mortality and the disability burden of Campylobacter-associated gastro-enteritis cases, reactive arthritis, Guillain-Barré syndrome and inflammatory bowel disease.

The cost of human illness includes direct health-care costs (doctor consultations, hospitalisation, drugs, rehabilitation and other medical services), direct non-health-care costs (travel costs of patients and any related payments made by patients for costs, such as informal care) and productivity losses from missed work (as a consequence of temporary absence, disability and premature mortality and third persons taking care of patients).

The direct intervention costs are estimated as annual total costs, which are comprised of the estimated annuity of non-recurrent costs and the annual recurrent costs. The non-recurrent costs are purchase costs for the required technology, plus the installation and reorganisation costs. Recurrent costs are the annual maintenance costs plus activity- and volume-dependent costs that would recur with each application of an intervention. Figure 2 below shows an example of the results for a number of proposed interventions.

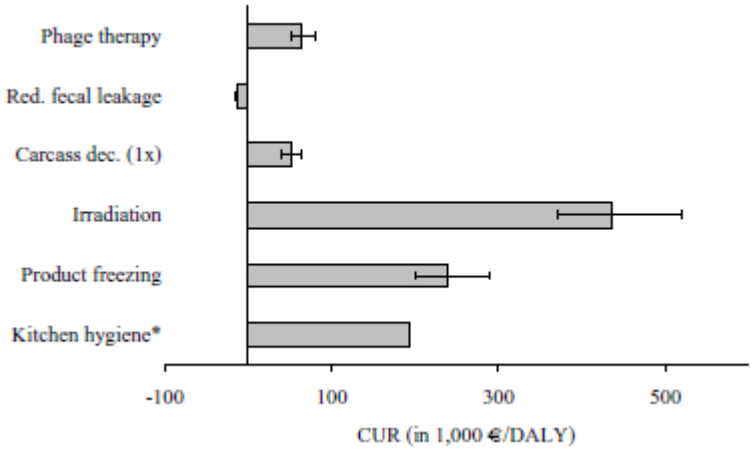



*Figure 2: An example of the CUR for a number of proposed interventions to limit Campylobacter infections from chicken meat.*

*Pros and cons of the assessment method*

The advantage of the method is that it produces an objective criterion to select the most efficient intervention to reduce the public health burden. A general problem of the method is its uncertainties and data gaps. Most data gaps concern the impact pathway from Campylobacter

contamination to illness, such as the incidence of Campylobacteriosis cases, the attributable fraction of this to chicken meat and the reduction of Campylobacter on chicken meat during the production and preparation process. There is also no detailed information available about trade flows (import and export of chickens and chicken meat) and the potential costs of some interventions.

5.1.2 *Dutch General Guidance Social Cost-Benefit Analysis (SCBA)*

A Social Cost-Benefit Analysis (SCBA) is a systematic inventory of all the costs and benefits to society of a policy measure, compared to doing nothing or taking another measure. The SCBA uses a broad perspective which involves the systematic identification and valuation (in monetary terms) of all the consequences (advantages and disadvantages). Currently, various SCBAs are being performed within RIVM in the areas of alcohol, drugs and toxoplasmosis.

*General description of the assessment method*

An SCBA is a systematic method of valuing the impact of (policy) measures. When performing an SCBA, the costs and benefits of all the parties involved are added together to form the net welfare effect for the society as a whole. This net welfare effect can either be positive or negative. In case of a positive net welfare effect, society as a whole benefits from the proposed measure. In contrast, a negative welfare effects means society as a whole is better off without the proposed measure. Following the Dutch Guideline SCBA (Romijn and Renes 2013), the research strategy is structured into eight steps (see Figure 3).

The necessary data is taken from existing reports, databases and literature. An SCBA is unlike many other forms of economic evaluation because it is not only the costs but also the benefits that are expressed in euros. In this way, the benefits can be directly compared with the costs. This also brings the effectiveness of measures into view. A measure which costs a little more, but has many more benefits will increase net welfare.

Step 1: Scoping the problem

The main aim of this step is to describe the state of affairs of the current regulatory policies in the Netherlands related to the problem.

Step 2: Defining the reference scenario based on current policies

Defining the reference scenario is an important step as the scenario with the new measures will be compared to it in order to determine the impact of these new measures. The reference scenario, therefore, describes the current state of affairs and how this is likely to develop, including expected changes (trends) in the future.


*Figure 3: Research steps of a Social Cost Benefit Analysis (adapted from Romijn and Renes 2013)*

Step 3: Defining the alternative scenario under the new policies
In this phase solutions are formulated for the policy issue (problem or opportunity). Concrete policy alternatives (measures, investments) based on these solutions are determined which will be integrated into the SCBA.

Step 4 and 5: Define and value the benefits and costs of the alternative scenario vis à vis the reference scenario
In these steps, the economic costs of implementing and maintaining new measures are assessed in relation to the reference scenario. First, the extent to which the measures will impact production and consumption is assessed. The impact of the measure is translated into the positive and negative consequences that may stem from the new measures and we take the step of assigning a monetary value (in euros) to the cost and the benefits of the various stakeholders relative to the reference scenario. Standard unit costs, e.g. for health economic valuations (Zorginstituut_Nederland-2 2015) are used as much as possible. Another source of information for cost estimates is the 'Werkwijzer MKBA in het sociaal domein', a guideline detailing methods and unit prices for SCBAs in the social sector (Koopmans, Heyma et al. 2016b).

Step 6: Conduct sensitivity analyses to assess the robustness of outcomes
The main analysis conducted in Steps 4 and 5 is subjected to sensitivity analyses to assess the robustness of the study's outcomes in relation to the different assumptions made.

Step 7: Assess the present value of costs and benefits and their distribution amongst stakeholders
In this step, the net present value of all costs and benefits is computed for the appropriate base year. Costs and benefits are shown for each group of stakeholders. Costs and benefits can be reviewed over a time period. Some intangible costs and benefits cannot be easily converted into monetary terms.

Step 8: Present the outcomes
The outcomes of the main analysis and the sensitivity analyses are reported in agreement with the guideline for reporting economic evaluations in a transparent and replicable way (Husereau, Drummond et al. 2013). This is done for each of the measures under review and includes a list of the non-monetised costs and benefits.

The general guidance of the Netherlands Bureau for Economic Policy Analysis/Netherlands Environmental Assessment Agency (CPB/PBL) sets out the principles for SCBAs that apply to all policy (Romijn and Renes 2013). In addition to this general guidance, 'SEO economic research' developed a working method cost-benefit analysis in the social domain (Koopmans, Heyma et al. 2016a). This working method covers the areas of four ministries: The Ministry of Health, Welfare and Sport (VWS), the Ministry of Education, Culture and Science (OCW), the Ministry of Social Affairs and Employment (SZW) and the Ministry of Foreign Affairs (BZK). Together, these areas are designated as the social domain. The working method provides practical and more specific guidance for actual implementation of the general SCBA in the social domain.

The working method cost-benefit analysis in the social domain describes different assessment methodologies that can be used in an SEA. In Table 6, paragraph 7.3, some of these instruments are explained and complemented with this project teams' experiences.

*Pros and cons of the assessment method*
The most important pros of an SCBA are:

- All effects are expressed in the same unit (money). This make measures comparable with each other
- The methods used are based on welfare economics (scientifically justified)

An SCBA has also cons:

- The valuation of policy effects based on welfare economics is often not well recognized by policy makers and politic
- In is not always possible to express the effects in a monetary value
- A full SCBA requires a lot of information, assumptions and choices. As a consequence, an SCBA is often seen as a 'black box'
- The performance of an SCBA is relatively expensive

### 5.1.3 *SEA in industrial chemicals legislation (REACH)*

In the REACH legislation, the use of an SEA is obligatory in the authorisation process if risks cannot be adequately controlled, for instance, for substances without threshold limits (carcinogenic or Persistent, Bioaccumulative and Toxic (PBT) substances). In addition,

SEAs can be performed in restriction proposals that tackle substances which are of specific concern because of their health or environmental effects. Ideally, an SEA such as this has the form of a societal cost benefit analysis (CBA) which weighs the societal costs of substituting the use of a hazardous chemical with less hazardous alternatives, with the benefits to society of the human health/environmental effects of not using the hazardous chemical. Quantification of health and/or environmental effects is sometimes difficult due to lack of knowledge and a detailed societal CBA is therefore not always possible. In practice, other types of assessments (e.g. partial CBA, break-even analysis, cost effectiveness analysis) are also performed and used as SEAs if there is not enough data to perform a full CBA or if a full CBA is not deemed necessary for the case at hand.

Positive effects (or 'benefits') described in this context could, for example, be the prevention of skin sensitisation, cognitive impairment, fertility effects or cancer. In some of those cases, clinical cases can be attributed to the specific chemical of concern (such as in the case of contact dermatitis), in others, this data is not available. Usually, the potential health effects can only be estimated based on what is known from animal studies and it will not be possible to perform a quantitative health impact assessment in terms of a reduction in clinical cases; the only description of the benefit on the policy measure (e.g. the restriction) will then, for example, be an estimate of the risk reduction. The negative effects (or 'costs') of the policy measure under study are often expressed as the extra costs that industry would incur to change the production process and/or to pay for the use of a more expensive (drop-in) alternative substance. These costs could be borne by industry and passed on to consumers. The exact scope of the SEA in terms of baseline and policy scenarios, what impact categories to include and what time and geographical scale to apply, is very case specific.

*General description of the assessment method*
An SEA helps us to get a grasp of the socio-economic impacts of a proposed policy measure compared to the situation in which no action is taken. It is helpful in decision-making, showing the positive and negative impacts of the measure and with that, the proportionality of the measure for society as a whole. Figure 4 illustrates the general process of an SEA as defined within the REACH framework. As can be noted from Figure 4, performing an SEA is an iterative process.

In an SEA, the impacts of different scenarios (policy scenario [PS]) are described and compared to the baseline (Business As Usual scenario [BAU]). In REACH, the following types of impact categories are identified: *human health and environment; economic; social; wider economic impacts (trade, competition and economic development).* In principle, those impacts are described separately though included in one SEA chapter. When the SEA is performed (by a Member State, ECHA or industry), SEAC will evaluate the assessment and evaluates whether benefits of the proposed measure outweighs costs.

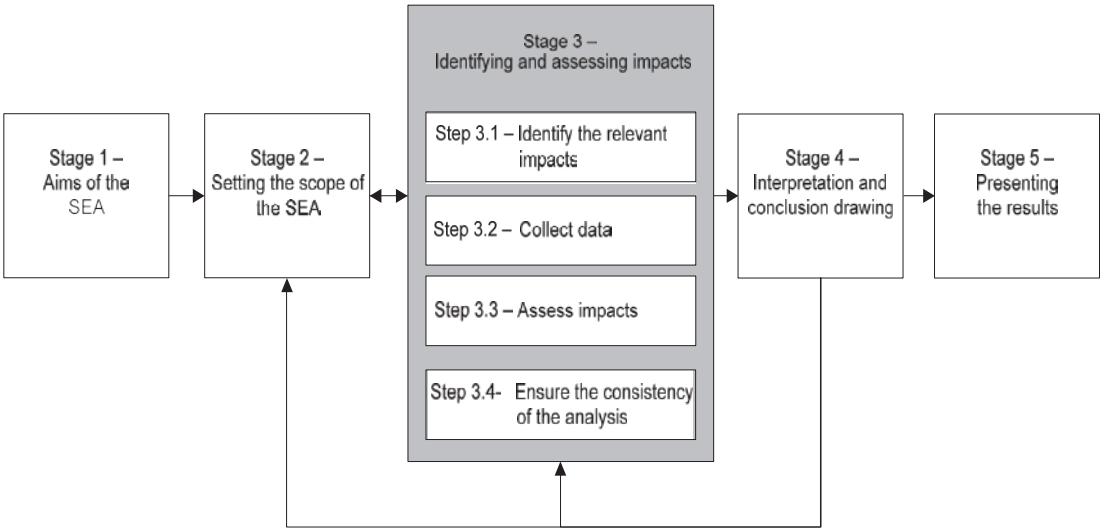



*Figure 4: General scheme of the SEA in restriction dossiers (ECHA 2008)*

In 2008, ECHA issued its technical guidance on how to prepare the SEA in restriction dossiers (ECHA 2008) and three years later a comparable guidance was published in regard to preparing SEAs in applications for authorisation (ECHA 2011). The aim is to answer the central question: 'What are the impacts of the 'proposed restriction' scenario compared to the 'baseline' scenario'? The general scheme for the identification and assessment of impacts, Stage three in the SEA, is depicted below in Table 3.

*Table 3: General scheme for the identification and assessment of impacts (ECHA 2008)*

| | |
|---|---|
| Identify the relevant impacts | - Create a list of impacts (ECHA has provided a general checklist)<br>- Screen the impacts and consider only the major ones |
| Collect data | - Conduct the analysis of impacts using a stepwise approach<br>- Focus on the differences in impacts between each scenario<br>- Try to reduce key uncertainties that may arise in the analysis when it is feasible to do so<br>- Avoid double counting an impact along the supply chain |
| Assess impacts | |
| Ensure the consistency of the analysis | - It's very important that all the assumptions that are made during the analysis are documented in a transparent way |

Ideally, all the relevant impacts indicated in the steps above should be quantified where suitable data sources exist and where such analysis is possible, practical and proportionate. Where possible, these impacts are expressed in monetary terms to enable easy comparison of the different impact categories. For example, the quantification and valuation of health impacts entail the prediction of the total health improvement, including morbidity and mortality, changes in health care costs (hospital costs, medicine etc.) and changes in production caused by sick leaves. It is possible to aggregate the health impacts, although this depends on

the quantification being carried out. However, in practice quantification and valuation is not always possible. There should be no bias towards impacts that are quantitatively described simply because it was possible to quantify them. There may be other impacts of greater importance that cannot be quantified for reasons of data availability. The ECHA Guidance on SEA for restrictions provides a more detailed description of the various steps and recommendations as well as a template for reporting an SEA (see Text box 2).

*Text box 2: Reporting template from ECHA Guidance on Socio-Economic Analysis – Restrictions (ECHA 2016).*

**1 The problem identified**
- 1.1 The hazard, exposure/emissions and risk
- 1.2 Justification for an EU-wide restriction measure
- 1.3 Baseline

**2 Impact assessment**
- 2.1 Introduction
- 2.2 Risk Management Options
- 2.3 Response to restriction scenario(s)
- 2.4 Economic impacts
- 2.5 Human health and environmental impacts
- 2.6 Other impacts
- 2.7 Practicability and monitorability
- 2.8 Proportionality to the risk (including comparison of options)

**3 Assumptions, uncertainties and sensitivities**

**4 Conclusion**

Annex A: Manufacture and uses
Annex B: Information on hazard, exposure/emissions and risk
Annex C: Justification for action on a Union-wide basis
Annex D: Baseline
Annex E: Impact Assessment
Annex F: Assumptions, uncertainties and sensitivities
Annex G: Stakeholder information

Usually, the results of the SEA will not be one aggregate number but rather a mixture of qualitative, semi-quantitative and quantitative information about the change in impacts of the proposed restriction or authorisation. Determining the level of quantification to be used is best achieved through an iterative process. Starting with a qualitative assessment of the impacts, further analysis is carried out in future iterations if this is necessary to produce adequate support for the decision-making. In some cases, a qualitative analysis will be sufficient to produce a robust conclusion and, in such a case, further quantification would not be necessary.

The process of developing and reviewing an SEA within REACH takes various steps: after the dossier submitter (member state, ECHA or industry) performs the SEA, it is scrutinized and reviewed by the scientific committee (SEAC) who develop an opinion on the matter that serves as input for the decision-making by the European Commission. In this process of scrutiny, interested parties have the opportunity to

respond to the SEA in one or two public consultations and make sure that all relevant information from other actors is taken on board in the evaluation.

*Pros and cons of the assessment method*
Judgement on the proportionality is often a complex process as the assessments and comparison of impacts are subject to uncertainties and assumptions. The SEA provides arguments for a case rather than proof. Great effort has been made in the recent years to investigate and compare different types of impacts, usually through some form of quantification and monetisation. Because of the assumptions and complexity of the calculation, the final number presented usually depicts a broad range instead of an exact figure. To enable the possibility of a balanced judgement to be made on the proportionality, a clear, structured description of the different impact assessments needs to be available. This description should focus on the scope and scenario setting, the expected impacts, the presentation of uncertainties and assumptions, and their influence on the results and conclusions. This transparency and clear structure of reporting appears to be essential for a good understanding of the results. This is especially important as the assessment is based on many steps, using many estimates and assumptions, to investigate various impact categories without using standard methods. Although some guidance is available for the assessment of the different impact categories in ECHA's guidance, in practice the method used largely depends on the case at hand and the data that is available. Because of this, the approach taken might lack in uniformity, although on the other hand, it appears to be useful in, and applicable to, a wide variety of cases. Furthermore, contributions from relevant actors and interested parties from the field is important especially in the more complex and ambiguous cases to make sure all relevant elements are covered.

In practise, the assessment mostly focusses on a cost benefit comparison of the quantitative economic and health impacts. This narrow view is often a consequence of data (un)availability and the latent impetus to present a quantitative analysis. The (wider) social impacts and a proportion of the health and/or environmental impacts are often not taken into account as information to get an understanding of these impacts is often lacking and the impacts are mostly of qualitative nature. Furthermore, people working on the SEA in REACH often have a background in chemistry or economics and tend to focus on these aspects. Assessors are often unfamiliar with the issues that could be addressed under (wider) social impacts. In case of environmental impacts, which are usually impossible to quantify and valuate, the approach taken usually involves some sort of cost-effectiveness analysis. Although quantification of impacts might be possible in some cases, practical experience of this is scarce.

Although some would argue that the SEA in REACH is far from comprehensive and scientific, it does initiate a scientific/policy debate about the proportionality of a proposed measure. The SEA is designed to try and identify the relevant information that needs to be taken into account by policy makers in the final decision-making, even when uncertainties and data gaps prevent a more scientific quantified analysis

and conclusion. Thus, performing an SEA is an attempt to underpin policy decisions on substances by widening the scope to beyond pure risk assessment.

5.1.4 *Framework for the socio-economic analysis of the cultivation of genetically modified crops*

The cultivation of genetically modified (GM) crops can have a number of socio-economic effects. For example, farmers using GM crops have seen effects on yields, pest management practices and gross margins. Socio-economic impacts can also be subject of political debates, which can influence the future development and adoption of GM crops.
The EU directive 2001/18/EC requires the European Commission to deliver an assessment of the socio-economic implications of GM cultivation. In 2015 the Joint Research Centre (JRC) Institute for Prospective Technological Studies developed a framework for the socio-economic analysis of the cultivation of genetically modified crops (Kathage, Gómez-Barbero et al. 2015).

This framework (described in the JRC reference documents) will enable a science-based assessment to be made of the socio-economic implications of the cultivation and use of GM crops in Member States across the EU. It is, therefore, purely an information gathering exercise and is not intended to serve any regulatory purpose.

Since April 2015 a new EU Directive 2015/412/EC is in force that enables the Member States to restrict or prohibit the cultivation of GM crops at national level. One of the grounds on which a national decision can be based is the socio-economic impact. This means that for GM crops the European authorisation, including a safety assessment, is separated from national decisions on cultivation based on other aspects, such as socio-economic impacts.

*General description of the assessment method*

Ensuring the quality of the assessment of the impacts of GM cultivation requires the use of a scientific approach, reliable methods and appropriate data sources. There are three main steps for performing the assessment. First, a definition of the scenarios that are to be compared is needed. One scenario includes cultivation (‘impact scenario’) of the GM crop/trait under study, while the second represents the situation without cultivation (‘baseline scenario’) of the GM crop/trait. Second, the value of the indicator(s) to be assessed must be estimated for each of the two scenarios. Third, the difference between the two values (‘impact’) is calculated.

This is particularly suitable when considering impacts on a single plot cultivated by a farmer (either the GM crop is grown on it, or not). However, assessments usually cover more than one plot (often whole regions, countries or groups of countries) and not only adopting farmers but also non-adopting farmers and non-farming groups (upstream and downstream industries as well as consumers). The impacts crucially depend on the (regional) adoption rate of the GM crop. Low or high adoption rates will have radically different impacts for most actors. Therefore, the impact scenario should always be described with reference to the actual or estimated adoption rates (between 0 and

100%). The baseline scenario will usually assume an adoption rate of 0% of the GM crop/trait under consideration, but positive adoption rates can be used, as long as these are lower than the ones applied in the impact scenario. A positive adoption rate in the baseline scenario can be useful if the GM crop/trait combination under study is already grown by some farmers, but the release of new events and/or cultivars is expected to further expand its adoption rate.

Defining the adoption rate under different scenarios can be approached in two ways. It can be estimated based on an explicit model (predictive), or it can be assumed in the absence of an explicit model (exploratory). In both cases, it is possible to employ varying assumptions to define multiple impact scenarios, which subsequently are assessed individually against the baseline scenario. The use of multiple impact scenarios can provide insight into the robustness of the results. A central question is how farmers and other stakeholders (e.g. upstream and downstream industries as well as consumers) behave under the impact and baseline scenarios. The adoption of a GM crop may lead farmers to choose different varieties or even different crops than the ones they would have grown in the absence of the GM crop, as well as modify their use of inputs and practices. Since only one scenario can be observed and the others are hypothetical, the most common approach is to compare adopters and non-adopters in the same area/region (Gomez-Barbero, Berbel et al. 2008), or to compare GM and non-GM plots within the same farm (Kathage and Qaim 2012). In both cases, the methodology should as much as possible control for the heterogeneity in environmental, economic and managerial characteristics among farmers and plots in order to avoid selection bias.

Assessing the effects of GM cultivation on upstream and downstream industries requires complex socio-economic models and a combination of primary and secondary data. Welfare economics provides tools for conducting such assessments. Aggregate analyses take into account effects such as the impacts of GM crop cultivation on regional and global supply and market prices, the effects on consumers (if prices change) and the effects on prices of agricultural inputs (e.g. seeds, pesticides) as well as on land and labour.

Analysis of the segregation between GM and non-GM products in the supply chain, from seed suppliers to retailers, requires integrated models with endogenous price mechanisms. These models need to determine, for instance, how the operators of the chain will react to the adoption of GM crops and the exploitation of the demand for non-GM food/feed (i.e. establishing identity preserved (IP) markets and price premiums on these products). Two main types of methodologies to elicit consumer preferences regarding GM/ non-GM products can be distinguished. Stated preferences are elicited in a hypothetical framework, resulting in the hypothetical willingness to pay (WTP). Revealed preferences are measured in real purchase situations, resulting in the actual WTP. Revealed preferences are more appropriate as they avoid socially desirable answers. Primary data from dedicated surveys are needed for this type of analysis.

*Pros and cons of the assessment method*

Methodologies have been developed by the scientific community for many of the topics and indicators (from simple partial budget analysis to complex aggregated models). However, the main constraint concerns the lack of data to conduct the analyses. Surveys of farmers, industry and consumers are necessary to assess the majority of topics. Fewer topics can be analysed by compiling secondary data from existing sources.

## 5.2 Description of useful elements in abovementioned frameworks

The DALY methodology used in the Microbiological Risk assessment modelling selects cost-effective measures to reduce the human disease burden. Using a cost-utility analysis such as this is a very informative methodology to compare different policy options. In the area of chemical food safety, cost-utility analyses could be applicable to compare different policy options and assess which option is most cost-effective, therefore the methodology used in the microbiological risk assessment is relevant for this project. Experiences in microbiology reveal general drawbacks which are also applicable to other types of socio-economic assessments, e.g. there can be significant uncertainties in the data, data gaps can exist. An advantage in the area of microbiological food safety is the availability of a dose-response between exposure and disease based on human data. For chemicals in food this correlation for humans is, in most cases, difficult to establish as only animal data is usually available.

The Dutch General Guidance Social Cost-Benefit Analysis provides a very useful systematic method for this project. Although the guidance is not specifically designed for the food safety area and focusses mainly on the social cost-benefit analysis (SCBA), the steps to come to the actual SCBA are uniform and can be used to develop a socio-economic assessment in the food safety area. The overview of the different assessment methods that can be used in an SEA is useful to differentiate between the various levels of scrutiny needed to support policy decisions.

The outline and the assessment steps in the socio-economic analysis in the cultivation of genetically modified crops is, to some extent comparable, although less detailed, with the steps as defined in the Dutch General Guidance of the SCBA. Some discussions in the GMO area regarding the relationship between agricultural GM crops and environmental effects and the intake of GMO crops and human health effects can be ambivalent, resulting in different consumer preferences of GM/non-GM products. Similarities also exist for chemicals in the food safety area. Currently however the framework for socio-economic assessment in the cultivation of GMO crops does not provide specific guidance on how to address the societal concern within the assessment methodology.

The industrial chemicals legislation REACH requires an SEA for hazardous substances that are in the process of being authorised or restricted. As REACH deals with chemicals and human exposure, the complete SEA methodology in the REACH legislation is useful for the area of chemical food safety. The toxicological dossiers and the risk

assessment methodology are, to some extent, comparable. Both REACH and the chemical food safety area generally evaluate risks based on animal toxicity data. Health impacts are quantified and monetised depending on the assessment strategy. Quantifying the health impacts of chemicals, in particular those based on animal toxicity data, is currently still a great challenge. The project team's experiences with the SEA within REACH revealed that SEAs could benefit from other factors besides the quantitative cost-benefit balance, e.g. considering the distribution of effects, economic feasibility, risk perception and societal concern if risk assessment is uncertain or ambiguous and stakeholders' perceptions are divided.

Based on the recognition that risk assessment can be uncertain or ambiguous, the project team decided to extend the focus to risk governance. In the next chapter this scientific area is further described and how it can aid in performing an SEA is discussed, especially in the context of chemical food safety.

# 6 Risk governance

## 6.1 Relationship between science and policy: a linear model of expertise

Traditionally, the relationship between science and policy is often (implicitly or explicitly) based upon linearity. The idea of such a linear model of expertise is that science produces facts (truth) that are used by policy makers to come to choices about policy actions. This is a linear and one-way process without much interaction between science and policy (see Figure 5).

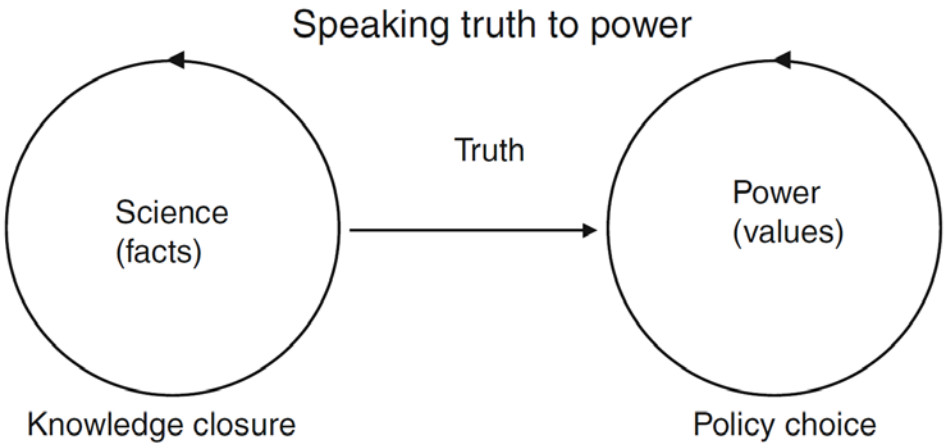



*Figure 5: Speaking truth to power (Jasanoff and Wynne 1998) adapted from Beck (2011)*

The way risk assessment and/or socio-economic analysis (SEA), as described in the previous paragraphs, is performed and implemented in policy making will often be based on traditional modernist approaches to knowledge production, which include the linear model of expertise, although not stated explicitly (see Box 2 for a discussion about modernist versus reflexive approaches).

Consequently, most of the abovementioned guidance primarily focus on various methods of determining the scientific parameters used to assess the net societal benefit between various scenarios. One of the underlying assumptions is the existence of an unambiguous net societal benefit and that more information (data) would lead to more certainly about the magnitude of this net societal benefit.

This linear model of expertise is based upon three propositions (Beck 2011):

1. More research will necessarily lead to more certainty.
2. More and better science will help to solve political disagreement.
3. By keeping problems away from the political 'whirl', science makes policies which are evidence-based and thus more rational

Using this linear model of expertise as a basis to approach simple risk problems and the resulting policy debates generally seems to work in practice, as discussion around such issues are often limited. However, there are also complicated risk problems and policy debates in which the above propositions appear not to be true and where the linear model appears to hamper the policy debate (e.g. climate adaptation as described by [(Beck 2011)). The scientific community, or other important stakeholders, might have different views on the causality or severity of assumed effects, or different views may exist on what facts are actually the most important for use as a basis for a policy decision which potentially leads to discussion and ambiguity. This should be strictly distinguished from political interference with the final conclusion.

*Text box 3: Modernist and reflexive approaches in knowledge production*

***The science of knowledge production***

Thinking about how knowledge is produced and the best way to produce it has been the subject of much debate recently. Some have suggested that there is a dichotomy between the 'old' way of producing knowledge (modernist approaches) and a new way (reflexive approaches), and that the latter is better suited to the demands of a changing society (the networking society) and its specific knowledge requirements (Gibbons, Nowotny et al. 1994; Nowotny, Scott et al. 2001; Shinn 2002).

The reflexive approach to scholarly work has constant interaction between theory and practice, between fundamental and applied knowledge, between various disciplines, and between scientists and non-scientists. It is not always clear whether the characterisation of the reflexive approach is a description of an actual change that has occurred or an appeal for such a change. Moreover, modernist approaches and reflexive approaches exist alongside each other and mixed forms are found as well.

| **Modernist** | **Reflexive** |
|---|---|
| Disciplinary | Interdisciplinary, or even trans-disciplinary (involving non-scientists) |
| University-based | In various institutions, think tanks, consultancies |
| Homogeneous | Heterogeneous |
| Linear model | Stakeholder model |
| Hierarchical | Horizontal |
| Theory-oriented | Application-oriented |
| Set procedures | Flexible and reflective |
| Classic peer review | New forms of quality control |

Instead of the rather closed science in the modernist approach, participation is an aspect of the 'new' way of producing knowledge in a reflexive mode. By allowing stakeholders to take part in research, one is making use of the many sources of knowledge present in the community. In this way, research is able to produce a more complete picture that is close to practice and is application-oriented. Participation also operates in this scenario as a new form of quality control.

It has to be born in mind that this more complex way of producing knowledge is not always necessary or desirable. A participative approach is more appropriate for complex issues, while a disciplinary approach may be perfectly adequate for more straightforward matters. In the context of this project, this means that, depending on the characteristics of the risk problem at hand, one could decide to differentiate in the approach taken to perform an SEA.

When developing a methodology to provide relevant scientific information basis for policy debates, it thus seems valuable to think about the relationship between science and policy and linked to that, look at what model of interaction would be appropriate for the context of the case at hand. This is especially true for the more complicated, uncertain and/or ambiguous policy issues that we might face in the context of chemical food safety.

Such cases would benefit from a more reflective approach of knowledge production (see Textbox 3), incorporating stakeholders in the process. In the next paragraph, this idea of a reflective assessment approach is

further explored by explaining the concept of Risk Governance introduced by the International Risk Governance Council (IRGC).

## 6.2 Risk governance as defined by the International Risk Governance Council (IRGC)

### 6.2.1 *IRGC framework*

In the search for a concept broader than the linear model of expertise, which is more widely applied than the reflexive mode of knowledge production, the value of the concept of risk governance introduced by the IRGC was investigated. The IRGC introduced a framework for risk governance that focussed on the interaction between a) the assessment sphere of science where knowledge is generated and b) the management sphere of policy makers where values are introduced, decisions are taken and actions are implemented (see Figure 6). It should be noted that the boundary between knowledge production and introduction of values in practice is often not very strict and explicit.

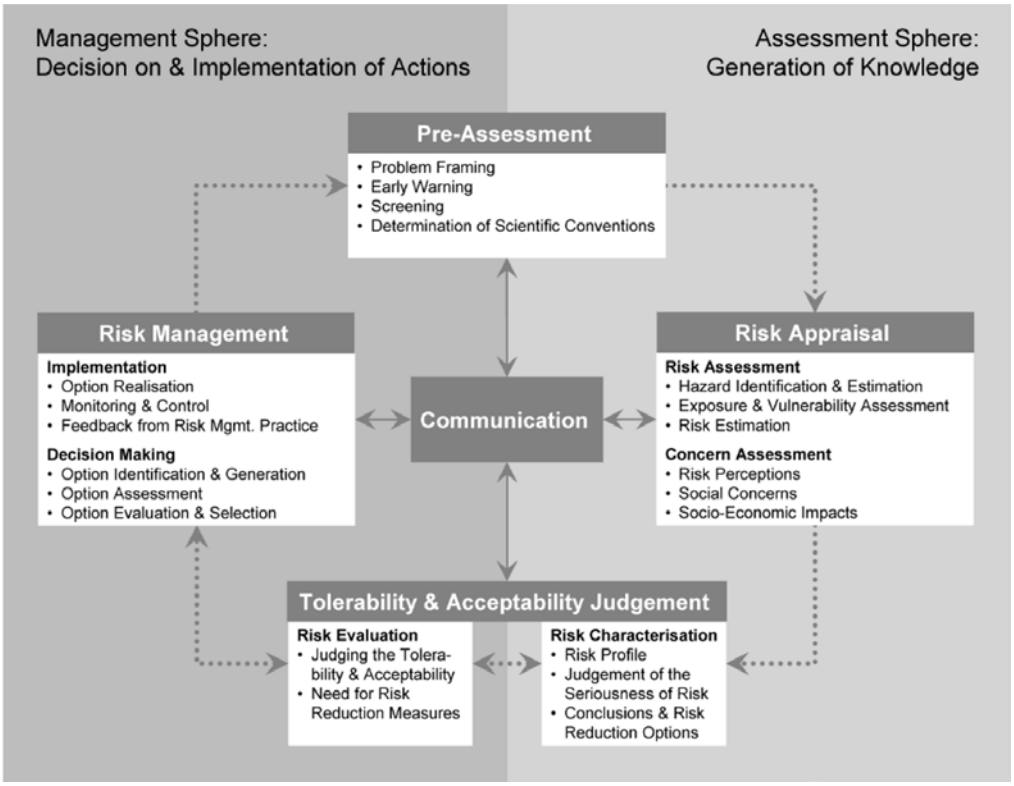



*Figure 6: IRCG Risk governance framework (International Risk Governance Council 2008)*

This framework consists of various steps:

1. A *pre-assessment* that is performed together by scientists, policy makers and other relevant stakeholders in which the problem is framed and categorised as a specific (dominant) risk type. It should be noted that this process of framing is very important as, to a large extent, it determines the further design of the process and, as various stakeholders can have very different viewpoints, it integrates interests, wishes, views, power and resources. It is

therefore very important to justify the choices made in the pre-assessment, including the choice of stakeholders involved.
2. The *risk appraisal* process performed by scientists that includes the risk assessment in which the hazard is identified, exposure and vulnerability is assessed and the risk is estimated. Followed by a concern assessment where risk perceptions, social concerns and socio-economic impacts are investigated. This concern assessment could provide insight that asks for a change to be made in the framing of the problem and the further analysis, for example, if the initial framing appears to be too narrow to incorporate concerns that are raised by various actors.
3. *Tolerability and acceptability judgement* that is ideally performed together by policy makers, scientists and potentially other stakeholders in which the information of risk appraisal is characterised and evaluated e.g. judging the tolerability and acceptability of the risk and the need for risk management.
4. *Risk management* that is predominantly performed by policy makers in which decisions on potential policy measures are taken and measures are implemented and monitored.
5. *Communication* between various actors that is relevant for the problem at hand. This involves scientists and policy makers, but could (and will often be) broader than that, involving other stakeholders as well. It should be noted that communication between various stakeholders can be designed in various ways (e.g. informing stakeholders versus giving stakeholders actual influence in the process).

A more extensive explanation of this risk governance framework can be found in the report by the International Risk Governance Council (2008). This framework was set up especially to deal with a novel type of so-called systemic risks. In its framework, the IRGC distinguishes various types of risk that can help to further design the risk governance process.

### 6.2.2 *Risk types*

According to the IRGC the following risk types can be distinguished: simple, complex, uncertain and ambiguous (see Table 4). Complexity, uncertainty and ambiguity are also somehow related. For example, complex situations are more likely to be faced with incomplete information and thus with uncertainty, whereas ambiguity might earlier occur in complex or uncertain situations. It might, therefore, not always be easy to define or propose the dominant risk type. Various actors, having various interests, wishes, views, power and resources, might also think differently about the dominant risk type of the problem at hand.

*Table 4: Risk characteristics and their implications for risk management (International Risk Governance Council 2008).*

| Knowledge Characterisation | Management Strategy | Appropriate Instruments | Stakeholder Participation |
|---|---|---|---|
| 1 'Simple' risk problems | *Routine-based:* | Applying 'traditional' decision-making | Instrumental discourse |
| | Tolerability/ acceptability judgement | ● Risk-benefit analysis<br>● Risk-risk trade-offs | |
| | Risk reduction | ● Trial and error<br>● Technical standards<br>● Economic incentives<br>● Education, labelling, information<br>● Voluntary agreements | |
| 2 Complexity-induced risk problems | *Risk-informed:* | Characterising the available evidence | Epistemological discourse |
| | Risk agent and causal chain | ● Expert consensus seeking tools:<br>*- Delphi or consensus conferencing*<br>*- Meta analysis*<br>*- Scenario construction, etc.*<br>● Results fed into routine operation | |
| | *Robustness-focused:* | Improving buffer capacity of risk target through: | |
| | Risk absorbing system | ● Additional safety factors<br>● Redundancy and diversity in designing safety devices<br>● Improving coping capacity<br>● Establishing high reliability organisations | |
| 3 Uncertainty-induced risk problems | *Precaution-based:* | Using hazard characteristics such as persistence, ubiquity etc. as proxies for risk estimates. Tools include: | Reflective discourse |
| | Risk agent | ● Containment<br>● ALARA (as low as reasonably achievable) and ALARP (as low as reasonable possible) | |

| Knowledge Characterisation | Management Strategy | Appropriate Instruments | Stakeholder Participation |
|---|---|---|---|
| | | ● BACT (best available control technology), etc. | |
| | *Resilience-focused* | Improving capability to cope with surprises | |
| | Risk absorbing system | ● Diversity of means to accomplish desired benefits<br>● Avoiding high vulnerability<br>● Allowing for flexible responses<br>● Preparedness for adaptation | |
| 4 Ambiguity-induced risk problem | *Discourse-based:* | Application of conflict resolution methods for reaching consensus or tolerance for risk evaluation results and management option selection<br>● Integration of stakeholder involvement in reaching closure<br>● Emphasis on communication and social discourse | Participative discourse |

The distinction between risk types should also not be seen as a very strict distinction but rather as a general orientation for the further assessment. The choice of a dominant risk type helps to further design the risk governance process. It can focus the questions to be asked to scientists in the risk appraisal process, it gives suggestions for the appropriate level of stakeholder involvement and the appropriate approach for risk management.

6.2.3 *Risk appraisal and risk management*

The IRGC states that *'when dealing with complex, uncertain and/or ambiguous risks it is essential to complement data on physical consequences with data on secondary impacts, including social responses to risks and insight in risk perception.'* This implies that simple risks could well be managed using traditional decision-making that is based upon modernist approaches including the linear model of expertise. Considering this, it could indicate that regular risk assessment and impact assessment could be used as a basis for regulatory decision-making. Cost-effectiveness and social cost-benefit assessments could be typical assessment methodologies to investigate societal impact of proposed policies as a basis for decision-making on preferred policy measures.

For complex risks traditional, modernist methods might be appropriate as the basis for risk management resulting in ‘risk-informed’ and ‘robustness-focused’ decisions. Assessment methodologies like cost-effectiveness and break-even analyses might be appropriate if no significant ambiguity surrounds the scientific input. However, complex risks often are also uncertain and/or ambiguous risks. According to the IGRC, uncertain risks are better managed using a reflexive approach such as a ‘precaution-based’ strategy, with the intention of ensuring the reversibility of critical decisions and to increase systems coping capacity. The idea is that the ‘true dimensions of the risks are not (yet) known’ and one should thus ‘pursue a cautious strategy that allows learning by restricted errors.’ This might imply that precautionary decisions are based on the available uncertain information and that decisions are not delayed for reasons of uncertainty. Uncertain risks benefit from a stepwise and flexible approach, with close interaction between risk managers and risk assessors, which allows the process to be changed should new information become available.

For ambiguous risk problems, modernist approaches, mainly focusing on the scientific underpinning of risks, do not appear give sufficient basis for decision-making. Insight into the differences in risk perceptions, ‘future visions, basic values and convictions, and the degree of confidence in the human ability to control and direct its own technological destiny’ is relevant as well. Ambiguous risks are best managed by a reflexive approach using a ‘discourse-based’ strategy that seeks to create tolerance and a mutual understanding of conflicting views and values. This implies that stakeholder analysis and stakeholder involvement are important elements in the regulatory decision-making process. The main challenge here is to organise a suitable discourse involving all relevant stakeholders.

#### 6.2.4 *Stakeholder involvement*

The IRGC explains that respectively simple, complex, uncertain and ambiguous risks would benefit from increased stakeholder involvement (see Table 3). Simple risks require relatively limited stakeholder involvement (indicated as ‘instrumental discourse’), while complex risk problems would benefit from an ‘epistemological discourse’ with the goal of involving all relevant experts and knowledge holders to resolve any cognitive conflict. Uncertain risk situations would benefit from even more stakeholder involvement involving policy makers, scientists and other relevant stakeholders to not only discuss the knowledge base but also the value various actors attach to it (so-called reflective discourse). Lastly, ambiguous risks require the most extensive stakeholder involvement aimed at developing consensus or obtaining insight into the variation in views that exist around the problem. With regard to simple and complex risks, stakeholder involvement tends to improve the evidence base of the problem, where stakeholder involvement in case of uncertain and ambiguous risks besides evidence base also tends to cope with values.

As the framing of the problem including the characterisation of the problem in type of risk largely influence the further process, it could be beneficial to incorporate stakeholders in this stage of the process to make sure the interests, wishes and views of various stakeholders have

been incorporated when framing the problem. Whether including stakeholders is accepted also depends on the ideas that the involved policy makers and/or scientists have of the roles and responsibilities of various actors.

## 6.3 The Dutch Scientific Council for Governmental Policy

In 2014, the Dutch scientific council for governmental policy ('Wetenschappelijke Raad voor het Regeringsbeleid' [WRR]) published an advisory report on an integrated approach for risk and safety issues in different policy dossiers of the Ministry of Infrastructure and Environment (WRR 2014). Several aspects in which risk issues can differ are described. In the first place, the risk issue differs between simple, complex, uncertain and ambiguous types of risk issues (as described by the IRGC). Secondly, several determinants of (perceived) safety are relevant in the societal and political debate:

- natural causes versus human actions
- (ir)reversibility of activity or damage
- extent of (un)voluntariness
- known and familiar versus intangible and daunting
- degree of controllability, potential for disaster and extent of societal disruption
- extent to which consequences are passed on to future generations (reprotoxic effects, future environment of our children)
- extent of justice (in relation to geographic, socioeconomic and demographic differences)

These so-called social psychological determinants of safety can be used when assessing policy issues and influence the level of acceptance of the risk issue by the public. Lastly, it is important to specify who or what could suffer from the damage and what can be done to prevent this. By specifying the 'who' or the 'what', the vulnerability or resilience comes into play, and the options that the potential victims have themselves to prevent or reduce the possible damage can be addressed.

In the WRR report several risk and safety policy dossiers, including plant protection products, are described and ten key questions are extracted that need to be addressed for a more consistent risk and safety policy. Table 5 addresses these key questions.

*Table 5: Overview of key questions from the WRR report and the case description for plant protection products (adapted from WRR 2014)*

| **Key questions from the WRR report** | **Description of the plant protection products case** |
|---|---|
| What is the case? Cause, public interest, nature and extent of the issue. | |
| *Is the public interest clear?* | Yes. The use of chemical plant protection products has not only advantages (production of affordable, good quality food; nice ornamental plants), but also poses risks for human health and the environment. |
| *What is the current state of knowledge about probabilities and possible effects?* | The opinions regarding potential risks are divided. The authorisation requirements are inevitably uncertain and, in addition, safety is not given sufficient priority by farmers. There is complexity regarding differences in susceptibility and |

| Key questions from the WRR report | Description of the plant protection products case |
|---|---|
| | exposure to multiple substances. The majority are of little concern; specific groups, such as people neighbouring agricultural pastures, environmental organisations and some scientists do have concerns. This is caused by the insidious character of the potential effects. Effects only show in the long-term and are difficult to trace back. |
| *Are the risk assessments scientific or socially disputed?* | Partially. There seems to be interpretative ambiguity. Scientists and other stakeholders, value the outcome or relevance of different studies or research methods very differently. In these diverging views various underlying value judgements (also between scientists from different disciplines) play a role. |
| *Which actors are involved in the hazardous activities and for which responsibilities can they be held to account?* | - Federal government: authorisation, regulation, enforcement, monitoring, policy development<br>- Local government: spatial planning, enforcement, complaint handling<br>- Industry: dossier build-up, information distribution, innovation<br>- Farmers: using hazardous substances, growing crops with hazardous substances<br>- Relevant organisations: information distribution, education, regulation, innovation<br>- Implementing parties: working in accordance with regulation, executing policy<br>- Civilians: purchasing behaviour, measures for own safety<br>- European Union: legal and regulatory framework for free movement of goods and services and for a high level of safety for civilians. |
| What kind of trade-offs have to be made? | |
| *Have the 'good possibilities' as well as the 'negative possibilities' been sufficiently assessed?* | Partially. Good possibilities are taken into account, whether this is sufficient, however, differs per actor.<br>- Good possibilities: a lot of affordable, good quality food, nice ornamental plants and economic benefits<br>- Negative possibilities: potential damage to human health, environment, resistance development (also cross-resistance to medicines). In addition, it suffers from complexity, uncertainty and ambiguity. |
| *What is the distribution of costs and benefits amongst the different actors, regions and in time, and is this justifiable?* | If the distribution of costs, benefits and risks is justifiable, it is harder to assess when the uncertainty increases as to whether the use of plant protections products actually causes damage, and if so, to what extent. Scientists have different views on the extent and the importance of this uncertainty. |
| *Are there dossier specific issues that require a customized approach?* | Yes. It is inherently difficult to assess whether problems would occur; potential problems can remain hidden for a long period of time. This calls for resilience: aim for integrated plant protection (already common policy), non-spraying zones and the use of (bio)monitoring as post-marketing surveillance. |
| Intervention and implementation | |
| *Are the policy interventions well justified and described?* | Yes, in principle. This involves the authorisation procedure, legal and regulatory framework for the applied use, information distribution and education, enforcement, enhanced integrated |

| Key questions from the WRR report | Description of the plant protection products case |
|---|---|
| | plant protection (chemicals as last resort) and monitoring. The current policy is based on a covenant between stakeholders. |
| *Is the communication strategy adequate?* | Partially. The common civilian, consumer and farmer have little concern, specific groups, such as people neighbouring agricultural pastures, environmental organisations and some scientists do have concerns. Until recently, communication was primarily focussed on reassurance and very little on transparency about uncertainties or improving personal guidance for action. That has created distrust. However, it seems this is changing. Participation of stakeholders in the whole policy cycle appears to be more accepted. This also applies for the plant protection regulation. |
| *Can members of the government publicly justify the policy and related considerations, even after damage has occurred or there have been human casualties?* | This question belongs in the political and public administration domain and hence can obviously not be answered by the advisory councils. |

## 6.4 Lessons learned from practice for our assessment framework

Insight into the relationship between science and policy makers is very valuable for understanding what the most appropriate way to approach a specific risk issue could be. In addition the risk governance framework of the IRGC provides valuable, more practical, input for using this insight in the development of our assessment framework. The differentiation between various risk types seems valuable for the contextual risk problems related to chemical food safety and the development of a framework for socio-economic assessment for that context as, in that context, there are also more complicated, uncertain and/or ambiguous risk problems expected. In this project, the IRGC framework and the various risks types are used as a tool to think about the most appropriate assessment method to apply to an SEA and the appropriate level of stakeholder involvement. The various dominant risk types are also meant as tool and should not be implemented too rigid. Furthermore, the risk appraisal process includes a concern assessment in which risk perception and social concerns are investigated together with the socio-economic impacts. This could be very relevant input for policy makers' decision-making, especially for the more complex, uncertain and/or ambiguous risk problems.

However, what is acceptable and implementable in the context of toxic substances in food also depends on the current situation in that context. As discussed in the introduction and Chapter 3, the issue of toxic substances in food relates to various (European) legislative regimes which all have their own specific characteristics. What seems to be in common, however, is that policymaking is currently mainly based upon risk assessment information provided by scientific experts (the modernist approach). Other information, like socio-economic factors or risk perceptions do not have a formal role in the decision-making process. Interaction between science and policy is currently rather linear

providing limited room for interaction between the two. Furthermore, there is currently no or limited formal stakeholder involvement in the process of the scientific underpinning of the problem and policy-making. The questionnaire to scientists in the area of chemical food safety also revealed that they have very limited experience with broader socio-economic assessment in this field.

### 6.4.1 *Implementation in proposed framework*

Our impression of the current situation of food safety management, prompts us to propose adding a limited number of new elements to the current practice. Proposing a full possible package of changes at once would, in our view, be too complicated and too ambitious in practice as it is too far away from current practice. The chance of successful implementation would probably be limited.

Therefore, most of our proposed framework for an SEA for the context of chemical food safety uses existing scientific methods and tools for an SEA. Lessons learnt in terms of the science – policy relation and interaction and stakeholder involvement are only incorporated into the framework in a limited way at this time for reasons described above and as the project team lacks in-depth knowledge about these topics. However, it will be included as one of the very relevant topics for further investigation and assessment in the future.

For the proposed framework, it means that we have included a sort of pre-assessment (Steps 1 and 2 of the IRGC framework) where the societal problem at hand is described based upon readily available information. This step also incorporates some kind of stakeholder analysis (and potentially stakeholder involvement) that would provide an initial impression of the problem framing by various actors. Based on that, the distinction in various risk types is then used to select the most relevant form of the further (scientific) assessment (in IRGC terms, the risk appraisal process). For the sake of simplicity, it was decided to only differentiate between two dominant risk types in the proposed framework instead of the four defined by the IRGC: (1) a category including simple risks and (2) a category including complex, uncertain and ambiguous risks. This will simplify the categorisation as such and would be sufficient for the further assessment process.

The simple risk type focusses on the risk and impact assessment with a linear model of expertise as major starting point. The complex/uncertain/ambiguous risk types involve more emphasis on an interpretation of evidence, values and moral principles. This includes insight into the various interests, wishes, views, differences in power and resources etc. of various stakeholders besides the evidence base. This can be considered as a reflexive approach where stakeholders' dialogues are more relevant.

# 7 SEA of regulatory measures on toxic substances in food (SEATS), a framework proposal

## 7.1 Introduction to SEATS

It was assumed, when starting to work with this framework, that some sort of SEA would have an added value for the case at hand. In this chapter, six main steps for a socio-economic evaluation of policy measures in the chemical food safety area are proposed. These six steps are based on, and developed from, the available literature described in the previous chapters and consist of:

1. Problem and context analysis
2. Identification of dominant risk type
3. Goal and scope definition of the assessment
4. Impact assessment
5. Uncertainty and sensitivity analysis
6. Interpretation and presentation of impacts

Each step will be further described in the following paragraphs. It should be noted that the framework here is presented as a linear stepwise approach, however, in practice performing an SEA will often be an iterative process back and forth through the framework depending on what comes up during the assessment.

## 7.2 Step 1: Problem and context analysis

This first step is based upon the information that is readily available without extensive research and aims to provide an initial overview of the situation at hand. This step is performed by the Assessment Team (Risk assessors and SEA experts), however, it could be beneficial to incorporate other actors in this step as well (for example, policy makers or other stakeholders when it comes to framing the problem, defining potentially relevant policy scenarios or when describing characteristics and positions of various stakeholders).

### 7.2.1 *Description of the current situation*

The following elements need to be considered:

a) Describe the reason(s) for starting the evaluation of the current limit value/accepted concentration:
   a. Concern on one of the following dimensions:
      i. (potential/perceived) environmental risk
      ii. (potential/perceived) human health risk
      iii. (potential/perceived) burden to (EU) economy
   b. Concern by one or more stakeholders
      i. Crop producers
      ii. Crop processors
      iii. Meat producers
      iv. Industry
      v. Retailers
      vi. Workers
      vii. Consumers
      viii. NGOs

ix. Public authorities/policy makers (Member states, EU commission)
x. Scientific community

b) Substance of concern
   a. Intentionally added substance: pesticide, biocide, food contact material, food additive, hormones, antibiotics, etc.
   b. Contaminant (heavy metals, natural toxins, dioxins, PAHs)
   c. Metabolites of intentionally added substance and/or contaminants
c) Use of focus of the substance: specific crop(s)/food product(s)/application of concern
d) Additional use/exposure to the substance: other relevant crops/food products, other relevant non-food exposure routes (relates to Acceptable Daily Intake [ADI] and other health based guidance values)
e) Relevant legislative regime and current regulatory situation: current limit value/(accepted) concentration
f) Investigation of relevant stakeholders (see 5.2.1a)
   a. In this investigation, one can consider individual actors and branch organisations, national and international (EU, world) actors. It includes at least the policy makers relevant for the case at hand and the assessors (scientific experts) of the case
   b. Here a description is given of the problem/risk perception of various relevant stakeholders. Furthermore, attention is given to the interests, wishes and views that stakeholders have of the problem and to the power and resources various stakeholders have.

7.2.2 *Description of potential policy scenarios*

The following scenarios could be considered:

a) Reduction (or change) of Maximum Residue Limit (MRL) or other residue value, specified for crop/food product/application and specific substance of concern. Realised via:
   a. Change in allowed use of the substance (e.g. concentration, frequency of use)
   b. Ban of the substance, replacement by an alternative substance (which results in destruction of batches/crops/food products that exceed the limit, stop import of crop/food products from countries that exceed the limit)
b) Reduction (or change) in allowed contamination level, crop/food product and substance specific
   a. Destruction of batches of crop/food products that exceed the limit
   b. Stop import of crop/food products (e.g. from specific countries/regions) that exceed the limit
   c. Processing of crop/food to reduce contamination level
   d. Abatement measures (excavation of top soil; restriction on fertilizer usage)
c) Measure related to ADI, substance specific
   a. Advice to (specific) population (groups) on food consumption of crops/products

## 7.3 Step 2: Identification of dominant risk type

Based on the information collected in Step 1, the Assessment Team will select a dominant risk type that is thought to best suit the case at hand. Two different categories can be distinguished (based on the IRGC framework):
(1) simple risk and
(2) complex, uncertain or ambiguous risks.
Cases that appear to be quite straightforward in terms of the scientific underpinning of the problem and that appear not to show substantial differences in problem perception among the various stakeholders would fall into Category 1. Cases that are more complicated and for which substantial uncertainties exists within the scientific underpinning of the problem and/or where various stakeholders tend to have different problem perceptions of the problem tend to fall within Category 2.

The categorisation at first is performed by the Assessment Team (scientific experts) based upon the information available from Step 1, but could benefit from further stakeholder involvement. The choice of dominant risk type is meant to help assessors arrive at a more optimal design of the further assessment for the specific situation and should not be seen as an absolute or definitive choice. The selected dominant type of risk problem will have consequences for the focus (evidence or value based) of the further assessment but can change during the course of the assessment when further insight is generated.

## 7.4 Step 3: Goal and scope definition of the assessment

### 7.4.1 *Definition of the goal/aim of the assessment*

The main question in Step 3 is what the actual purpose of the assessment will be. In all likelihood, this has to do with providing relevant (scientific) information for decision makers to make well-informed decisions on the need for, and appropriateness/proportionality of, policy measures to regulate the (perceived) societal risk problem at hand. This aim or goal can be formulated as a main research question for the following assessment. An overall underlying goal of the assessment is to make the decision-making process more transparent and to be clear about what information is used as the basis for decision-making. As an overview, goals of the assessment could be:

a. Show the societal consequences or costs of the proposed measure
b. Show whether society as a whole is better off when the measure is implemented
c. Show how impacts of the measure are distributed over various actors/stakeholders
d. Providing relevant (multidisciplinary) information to policy makers to underpin decisions
e. Providing transparent basis for decision-making
f. Make the ambiguity of the perceived risk transparent

### 7.4.2 *Definition of Business As Usual scenario (BAU)*

This section should clarify the baseline, i.e. the BAU scenario used in the socio-economic assessment to which the policy scenario is compared. This description is mainly based on information from the current

situation description (Step 1) that has already been collected and involves at least:

a. Substance, application and crop(s) of concern
b. Use and trend in the use (amounts and exposures), price and expected price developments
c. Current regulatory situation

Note that the scenario described here is the scenario used in the actual assessment. This can deviate somewhat from the actual real life situation, for example, if available information is limited or has a slightly different scope. One should be explicit about the chosen scope, the basis of it and the assumptions made to define the scope.

7.4.3 *Selection of most relevant Policy Scenarios (PSs)*

Here the most relevant policy scenario(s) that will be compared to the BAU to assess the main differences in impacts will be described. This could include measures which policy makers are considering to take. However, what PS would be most appropriate depends on the actual goal of the assessment. This scenario can make use of the information already described in the first step. In defining this scenario, it is important to describe what actual changes are expected due to the proposed policy measure. For example, what is industry expected to do in case of a reduction in MRL? If that is not fully clear, one can decide to select a variety of potential scenarios that could represent the range of potential responses. Be clear about the assumptions taken here and the available underpinning of the assumptions. Note that the type of policy measure, and subsequent scenario, could differ substantially between Type 1 and Type 2 risks. Policy measures in Type 1 risks will be more focussed on traditional restrictions/bans whereas the policy measures in Type 2 risks can focus more on monitoring, dialogues and communications.

7.4.4 *Selection of possible/most suitable assessment methodology*

With the information from Step 1 (problem and context analysis), Step 2 (dominant risk type) and Step 3 (goal and aim of the assessment) a relevant assessment methodology should be chosen. This assessment methodology should be fit for purpose and focus on policy decision support. It is recommended that a first tier qualitative Impact Assessment is performed first to get an impression of all the relevant impacts of the case for the various stakeholders. This should give an impression of direct/indirect and major/minor impacts and possible distribution effects.

In Table 6 and Figure 7, various methodologies that can be useful for performing an SEA are presented and a brief overview of the characteristics and conditions of the assessment methodologies is given. To select the most appropriate assessment methodology from the table for the case at hand, the following aspects need to be considered:

a) What level of scrutiny for the assessment is appropriate/proportionate for the case at hand? Consider data, time, human resources, budget in the context of the project at hand (Steps 1-3).

b) What level of stakeholder involvement is required/appropriate? This relates e.g. to the dominant risk type defined earlier (Step 2).
c) What level of assessment is possible considering the available data?
   a. Is quantification of the most important positive and/or negative impacts possible?
   b. Is monetisation of the most important positive and/or negative impacts possible?

It is possible that multiple assessment methodologies are used. For instance, it is recommended to always start with an qualitative impact assessment. Furthermore, the outcome of the assessment methodologies based on welfare economics could be used as input in a Multi-Criteria Analysis in cases (policy) arguments are relevant that cannot be captured in for instance a Societal Cost Benefit Analysis. Figure 8 is an illustrative flowchart of how the context of the case influences the most appropriate assessment methodology.

*Table 6: Different assessment methodologies, and their characteristics, which may be appropriate for use in an SEA (modified from Koopmans, Heyma et al. 2016b).*

| **Assessment methodology** | **Purpose** | **Result** | **Characteristics and conditions** |
|---|---|---|---|
| *Based on welfare economy principles* | | | |
| Societal Cost Benefit Analysis (SCBA) | Estimates the net welfare change for society as a whole | Net welfare change expressed in monetary terms | - All expected impacts are qualitatively described and the most important costs and benefits can be quantified and monetised.<br><br>–No standard involvement of stakeholders, although stakeholders can be involved e.g. to help to frame the assessment, to verify input parameters, etc.<br>-High data and resource requirements.<br>-Not the first choice when there are signs of significant ambiguity, as results might not be accepted by stakeholders (in case of no stakeholder involvement). |
| Cost Effectiveness Analysis (CEA) | Estimates the relative costs to its effects. Focusses on maximization of the effects for the least costs | Cost-effect ratio | -The most important costs and benefits can be quantified.<br>-Costs can be monetised.<br>-Benefits can be aggregated into one central indicator or one benefit is the main focus, no monetisation possible/required.<br>-Other costs and benefits may be described qualitatively.<br>–No standard involvement of stakeholders, although stakeholders can be involved e.g. to help to frame the assessment, to verify input parameters, etc.<br>-Less data and resource intensive compared to SCBA.<br>-Not the first choice when there are signals of significant ambiguity, as results might not |

| Assessment methodology | Purpose | Result | Characteristics and conditions |
|---|---|---|---|
| | | | be accepted by stakeholders (in case of no stakeholder involvement). |
| Break-even Analysis (BEA) | Estimates the minimal costs or benefits needed to break-even | Minimal benefits to offset the costs or vice versa | -The most important costs and benefits can be monetised, but only one can be quantified.<br>-Other costs and benefits may be described qualitatively.<br>–No standard involvement of stakeholders, although stakeholders can be involved e.g. to help to frame the assessment, to verify input parameters, etc.<br>-Less data and resource intensive compared to SCBA.<br>-Not the first choice when there are signs of significant ambiguity, as results might not be accepted by stakeholders (in case of no stakeholder involvement). |
| *Not based on welfare economy principles* | | | |
| Impact Assessment (IA) | Creates a transparent overview of both quantitative as qualitative impacts without comparing them | Overview of all relevant impacts | -Qualitative IA always recommended as first tier assessment before any further assessment is done.<br>-(Semi) Quantitative IA also possible as a next step.<br>-Monetisation not part of the assessment.<br>-The least data and resource requirements, however depends on whether impacts are to be quantified.<br>–No standard involvement of stakeholders, although stakeholders can be involved e.g. to help to frame the assessment, to verify input parameters, etc.<br>-Not the first choice when there are signs of significant ambiguity, as results might not be accepted by stakeholders (in case of no stakeholder involvement). |
| Multi-Criteria Analysis | Weighing of semi-quantitative or qualitative impacts using user preferences | A score based on the subjective weights | -Not all impacts need to be quantified or monetised.<br>-Data and resource requirements depend on the level of stakeholder involvement and whether impacts are to be quantified and monetised.<br>-Standard stakeholder involvement needed to obtain weights.<br>-Standard involvement of stakeholders makes the methodology suitable for complex, uncertain and ambiguous risks. |

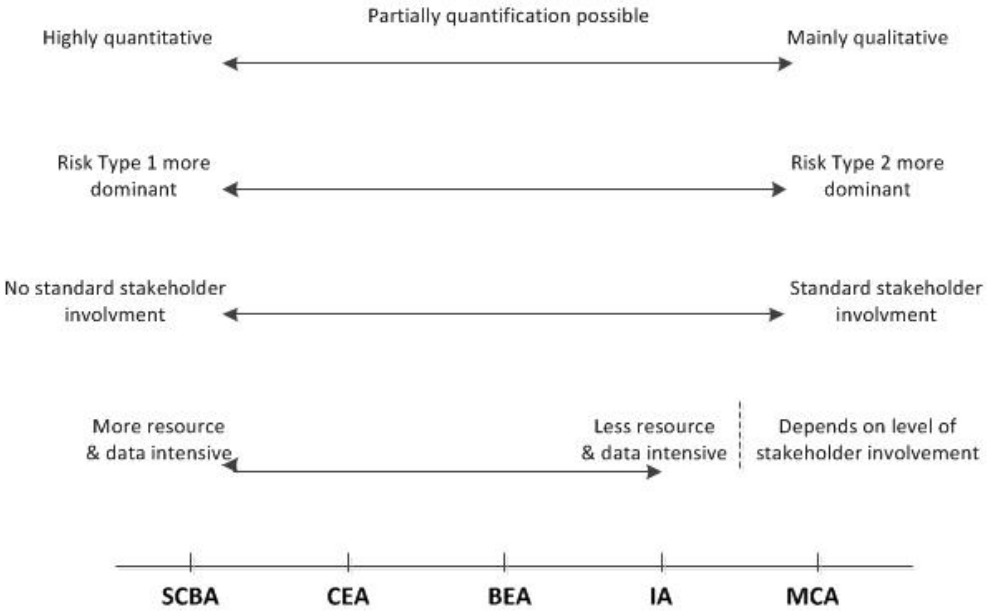



*Figure 7: The different assessment methodologies and their relationship to a number of characteristics.*

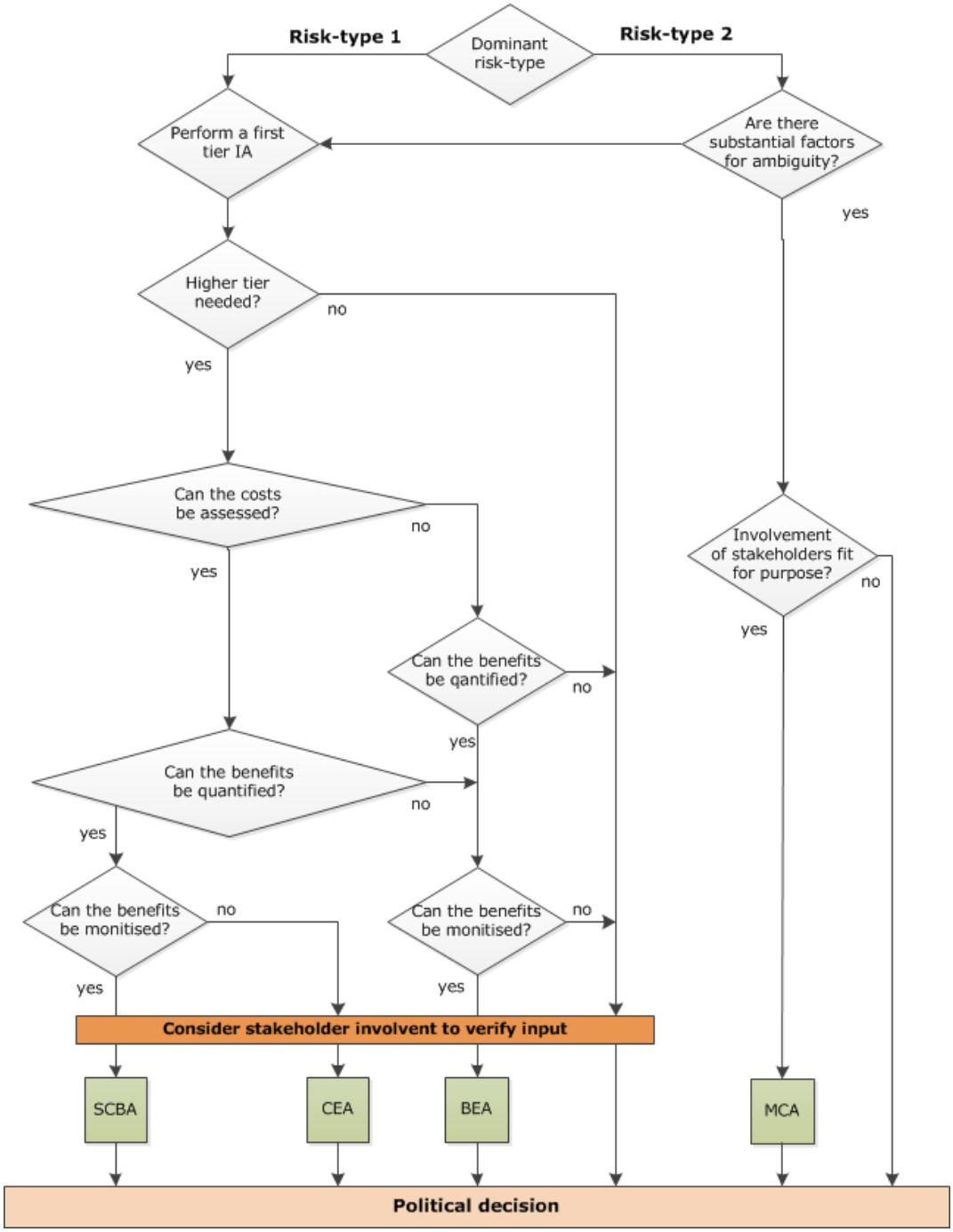



*Figure 8: Illustrative flow chart of how the characteristics of case (data availability and risk type) determines the most appropriate assessment methodology.*

### 7.4.5 *Clarification of the scope of the assessment*

a) Focus of the assessment
   When the overall goal of the assessment relates to the potential implementation of policy measures, the most appropriate focus of the assessment is the (EU) society as a whole. However, depending on the actual goal, the focus can also be on a single specific (group of) actor(s).
b) Investigation of relevant impact categories
   Impacts of the change from BAU to PS need to be investigated. Some impacts will be positive others will be negative. To obtain an overview of all relevant impacts that can be expected, one needs to structurally re-examine all potential areas of impact. To do this, it can be helpful to have a framework of impact categories that might occur in case of changes in policies to substances in food (see Table 7).
c) The timeframe
   The appropriate timeframe e.g. depends on the timing of the proposed measure and the period over which impacts are expected. Especially the latter might vary largely per case and will often be driven by the expected latency time between exposure of the substance and its effect(s) (e.g. environmental or human health effects).
d) The appropriate discount rate
   When quantifying (and monetising) impacts, impacts are often expressed over a certain timeframe or for a certain year. There might be a difference in timing of the various impacts that are expected to occur. Some impacts occur directly after implementation of the measure, others will only occur years after the measure has been taken. People value current impacts in a different way to impacts in the future. To account for this difference, discounting should be applied to the monetised figures. The choice of the applied discounting rate can significantly influence the overall results of the assessment and it might therefore be appropriate to apply a range of discount rates. The discount rate(s) to choose can, for example, be based upon the actual economic situation at the time of study in the geographical region of study (EU), or one can decide to take a standard rate for all the assessments done.
e) Geographical scale
   The appropriate geographical scale depends on the geographical scale of the policy measure and the society of interest. Very often therefore, the geographical scale of the European Union will be most appropriate. However, impacts might occur outside of this geographical scale which might be relevant to take into account. Impacts outside Europe can be translated to impacts within Europe or it can be a matter of correctly framing the impact respecting the chosen scope (e.g. costs for industry actors outside Europe will often be passed on to European downstream users). Additionally the health impacts can be different within and outside of Europe. This can result from environmental differences (e.g. soil contaminant level, climatological differences resulting in certain contaminants) or differences in diet. Therefore, some populations are more at risk.

## 7.5 Step 4: Impact assessment

Once the goal and scope of the assessment are set, the actual impact assessment of one or more policy measures compared to the current situation can be conducted. This need to be done for the relevant impact categories and various methods and models might be available to estimate the expected effect. The level of qualification/quantification/monetisation will often vary between the impact categories and depends on the available information, methods, models and most appropriate assessment methodology selected. As noted earlier, it is recommended to always first perform a qualitative impact assessment (IA) using the format of Table 6, to get an impression of the main impacts of the case at hand for the various stakeholders, as a first tier assessment. The selected SEA methodology can then be used for the further, more extensive SEA if deemed proportional and possible for the case at hand.

## 7.6 Step 5: Uncertainty and sensitivity analysis

The uncertainty and sensitivity analysis is very important in this type of assessment based on scenarios which include many different parameters. As data availability will often be limited, at least for part of the assessment, purely quantitative uncertainty and sensitivity analysis will often not be possible. This part of the framework is likely to include an overview of dominant decisions, choices, and parameters e.g. that are expected to significantly influence the end results. An uncertainty and sensitivity analysis might be performed using a table of elements that need to be considered in terms of their uncertainty and potential consequences on the end results. Parts might be assessed quantitatively by included ranges (average, upper and lower values) of the included estimates. Others will only be presented qualitatively, possibly by using a plus and minus system to indicate the direction of uncertainty to the end results. Guidance to perform an uncertainty and sensitivity assessment for the health impact of chemicals in food is outlined in the draft EFDA Guidance for uncertainty assessment (EFSA Scientific Committee 20xx).

## 7.7 Step 6: Interpretation and presentation of impacts

What will be possible and needed here depends on the dominant risk type, the goal of the assessment, the available information per impact category and the chosen assessment method. In essence, this includes application of the available assessment method using the results of the various impact categories. In this assessment one tries to answer the main research question. Only if all relevant effects can be quantified and monetised, will the comparison of impacts give the net welfare change, in monetary terms, expected due to a policy measure. Some assessment methodologies, like the multi criteria analyses and impact assessment, are not based on the welfare economic theory and therefore will not result in a net welfare change.

Often the comparison consists of quantitative, semi-quantitative and qualitative elements. In that case, the available information needs to be presented in a transparent manner; the valuation and prioritisation of various elements can be left for policy makers.

7.7.1 *Identification of relevant distribution effects*

Here the distribution of effects over various actors is analysed and discussed. For example, costs and benefits may apply for various stakeholders. Issues like inequity and injustice can become relevant here.

*Table 7: Relevant impact categories, stakeholders and description of potential effects for chemical food safety. Main goal is to describe, and quantify if possible, the various impacts, sources of uncertainties, distribution of positive and negative effects and change in (risk)perceptions among stakeholders.*

| **Impact category** | **Relevant stakeholders** | **Description of potential effects of PS** | **Quantification and monetisation of effects** |
|---|---|---|---|
| Economy | -Substance producers<br>-Crop producers<br>-Crop processors<br>-Meat producers<br>-Meat processors<br>-Retailers | -Change in one-off costs and operational costs (e.g. investments, R&D, costs due to process changes, reporting and monitoring systems)<br>-Change in quantity and/or quality of output product<br>-Change in profitability/viability<br>-Supply chain consequences<br>-Changes in trade, competition and innovation<br>-Change in public perception of stakeholder<br>-Availability of alternatives<br>-Affordability of transition costs | -Producers surplus change<br>-Substitution costs<br>-… |
| Society | -Workers<br>-Consumers<br>-NGOs<br>-Scientific community | -Employment effects (changes in job security, number of jobs, wages, distribution of jobs)<br>-Changes in availability, costs and quality of food products (consumers choice)<br>-Changes in food consumption patterns<br>-(Changes in) societal concern and risk perception | -Cost of job loss<br>-Consumer surplus change<br>-… |
| Health | -Workers<br>-Consumers | -Changes in health effects due to changes in exposure to substance of concern<br>-Change in distribution of health effects (vulnerable groups?)<br>-Changes in risk perception of health effects | -Costs of illness (direct and indirect costs of health effects)<br>-Intangible costs of health effects |
| Environment | -Consumers<br>-NGOs<br>-Scientific community | -Changes in environmental quality due to changes in exposure of substances of concern (water, soil, air quality, ecology)<br>-Changes in use of resources due to changes in production processes (land use, water use, energy use)<br>-Changes in risk perception on environmental effects | -Valuation of ecosystem services<br>-… |
| Government | -Public authorities<br>-Consumers<br>-Workers<br>-Industries | -Legislation implementation costs<br>-Control costs<br>-Enforceability<br>-Change in public perception (political pressure) of government | -… |

# 8 Case studies applying SEATS

## 8.1 Introduction to the cases

Socio-economic evaluations can aid policy decisions in cases where decisions based on the regular assessment methodology (toxicological risk assessment) are not sufficient, and where other arguments like economic impact, and social concern play a role. Our SEATS approach , presented in Chapter 7, will be tested in two cases: one on triazole pesticide representing a substance intentionally added to the food chain and a second one on lead representing an environmental contaminant. The triazole case was chosen because of the data availability and because there is some degree of uncertainty and ambiguity around the expected exposure and health related impact. Despite the regular risk assessment for authorisation concluding that there was no concern, societal concern, however, still exists.
The lead case was chosen because of its data availability and since no “safe” level of lead exposure can be defined. The health impact from lead is applicable for the whole population and especially for the vulnerable group of young children. Furthermore, lead exposure from food is not easily regulated as it is an environmental contaminant.

## 8.2 Case study Pesticide (azole fungicide)

In recent years, Aspergillus resistance to azole medication appears to have been increasing in several European countries (Snelders, van der Lee et al. 2008; Howard, Cerar et al. 2009; Verweij, Snelders et al. 2009). Although azole resistance may develop in patients who are treated with medical azoles, there are strong indication that this is rare and that this azole resistance has evolved in the environment and is driven by the selective pressure of the azole fungicides which are used in non-medical applications. However, the available scientific data is not sufficient to establish a link between the use of azole fungicides and Aspergillus resistance to azole medication. A socio-economic assessment could be helpful for policy makers to underpin their policy measures of the use of azole in non-medical applications. To use our socio-economic assessment approach as suggested in Chapter 7, and to ease applicability of the assessment we will use a rather extreme (unrealistic) theoretical scenario in this case study. It should be noted that the health benefits from the chosen policy measure in this case study is not proven and considered theoretical for proof of principle of the assessment approach. A recent study shows that actual triazole-resistant Aspergillus predominantly grows in composting sites (CLM, WU et al. 2017).
In this case study we focus on the total ban of azole fungicides from the market, accompanied by a lower level of the food safety measure. The ban of azoles in EU agriculture and the limitation of maximal residue levels in food would have a big impact on the agricultural sector (Schmitz, Matthews et al. 2011). The involvement of stakeholders in the SEA may be beneficiary due to the uncertainty in the available scientific data and the significant consequences for the agricultural sector.

*Text box 4: Information about the azole fungicide*

Azoles are chemicals with anti-fungal mode of action (i.e. fungicide). Azoles can be divided into imidazoles and triazoles. Only triazoles are used in anti-fungal medication for humans and animals. Both imidazoles and triazoles are used as cosmetics, plant protection products and biocides, where triazoles are the most used substances in agriculture.

Moulds in general are very prone to develop resistance to azoles. In agriculture, fungal plant diseases are treated with a combination of fungicides from different chemical classes (i.e. azoles and non-azoles) to limit the resistance development of the mould.
Human mould disease treatment mainly relies on triazole medication, to limit resistance development some triazole medication is only available with a prescription or only used in a hospital setting.

Examples of triazoles for pesticidal use are: Difenoconazole, Epoxiconazole, Tebuconazole
Examples of triazoles for medicinal use are: Vorticonazole, Itraconazole, Posaconazole

8.2.1 *Step 1: Problem and context analysis*

Description of the current situation
The following description of the current situation is predominantly based on the technical analysis of the European Centre for Disease prevention and Control (ECDC 2013).

The term aspergillosis refers to a group of diseases which can result from an infection of the mould Aspergillus. It includes allergic bronchopulmonary aspergillosis (ABPA), chronic pulmonary aspergillosis (CPA), aspergilloma and the most severe form, invasive aspergillosis (IA). Some asthma patients with very severe asthma may also be sensitised to mould-like Aspergillus (SAFS). Aspergillus fumigatus is by far the most common species in human Aspergillus infections, constituting more than 80–90% of the isolates in most series (Lass-Florl, Griff et al. 2005). People with a weak immune system are particular vulnerable and therefore at risk for aspergillosis. The number of Aspergillus infections has increased because more patients are at risk of being exposed to this opportunistic pathogen (due to high frequencies of allergies and asthma, the aging population, the increase in cancers and their treatment and the expanding indications for transplantation) and it is difficult to prevent the diseases it causes. It should be noted thought that also an increased Aspergillus screening could explain these increased figures. Patients with established Invasive Aspergillosis (IA) have poor recovery outcomes. Successful therapy depends on early diagnosis, which is difficult to establish, and timely and effective use of antifungal agents. Antifungal agents have been developed for the treatment of aspergillosis. The newer azoles, in particular, have become the mainstay of therapy and are the recommended first line drugs in the treatment and prophylaxis of aspergillosis.

The overall mean ‘burden of disease’ estimate of all forms of aspergillosis in the European region, including the Russian Federation, is approximately 2,400,000 affected individuals annually based on 2010 figures (ECDC 2013). These numbers do not include the estimated

1,870,000 individuals with allergic fungal rhinosinusitis; it has yet to be demonstrated whether these individuals will respond to antifungal therapy. It is estimated that 63,250 of these patients develop IA, a disease with a high mortality rate requiring urgent therapy.

Case series consistently show high failure rates effective treatment of patients with azole-resistant Aspergillus diseases to azole therapy. In patients with chronic Aspergillus diseases a failure rate of 89% is observed. In patients with azole-resistant IA 88% of patients died within 12 weeks of obtaining a positive culture (van der Linden, Snelders et al. 2011). The majority of azole-resistant A. fumigatus isolates are multi-azole-resistant. In a recent Dutch survey, 82 clinical azole-resistant isolates were all resistant to itraconazole (MIC > 2 mg/l), 79% were resistant to voriconazole (MIC > 2 mg/l) and 65% to posaconazole (MIC > 0.25 mg/l). As a consequence, at best only a marginal role remains for azoles in the treatment of azole-resistant Aspergillus diseases

Resistance in Aspergillus has long been considered a rare event and has only been reported at low frequency, mainly in case reports. However, the situation has changed considerably as there is an increase in the frequency of azole resistance in A. fumigatus. Slightly more than 2.3 million patients with allergic or chronic aspergillosis could potentially benefit from long-term oral azole therapy. Azole resistance is therefore potentially highly problematic for both groups of patients (ECDC 2013).

Resistance development might occur through exposure of A. fumigatus to azole compounds in our environment. Exposure of moulds to azole compounds could take place in non-medicinal applications. The fungicides are applied repeatedly over a long period of time creating a persistent pressure of azole compounds on moulds (Verweij, Snelders et al. 2009). It should be stressed, however, that there is no full proof evidence of a causal link between the non-medicinal use of azoles and the development of azole-resistant Aspergillus fumigatus.

Since their introduction more than thirty years ago, azoles have been intensively used in cosmetics, plant protection products, biocides and (veterinary) drugs. Azoles have played an important role in agriculture and horticulture. Because of their excellent systemic broad-spectrum eradicant and protectant properties, azoles are, for many crops, (e.g. cereals and soybean) the most important fungicide group to protect crops from diseases, therefore ensuring yields and preventing fungal contamination of products, thus ensuring product quality (Russell 2005). Triazoles and the imidazole prochloraz are most commonly used on arable crops (e.g. wheat, barley, oilseed rape and beans), controlling septoria leaf blotch, rhynchosporium, Fusarium, rusts and mildews. These are therefore used over the largest areas and in the highest amounts. Some azoles are used as seed treatments for cereal crops to control Fusarium seedling blight on wheat and loose smut and leaf stripe on barley. They are also used to control diseases of outdoor bulb/flower crops, vegetables, soft fruit, ornamental crops and orchards (e.g. Alternaria fruit rot, Botrytis crown rot, apple scab, downy mildew and mildew).

Fungal diseases such as Septoria are extremely difficult to control in agriculture without the use of fungicides, in particular azole-based fungicides. They are highly effective for controlling Septoria and rust pathogens, which represent the greatest disease threat to cereal production. According to the European Landowners' Organisation (ELO 2013b), fungicides prevent losses estimated to be between 15-30% of global wheat harvests. Like other authorised crop protection products, fungicides need to be used safely and effectively under practical agricultural conditions, they should be used according to the label instructions and applied by professionals. The issue of azole-based resistance in mould species is not assessed if a fungicide is authorised on the market because Aspergillus is not a target species; Aspergillus is not a plant pathogen.

*In summary*
There is currently a concern about the number of azole-resistant Aspergillus infections in humans. An important uncertainty in this case study is the question as to whether the resistant form of Aspergillus fumigatus is developed by the non-medicinal use of azoles, e.g. the use of plant protection products (as is suggested for this non-realistic theoretical case study). Azole-based fungicides are essential for retaining the current yields in agriculture and stricter regulation on the use of these fungicides will have a significant economic impact on the supply chain and end-consumers. On the other side, azole-resistant Aspergillus infections lead to increased mortality in an already vulnerable group. This trade-off between economic consequences for a powerful, influential sector and mortality or severe health consequences in a vulnerable group could introduce ambiguity.

*Concern assessment and relevant stakeholders*
The potential ambiguity of the problem makes it valuable to have an idea of the relevant stakeholders related to the problem and their role and concern in the situation at stake. Therefore, a (limited) investigation of stakeholders was performed based on an internet search. This concern assessment is based on publicly available information and no stakeholders were contacted to verify the information. It should be noted, however, that a more extensive case study (relating to an issue of ambiguity) would benefit from a more extensive stakeholder analysis and stakeholders involvement in the process.

Identified relevant stakeholders are:

- Patient groups
- NGOs
- Pharmaceutical industry
- Medical personnel
- Manufactures of azole-based fungicides
- Farmers
- Consumers (residue)
- Consumers (prices)
- Academics

*Patient groups and NGOs:*
In this case, patients are quite organised and represented via two organisations. One online patient support group for aspergillosis

(www.aspergillus.org.uk) based in the United Kingdom could be found through a short internet search. The information mainly focusses on providing a platform for aspergillosis patients, a scientific section with background information on moulds, and a medical section on diagnosis, treatment options and drugs. A small commentary is written about the link between antifungal drug resistance and the agricultural use of azoles, based on an academic article that suggested this link in 2009 (Verweij, Snelders et al. 2009). The commentary concluded that: "*this is enough to require us to think carefully about allowing the large scale use of azoles in agriculture*".

The Health and Environment Alliance (HEAL, www.env-health.org), an NGO addressing issues related to the environment and how they affect health within the European Union, issued a press release based on the same academic article. Based on the academic findings HEAL states that: "*these new findings help to re-inforce calls from the NGO community to bring about a ban of the use of the azoles-group in pesticides".*

It appears that the role of NGOs and patient groups in the public debate at this moment is limited. This is remarkable as the health effects of azole-resistance of Aspergillus are severe. However, the patient groups might lack resources (in terms of money and knowledge) to express their concerns.

*Pharmaceutical industry*
The pharmaceutical industry has an important role in the problem around aspergillosis disease as they developed and provide the antifungal agents used for the treatment of aspergillosis. The first line drugs for the treatment of aspergillosis are azole-based antifungal drugs. No information could be found showing any concerns in the pharmaceutical industry around the issue of growing resistance to azole-based therapies.

The pharmaceutical industry is usually well organised with sufficient resources to express their concerns. If resistance to azole-based drugs were to continue to increase, this could potentially have a significant impact on their business, then one would expect the industry to pro-actively react to such developments by, for instance, increasing funds for alternative medication or research.

*Medical personnel*
The main role of this stakeholder is the treatment of aspergillosis, especially invasive aspergillosis in patients with immune deficiency. The mortality rate of untreated aspergillosis can be very high, depending on the invaded organs and condition of the patient. An effective treatment is, therefore, very important. Azole therapy is the recommended first line drug in the treatment of aspergillosis; an increase in the frequency of azole-resistant Aspergillus severely limits the effective treatment options resulting in an increased mortality rate or chronic disease.

A first screening of the (medical) academic research papers related to aspergillosis shows that, in the last 15 years, the main area of research has been the diagnosis and treatment of aspergillosis. In about 5% the

word azole is mentioned in the abstract and 1-2% of the articles on aspergillosis is aimed specifically at the link between aspergillosis and azole resistance or use. This percentage has increased from <1% in the first years to 3% in 2016.

No thorough analysis was performed on the contents of these articles, but, at first glance, the articles tend to signal an increase in azole resistance and a potential health risk for immunocompromised patients, but fail to find the underlying causes of this increase.

*Manufactures of azole-based fungicides.*
The manufactures of azole-based fungicides and the European Landowners' Organisation (ELO) have disseminated several information leaflets on the use of azoles in agriculture (ELO 2013b; ELO 2013a). The main issue raised, and probably the incentive for the development of the leaflets, is the potential effect of changes in EU legislation on the use of azoles based on potential endocrine disrupting effects. The potential endocrine disrupting effects of azoles has been put outside the scope of this assessment, as it would make the case study overly complex.

Human health and environmental safety concerns focussing on the stringent safety testing system that is applied. This is said to ensure that the fungicides can be used safely and effectively under practical agricultural conditions, if used according to the label instructions and applied by professionals.

A limited internet search did not reveal any official statements about the hypothesised link between the agricultural use of azole-based fungicides and increased prevalence of azole-resistant Aspergillus and subsequent public health risk.

The manufacturers of azole-based fungicides are well-organised and have the resources to react to protect their business. They could be a powerful stakeholder in a public debate. The industry have installed the Fungicide Resistance Action Committee (FRAC) long ago to manage resistance development in crop treatment. The FRAC is currently also funding research on resistant Aspergillus. At the same time, the subgroup of triazoles if promoted as most effective antifungal treatment currently available. It is particularly this group that is chemically most related to the medical triazoles.

*Farmers*
The above-mentioned leaflets focus on the important function of azole-based fungicides in agriculture and the impacts on society that would occur if these fungicides were restricted or banned. Resistance development by moulds against some azole-based fungicides is used as an argument to retain access to a diversity of different azole fungicides.

A limited internet search did not reveal any official statements about the hypothesised link between the agricultural use of azole-based fungicides and increased prevalence of azole-resistant Aspergillus and subsequent public health risk.

Historically, farmers have been organised in strong unions and organisations. It can be expected that, as with the pharmaceutical industry and the manufacturers of fungicides, they will have sufficient resources to play a significant and powerful role in a public debate. However, it this group often lacks the knowledge to interfere in the debate. Advice is nowadays provided by the chemical industry.

*Consumers*
It appears that the consumers do not have a specific concern related to the use and residues of azole-based fungicides. In general, some consumers are concerned about the residues of plant protection products in, or on, their food. In general, consumers are sensitive to products costs, therefore any difference in price due to the policy scenario will affect them. In debates, public opinion can exert a strong influence on policy decisions. Public opinions are often not based on purely scientific information.

*Research institutes*
EFSA's Pesticides Unit is responsible for the EU peer review of risk assessments of the active substances used in plant protection products, in close cooperation with EU Member States. The risk assessment of active substances evaluates whether, when used correctly, these substances are likely to have any direct or indirect harmful effects on human or animal health. For example, through drinking water, food or feed quality.

The European Centre of Disease Control (ECDC) has published a risk assessment report on the impact of the environmental usage of azoles (ECDC 2013). The development and spread of resistance to azoles in Aspergillus species indicates an environmental route of resistance development. Several observations are stated that support an environmental route of azole resistance development, including: azole resistance observed in azole naïve patients, isolates harbouring the TR34/L98H resistance mechanism are found in the environment, azole fungicides used in agriculture have a similar molecular structure to medical azoles and absence of genotypical wild-type isolates related to those with TR34/L98H.

However, the report concludes: "*In spite of the data supporting an environmental origin of the multi-azole resistance […], several uncertainties still exist. Estimates of the prevalence and spread of multi-azole resistance in A. fumigatus due to the TR34/L98H mutation are currently based on a small number of studies from a few European countries. Existing data show a strong variation in the frequency and composition of the mutations associated with azole resistance between the centres within and between European countries. Although as shown there is accumulating evidence for an environmental origin of multi-azole resistance in A. fumigatus, this link still needs to be proven. Association of certain azole fungicides with the observed resistance mechanism appears likely, yet it is unclear which exposures represent the main drivers for resistance development in Aspergillus spp.*"

Research institutes, like the ECDC, can act as an early warning system by signalling potential trends and concerns among academics. Usually,

they are well organised and will state their concerns if needed. Whether these concerns influence the public debate normally depends on whether there is also media involvement and public interest.

*Description of potential policy scenarios*
In this theoretical (and rather extreme and unrealistic) case, the aim of the policy scenario is to ban the use of azole fungicides to prevent further resistance development of Aspergillus.

The hypothetical policy scenario considered in this case study would be: Withdrawal of azole fungicide from the pesticide market and reduction of the maximum residue limit in azole treated crops. *It is stressed that the policy scenario is hypothetical.*

8.2.2 *Step 2: Identification of dominant risk type*
In this step, the Assessment Team selects a dominant risk type that is assumed to best suit the case at hand considering the information gathered in Step 1.

The relationship between high failure rates of patients with azole-resistant Aspergillus diseases to azole therapy seems undisputed between stakeholders. Also stakeholders' views on the increase in occurrence of these azole-resistant *A. fumigatus* does not seem to diverge. A link between the use of azole-based fungicides and the reported increase in the prevalence of azole-resistant Aspergillus diseases has been hypothesised in the academic sphere (Verweij, Snelders et al. 2009) and is supported by the ECDC, albeit with uncertainties. However, this causality has not been proven and several uncertainties exist. The lack of causality has not caused divergent perceptions on the role of agriculture in the development of azole-resistant Aspergillus diseases in this limited concern analyses. The patients groups and NGOs would like to restrict the use of azole-based fungicides due to an increase of azole-resistant Aspergillus. No strong opinion on the link between the agricultural use of azole-based fungicides and the increase of azole-resistant Aspergillus could be found from the manufactures and farmers. At this moment, it is uncertain whether more scientific research or expert consensus tools would reduce the uncertainty about causality. Causality can be extremely difficult to prove in this case, even with more research. Based on the limited stakeholder analyses, it seems that the most dominant risk type would be primarily driven by the uncertain scientific underpinning of the perceived problem. Furthermore, the problem has the potential to become ambiguous. This limited stakeholder analysis did not reveal substantial ambiguity, however, a more thorough stakeholder analysis should be considered to reveal whether there are indeed no ambiguous elements.

Considering the above, Type 2 risk is chosen as the most dominant risk type.

8.2.3 *Step 3: Goal and scope definition of the assessment*
*Definition of the goal/aim of the assessment*
The main goal of an SEA assessment is to show whether society as a whole benefits from the proposed policy and how impacts are distributed

over various actors/stakeholders. In addition, the aim could also include to make the uncertainty surrounding the causal relationship between the agricultural use of azole fungicides and the resistance development of Aspergillus more transparent, explore potential factors for ambiguity and, if necessary, increase mutual understanding between stakeholders and provide relevant objective multidisciplinary information to support policy makers in the policy decision-making process.

In light of the limited time and exploratory purpose of this case, an in-depth SEA is not deemed possible and the main aim for this SEA is to use and evaluate the usefulness of the proposed SEA framework.

*Definition of Business As Usual scenario (BAU)*
Azole-based fungicides are used in various situations, e.g. as biocide, pesticide, veterinary drugs, in cosmetics and in biocides treated articles. The most intensive use of the azoles is the triazole use in agriculture; to be more specific, the use of azole fungicides in cereal crops.
Therefore, in this case study, we focus on the use of azole agriculture (pesticide use) on wheat. In Europe, the azoles prothioconazole, epoxiconazole, tebuconazole, cyproconazole, metconazole, propiconazole, difenoconazole and flusilazole are used in several cereal crops among others on wheat.

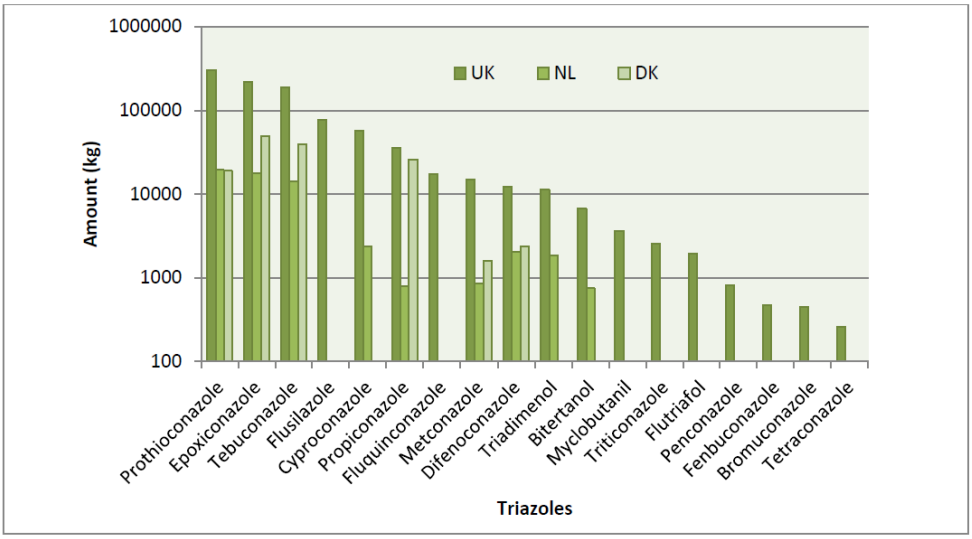
*Figure 9: Example of tebuconazole use.*

| Crop and/or situation (a) | MS or NEU /SEU or Country | F G or I (b) | Pest or group of pests controlled (c) | Formulation | | Application | | | | Application rate per treatment | | | PHI (days) (l) | Remarks (m) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | type (d-f) | conc. a.s. (i) | Method kind (f-h) | Growth stage & season (j) | Number min-max (k) | Interval min-max | g/hL min-max | Water L/ha min-max | g/ha min-max | | |
| Wheat, rye | NEU and SEU | F | *Erysiphe graminis, Septoria nodorum, Septoria tritici, Puccinia recondite, Fusarium spp*. | EC | 107 g/L | Foliar spray | BBCH 30-69 | 1 | | 30 - 90 | 150-400 | 128 | | |

Remarks:

(a) For crops, EU or other classifications, e.g. Codex, should be used; where relevant, the usage situation should be described (e.g. fumigation of a structure)
(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c) e.g. biting and sucking insects, soil-born insects, foliar fungi, weeds
(d) e.g. wettable powder (WP), water soluble granule (WG)
(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
(f) all abbreviations must be explained
(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants. Type of equipment used must be indicated
(i) g/kg or µg/L
(j) Growth stage at last treatment (Meier U, 2001. Growth Stages of mono- and dicotyledonous plants. BBCH Monograph, 2nd Ed., Federal Biological Research Centre of Agriculture and Forestry, Braunschweig, Germany, 2001), including where relevant, information on season at time of application
(k) The minimum and maximum number of application possible under practical conditions of use must be provided
(l) PHI - minimum pre-harvest interval
(m) Remarks may include: Extent of use/economic importance/restrictions

The example in Figure 9 shows the intended use of tebuconazole, which is one spray application on young wheat and rye plants with an application rate of 128 gram per hectare. The total use of azoles is estimated to be between 55,000 to 130,000 kilos a year in the Netherlands. However, azoles are used widely all over Europe (see Figure 10).




UK:data were collected by the Pesticide Usage Survey Teams at the Food and Environment Research Agency (FERA) and the Scottisch Agricultural Science Agency (SASA). Fungicide use by government, industry/forestry and garden/household is not included.
NL: Data were obtained from the Central Bureau of Statistics (Statistics Netherlands). Data on fungicide use by government, industry/forestry and garden/household is included.
DK: Data collected by the Danish Environmental Protection Agency (Miljøstyrelsen) 4/2009
*Figure 10: Use of azoles in agriculture in the United Kingdom, the Netherlands and Denmark, 2008 (ECDC 2013)*

Using the azole pesticide according to the label of the product results in residues in a consumable raw agricultural commodity, e.g. residues in wheat cereal grains. Maximal Residue Levels (MRLs) are set based on these expected residues in the consumable part of the crop. The MRL is the legal limit which enforcement agencies use to monitor the market (see Table 8). The MRL is the food safety standard. The risk assessment that these legal limits are based on established that it was safe for high incidental exposure to the pesticide residues and also covered chronic (life-long) average exposure to pesticide residues. The relation to possible medicinal azole resistance in Aspergillosis from azole use and the relation to the related additional burden of disease was not assessed during the authorisation process of this (and other) pesticide(s).

For agricultural use, azoles are essential to reduce mould development and reduce crop loss. Azoles are used in combination with other fungicides. The combination is essential to reduce resistance development of the plant pathogen. Therefore azoles cannot be replaced by other types of fungicides and are considered essential for the economically profitable production of crops. In the ‘business as usual’ scenario the use of azoles in the agriculture of wheat remains unchanged and is assumed to remain constant over time.

*Table 8: Actual Azole Maximal Residue Levels*

| **Azole substance** | **Maximal Residue Level (MRLs) for wheat (mg/kg)** |
|---|---|
| Cyproconazole | 0.1 |
| Difenoconazole | 0.1 |
| Epoxiconazole | 0.6 |
| Flusilazole | 0.01* |
| Metconazole | 0.15 |
| Propiconazole | 0.05* |
| Prothioconazole | 0.1 |
| Tebuconazole | 0.3 |

* MRL is equivalent to the analytical limit of detection

*Selection of most relevant Policy Scenario(s, PS)*
In this theoretical policy scenario, we focussed on the total ban of azole fungicide from the market. As azoles can no longer be used in agriculture, the ban will result in a lower level of the MRL (see Table 9). Azoles are always used in combination with other non-azole fungicides to reduce resistance development and cannot, therefore, be replaced. It is assumed in the PS that the use of these other fungicides remains. The main impact on agriculture will be lower crop yields for wheat (about 14%). The yield loss results in a decreased production of 18.6 million tons in the EU (in 2020). This is equivalent to a loss of 4.6 billion euros. (Nomisma 2012)

*Table 9: Azole Maximal Residue Levels, as chosen in a theoretical policy scenario*

| **Azole substance** | **Maximal Residue Level (MRLs) for wheat (mg/kg)** |
|---|---|
| Cyproconazole | 0.01* |
| Difenoconazole | 0.01* |
| Epoxiconazole | 0.01* |
| Flusilazole | 0.01* |
| Metconazole | 0.01* |
| Propiconazole | 0.01* |
| Prothioconazole | 0.01* |
| Tebuconazole | 0.01* |

* MRL is equivalent to the analytical limit of detection

*Selection of possible/most suitable assessment methodology*
In this case study, the uncertainty concerning the relationship between the application of azole-based fungicides and the prevalence of azole-resistant Aspergillus diseases means that the quantification of health impacts is not possible. We have already established that the most dominant risk type is Type 2 and from the limited stakeholder analyses no substantial factor for ambiguity arises.

An appropriate first-tier framework would be to start with a qualitative investigation of relevant impacts, although available quantitative information can be used in this arena as well. This will provide a first impression of the relevant multidisciplinary information that can serve

as a basis for further policy as it increases transparency about the impacts considered.

The questions raised for the selection of a more extensive, second tier, assessment methodology are:

a) What level of scrutiny for the assessment is appropriate/proportionate for the case at hand?
b) What level of stakeholder involvement is required/appropriate?
c) What level of assessment is possible considering the available data?
    a. Is quantification of the most important positive and/or negative impacts possible?
    b. Is monetisation of the most important positive and/or negative impacts possible?

In this case study, we chose to limit the analysis to this first step of a qualitative analysis because of the resource constraints in this project. If more resources were available, some level of stakeholders' involvement would be beneficial to verify whether a) indeed there is no significant ambiguity, b) all relevant impacts have been taken into account and c) the appropriate input parameters are used.

Considering the available data, it appears that a break-even analysis might be fit for purpose. In this case, a break-even analysis could be performed as both the costs to the agricultural sector can be estimated and the (in)tangible costs of a case of azole-resistant Aspergillus disease. The break-even analysis estimates the number of azole-resistant Aspergillus disease cases needed to offset the costs of banning azole-based fungicides. One should be alert to the fact that the usefulness and representativeness of the outcome of a break-even analysis is dependent upon whether the most relevant impacts are taken into account.

A quantitative break-even analysis and stakeholder involvement is suggested for this case study, but not performed due to project budget constraints.

*Clarification of scope of the assessment*
*Focus of the assessment*
The scope of the assessment will be European society as a whole, because plant protection legislation is implemented European wide for the active substances. Furthermore, it is expected that the baseline and policy scenarios are applicable all over European society.

*Investigation of relevant impact categories*
Table 10 states the most relevant impact categories: economy, society, health effects, environment and government. In Section 8.2.1 the relevant stakeholders for the concern appraisal are identified: potential patients, NGOs, medical personnel, pharmaceutical industry, farmers, manufactures, consumers (residue) and academics. Not all the stakeholders, such as the academics for instance) are affected by the policy scenario.

In Table 10 the relevant stakeholders are placed within the different impact categories. In Step 4 the actual impacts per category will be further described.

*Table 10: Relevant impact categories*

| **Impact category** | **Stakeholder** |
|---|---|
| Economy | Patients<br>Medical personnel/public health care sector<br>Pharmaceutical industry<br>Farmers of crops treated with azole-based pesticides<br>Retail<br>Manufactures of azole-based pesticides<br>Consumers (prices)<br>Government |
| Society | Patients<br>NGOs<br>Medical personnel/public health care sector<br>Pharmaceutical industry<br>Farmers<br>Consumers (residue)<br>Residents near agricultural fields (concern about spray residue) |
| Environment | NGOs<br>Farmers of crops treated with azole-based pesticides |
| Health effects | (future) Patients<br>Food consumers |

*Timeframe*
An active substance of a plant protection product can be excluded from approval based on unacceptable health risks; the withdrawal is for an undefined period of several months. In this assessment, the permanent withdrawal of azole-based fungicides from the market is anticipated. No information is available on time-specific impacts and, as a first tier qualitative impact assessment is foreseen, no set time period needs to be defined.

*Discounting*
Common practise within the European Union is to use a 4% discount rate for both costs and benefits that will occur in the future.

*Geographical scale*
The logical geographical scale of any policy scenario regarding withdrawal, or change, of pesticide MRLs, is the European Union (EU-28) because MRLs have been widely harmonised across the EU-28. For this case study we assume the environmental and human health consequences (applied use and environmental pressure) will remain within the European Union.

8.2.4 *Step 4: Impact assessment*
The impact assessment is based on a qualitative impact assessment framework. In this exemplary case study, and in this report, no stakeholder involvement to verify or provide additional information on

the impacts is performed. Table 11 provides the qualitative impact assessment.

*Table 11: Qualitative impact assessment of a potential ban on the agricultural use of azole-based fungicides*

| **Impact category** | **Description of impact** |
|---|---|
| Economy | **Patients**<br>• Depending on the general health of recovered patients, a potential decrease in mortality due to a reduction of azole-resistant aspergillosis could lead to more ex-patients available for the labour market<br>• It is expected that the medical treatment of azole-resistant aspergillosis is associated with more severe comorbidity and a longer recovery. A reduction in azole-resistant aspergillosis could therefore potentially lead to increased earnings from increased labour productivity.<br><br>**Medical personnel/public health care sector**<br>• Depending on the difference in the medical treatment of azole-resistant aspergillosis, costs associated with a reduction in the number of azole-resistant aspergillosis could be higher or lower (estimated health care costs of Aspergillus diseases are approx. 350-950 euro a day, (Verweij 2010), Aspergillus treatment costs approx. 37-60k USD (Krueger and Nelson 2009).<br>• It is expected that due to a decrease in mortality, there will be an increase in health care costs of the ex-patients (health care costs related to additional years of life).<br><br>**Pharmaceutical industry**<br>• Depending on the difference in medical treatment in case of azole-resistant aspergillosis, there could be a potential increased or decreased profit associated with the medical treatment of Aspergillus diseases (The world market for antifungal agents is currently in excess of 6 billion USD with consistent annual growth [www.f2g.com], no EU specific sales numbers were found).<br><br>**Farmers and retail**<br>• Potential loss of profit within the supply chain (farmers and retail, due to crop losses). Most of these costs are passed on to the consumers, however some might be borne by the farmers. Wheat example: the yield loss results in a decreased production of 18.6 million tons in the EU (in 2020). This is equivalent to a loss of 4.6 billion euros, (Nomisma 2012) A yield reduction of 15% could lead to a decline in farm net income of between 20 to 70% (Schmitz, Matthews et al. 2011).<br>• Loss of world market share due to lower yields per hectare in Europe. Wheat example: EU produces 21% |

| | |
|---|---|
| | of the total world production (BAU scenario), a total ban would lead to an EU production of 18.5% of the world production (Nomisma 2012).<br>• Increase in import of crops from outside the EU. Wheat example: decreased yield results in a situation where the EU is no longer self-sufficient. The production/demand ratio is 1.09 in the BAU scenario and, in regards to a ban, results in a ratio of 0.93-0.98 (Nomisma 2012).<br>• Loss of world market share and increase in import of crops from outside the EU could lead to farmers going out of business and subsequent friction costs of finding new employment. Wheat example: To be self-sufficient (demand for wheat = production + import) export should decrease by 103% or imports should increase by 337% (Nomisma 2012).<br><br>**Manufactures of azole-based fungicides**<br>• Loss of sales (and potential profit) and change of market volumes (in the Netherlands about 50,000 – 130,000kg azoles are used annually (Schoep and Sterenborg 2013), no detailed information is available about corporate profits.<br><br>**Consumers**<br>• Increased cost for food consumption, Wheat example: Expected increase in wheat prices of 17-30% (Nomisma 2012).<br><br>**Government**<br>• Depending on the difference in medical treatment between azole-resistant aspergillosis, increase/decrease in public health spending for the treatment.<br>• A potential decrease in mortality due to a reduction of azole-resistant aspergillosis could lead to:<br>o Increased public health care costs due to health care provision in the remaining years of life of ex-patients.<br>o Depending on the general health of recovered patients, an increase in spending on welfare benefits for ex-patient who are (partially) unfit for work. |
| Society | **Patients**<br>• Potential decrease of the emotional impact of suffering from aspergillosis for the patient and patient's family or acquaintances.<br>• Potential decrease of the emotional impact of premature death due to aspergillosis for the patient and patient's family or acquaintances.<br><br>**NGO**<br>• Decreased attention to addressing azole usage.<br>• Decreased concern regarding prevalence of azole- |

| | |
|---|---|
| | resistant Aspergillus diseases.<br><br>**Medical personnel / public health care sector**<br>• Potential increased emotional impact of work-related effectiveness of Aspergillus treatment.<br><br>**Pharmaceutical industry**<br>• Potential loss of business case to develop new, non-azole based antifungal agents.<br><br>**Farmers**<br>• Loss of world market share and increase in import of crops from outside the EU could lead to job losses in the agricultural sector.<br>• Increased emotional impact and concerns from economic impact based on reduced yields.<br>• Fewer perceived health risks from pesticide usage.<br><br>**Consumers**<br>- Decreased societal concern regarding pesticide residues on food (if no other fungicide is used).<br>- Increased societal concern regarding food prices and available choices, economic impact on society. |
| Environment | **NGO**<br>- Decreased concern regarding azole pesticides in environment.<br><br>**Farmers**<br>- Decreased concern regarding environmental pollution by pesticide usage.<br>- No residue of azole-based fungicides in the soil.<br>- Less ecological toxicity as a result of fungicide application.<br>- Increased use of area for agriculture to compensate lower crop yield. Wheat example: 1.7-7.5% increase (Nomisma 2012). |
| Health effects | **Patients**<br>- Potential reduction in prevalence of azole-resistant Aspergillus diseases.<br>- Potential reduced mortality and morbidity from Aspergillus diseases.<br><br>**Consumers**<br>- No increase in health risks are expected due to an increased prevalence of moulds on the crops. |

8.2.5 *Step 5: Uncertainty and sensitivity analysis*

In this assessment framework, a qualitative description of potential impacts, an extensive sensitivity analysis is not anticipated. The main uncertainty lies in the link between the environmental pressure coming from the agricultural use of azole-based fungicides and the prevalence of azole-resistant Aspergillus diseases. The impact assessment in this case study tries to identify the major potential impacts of the policy scenario.

The impacts are assessed based on a limited screening of the literature and no stakeholder consultation was performed, therefore, another central uncertainty is whether or not all relevant impacts are described.

A limited uncertainty analysis of the main identified impacts of Table 12 was performed by indicating qualitatively the uncertainty in the likelihood of the impact occurring in the policy scenario. A division is made between the likelihood of main impacts occurring (like reduced mortality) and all subsequent impacts (such as decreased private health care spending due to reduced mortality) that would follow if the main impact occurred. The uncertainty table is performed to give an impression of how this could look like in practice. However, it is recognised that further scrutiny of the table could improve understanding of the most relevant uncertainties in the case study.

*Table 12: Uncertainty analysis of main impacts*

| **Main impacts** | **Subsequent impacts if main impact occurred** | **Level of uncertainty re. occurrence** |
|---|---|---|
| *Reduced mortality and morbidity of Aspergillus diseases* | | *Highly uncertain* |
| | Increase in labour force as more ex-patients are available for the labour market. | Medium uncertainty |
| | Increased earnings from increased labour productivity due to a better recovery in case of non-resistant aspergillosis. | High uncertainty |
| | Increased public health costs due to health care cost in the years of life gained. | Low uncertainty |
| | Change in public health costs due to differences in medical treatment of resistant and non-resistant aspergillosis. | Medium uncertainty |
| | Increase in spending on welfare benefits for ex-patients who are (partially) unfit for work. | High uncertainty |
| | Decreased emotional impact due to suffering and premature death from aspergillosis. | Low uncertainty |
| | Profit change associated with medical treatment of Aspergillus diseases. | High uncertainty |
| | Increased emotional impact on work-related | High uncertainty |

| Main impacts | Subsequent impacts if main impact occurred | Level of uncertainty re. occurrence |
|---|---|---|
| | effectiveness of Aspergillus treatment. | |
| *Loss of crop yield* | | *Low uncertainty* |
| | Potential loss of profit within the supply chain | Low uncertainty |
| | Loss of world market share | Low uncertainty |
| | Increase in import of crops from outside | Low uncertainty |
| | Job losses | Low uncertainty |
| | Loss of sales (and potential profit) and change of market volumes of azole-based fungicides | Low uncertainty |
| | Increased cost related to food consumption | Low uncertainty |
| | Increased emotional impact of economic impact based on reduced yields. | High uncertainty |
| | Increased societal concern regarding food prices and available choices, economic impact on society. | Low uncertainty |
| | Increased use of area for agriculture to compensate lower crop yield. | Low uncertainty |
| | | |
| *Other impacts* | | |
| | Decreased concern regarding prevalence of azole-resistant Aspergillus diseases | Low uncertainty |
| | Less perceived health risks from pesticide usage | High uncertainty |
| | No increase in health risks due to an increased prevalence of moulds on the crops. | Low uncertainty |
| | Loss of business case to develop new, non-azole based antifungal agents. | High uncertainty |
| | Decreased concern regarding pesticide residues on food (if no other fungicide is used). | High uncertainty |
| | Decreased concern regarding azole pesticides in environment. | Low uncertainty |
| | Less ecological toxicity as a result of fungicide application. | Low uncertainty |

8.2.6 *Step 6: Comparison of impacts.*

In this assessment framework no comparative step is anticipated. However, cross-tables (see Tables 13-16) have been made to give an impression of the distribution of positive and negative impacts over stakeholders and to show the transfers of effects over stakeholders to avoid double counting of costs. The tables show that the negative effects of the proposed measure fall on the manufacturer of azole-based pesticides, farmers and consumers (tax payers) and potential positive effects could occur for patients, public health sector and NGOs. The overall balance of costs and benefits for society as a whole cannot be given based on the provided analysis, therefore, further (quantitative) analysis would be required.

*Table 13: Costs: Distribution and transfer of impacts*

| **Impact** | **Distribution and transfer of impacts over different stakeholders** | | | | | | | | | **Total** |
|---|---|---|---|---|---|---|---|---|---|---|
| | Pharmaceutical industry | Manufacturer of azole based antifungal agents | Farmer | Retail | Patient | Public health sector | Government | Consumers (tax payers) | NGO | |
| ***Costs*** | | | | | | | | | | |
| Crop losses and decrease of overall yield | | | - | | | | | | | **-** |
| Import of crops | | | | - | | | | | | **-** |
| Higher food prices | | | | + | | | | - | | **0** |
| Loss of jobs | | | - | | | | | | | **-** |
| Loss of antifungal sales | | - | + | | | | | | | **0** |
| Loss of profit antifungal sales | | - | | | | | | | | **-** |
| Increased health care costs for remaining life years recovered patients | | | | | | - | | | | **-** |
| Increased public health spending | | | | | | + | - | | | **0** |
| Increase in premium for health care insurance | | | | | | | + | - | | **0** |
| Increased earnings due to increase in labour productivity of recovered patients | | | | | + | | | | | **+** |

| **Impact** | **Distribution and transfer of impacts over different stakeholders** | | | | | | | | | **Total** |
|---|---|---|---|---|---|---|---|---|---|---|
| | Pharmaceutical industry | Manufacturer of azole based antifungal agents | Farmer | | Patient | Public health sector | Government | Consumers (tax payers) | NGO | |
| Increase in welfare benefits for ex-patients that are (partially) unfit to work | | | | | | | - | | | **-** |
| Increase in premium for unemployment insurance | | | | | | | + | - | | **0** |
| Change in volume and subsequent profit of antifungal medicine sales | ? | | | | | | | | | **?** |
| **Balance** | **?** | **-** | **-** | **0** | **+** | **0** | **0** | **-** | | **?** |

*Table 14: Health: Distribution and transfer of impacts*

| **Impact** | **Distribution and transfer of impacts over different stakeholders** | | | | | | | | | **Total** |
|---|---|---|---|---|---|---|---|---|---|---|
| | Pharmaceutical industry | Manufacturer of azole based antifungal agents | Farmer | Retail | Patient | Public health sector | Government | Consumers (tax payers) | NGO | |
| ***Health*** | | | | | | | | | | |
| Potential reduced mortality and morbidity of Aspergillus diseases | | | | | + | | | | | **+** |
| **Balance** | **0** | **0** | **0** | **0** | **+** | **0** | **0** | **0** | **0** | **+** |

*Table 15: Society: Distribution and transfer of impacts*

| **Impact** | **Distribution and transfer of impacts over different stakeholders** | | | | | | | | | **Total** |
|---|---|---|---|---|---|---|---|---|---|---|
| | Pharmaceutical industry | Manufacturer of azole based antifungal agents | Farmer | Retail | Patient | Public health sector | Government | Consumers (tax payers) | NGO | |
| ***Society*** | | | | | | | | | | |
| Potential decrease of the emotional impact of suffering and premature death from aspergillosis | | | | | + | | | | | **+** |
| Decreased concern about azole resistance | | | | | | | | | + | **+** |
| Loss of jobs | | | - | | | | | | | **-** |
| Increase of ex-patients available for the labour market | | | | | + | | | | | **+** |
| Loss of business case to develop new, non-azole based antifungal agents | - | | | | | | | | | **-** |
| Emotional impact of reduced yield, loss of market share and economic consequences | | | - | | | | | | | **-** |
| Less perceived health risks about the use of pesticides | | | + | | | | | + | | **+** |
| Potential increased emotional impact of work | | | | | | + | | | | **+** |

| Impact | Distribution and transfer of impacts over different stakeholders | | | | | | | | | Total |
|---|---|---|---|---|---|---|---|---|---|---|
| Increased societal concern regarding food prices and available choices | | | | | | | | - | | - |
| Less perceived health risks about the use of pesticides | | | + | | | | | + | | + |
| Potential increased emotional impact of work | | | | | | + | | | | + |
| Increased societal concern regarding food prices and available choices | | | | | | | | - | | - |
| **Balance** | **-** | **0** | **?** | **0** | **+** | **+** | **0** | **?** | **+** | **?** |

*Table 16: Environment: Distribution and transfer of impacts.*

| Impact | Distribution and transfer of impacts over different stakeholders | | | | | | | | | Total |
|---|---|---|---|---|---|---|---|---|---|---|
| | Pharmaceutical industry | Manufacturer of azole based antifungal agents | Farmer | Retail | Patient | Public health sector | Government | Consumers (tax payers) | NGO | |
| ***Environment*** | | | | | | | | | | |
| Decreased concern regarding azole pesticides | | | + | | | | | | + | + |
| Less ecological toxicity as a result of fungicide application | | | + | | | | | | | + |
| Increased use of area for agriculture to compensate lower crop yield | | | - | | | | | | | - |
| **Balance** | | **0** | **?** | **0** | **0** | **0** | **0** | **0** | **+** | **?** |

## 8.3 Case study lead

Recent RIVM research has shown that the current dietary exposure of young children to lead in the Netherlands may give rise to a potential health concern with respect to their neurodevelopmental development (Boon, te Biesenbeek et al. 2017). This concern may be removed by reducing lead levels in food by re-evaluating current food safety standards (EU Maximum Limits (MLs)) for lead in food. Such a policy decision, however, requires the costs and benefits to be carefully balanced. An SEA may assist in such a policy decision.

In this case study, an SEA was performed on the effect of a policy decision to reduce the intake of lead by young children in the Netherlands to a level which complies with EFSA's benchmark for lead exposure (EFSA 2012).

### 8.3.1 *Step 1 Problem and context analysis*

*Description of the current situation*

Being an environmental contaminant which is present in soil, lead is taken up by plants and transported to the consumable parts of crops. Lead may also be ingested by animals via soil ingestion or contaminated animal feed such as grass. In this way, lead may be transferred to edible products such as meat or milk.

Food, drinking water, and ambient air are the major sources of the human exposure to lead (EFSA 2012). In addition, in contaminated areas, children may be exposed to lead via soil and dust, in particular in contaminated urban areas. However, in general, exposure via food is the most important route of exposure. EFSA (2010; 2012) identified neurodevelopmental toxicity in young children as a critical effect for the risk assessment of lead. In the case of young children, the EFSA concluded that the dietary exposure was such that the possibility of an effect from lead cannot be excluded.

In the Netherlands, the dietary exposure of young children to lead has recently been determined by Boon, te Biesenbeek et al. (2017). The results of this analysis, which are presented in Table 17, confirm the EFSA's conclusion that the current exposure of Dutch children exceeds EFSA's exposure benchmark of 0.50 µg/kg body weight per day[1] as set for developmental neurotoxicity by a factor of maximally 2. The exposure was found to be diffuse, i.e. to arise from many food products. The food groups that contributed more than 10% to the total exposure were 'grains and grain-based products' (22%), 'fruit and fruit products' (16%), 'milk and dairy products' (16%) and 'vegetables and vegetables products'(10%). Together, these food groups contributed in total 64% to the total exposure. Reducing the MLs of these food groups will be most effective in reducing the total dietary exposure to lead.

[1] This benchmark corresponds with a 1 point decrease in the IQ score

*Table 17: The median[1] age-dependent long-term dietary intake of lead (µg/kg bw per day) in children aged 2 to 7 (EFSA's exposure benchmark; 0.50 µg/kg bw per day[2] (Boon, te Biesenbeek et al. 2017).*

| Median age | Intake of lead (µg/kg bw per day) |
|---|---|
| 2 years | 1.00 (95% CI 0.99-1.20) |
| 3 years | 0.96 (95% CI 0.88-1.10) |
| 4 years | 0.88 (95% CI 0.82-0.99) |
| 5 years | 0.81 (95% CI 0.76-0.93) |
| 6 years | 0.74 (95% CI 0.69-0.83) |
| 7 years | 0.76 (95% CI 0.73-0.82) |

[1] Medium bound scenario: undetected samples were assigned a lead concentration equal to half the relevant analytical limit value.
[3] $BMDL_{01}$ values, i.e. 95$^{th}$ percentile lower confidence limit of the benchmark dose of 1% extra risk

The maximum limits (MLs) for lead are set in Commission Regulation (EC) No. 1881/2006. These MLs are regularly evaluated to keep the intake of lead, and other contaminants, controlled As Low As Reasonably Achievable (the ALARA principle). Current MLs for lead vary between 0.02 mg/kg for raw milk products and 1.5 mg/kg for molluscs. Fruit, vegetables and cereals have MLs between 0.1 and 0.3 mg/kg. Comparison of the monitoring data used to assess the exposure to lead in children (Table 17) with the MLs showed that most of the samples had substantially lower lead concentrations than the current EU MLs (see Table 18). Note that even though the monitoring data were well below the EU MLs, the corresponding intake in children aged 2 to 7 exceeded EFSA's human exposure benchmark for developmental neurotoxicity, thereby illustrating that MLs are not based on the toxicity of the contaminant. Consequently, when the concentration of a contaminant like lead in food is lower than the relevant MLs, the intake may still result in a potential health concern.

*Table 18: EU maximum limits (MLs) and monitoring results as used in Dutch intake calculations of children (Boon, te Biesenbeek et al. (2017)*

| Food category | ML (mg/kg) | Concentration (mg/kg) used in intake calculations |
|---|---|---|
| Raw milk products | 0.2 | 0-0.011 |
| Fruit/vegetables | 0.1 | 0-0.047 (fruiting vegetables)<br>0.016-0.060 (leaf vegetables)<br>0.005-0.013 (legume vegetables) |
| Cereals | 0.3 | 0-0.179 (bread, breakfast cereals, rice, etc.) |

In summary, there may be a potential health concern about the dietary lead exposure of young children in the Netherlands. Reducing such exposure needs a policy decision to be taken to lower lead levels in food. An SEA can provide valuable information to assist in such a decision.

*Concern appraisal and relevant stakeholders*
The EFSA has derived benchmark exposure levels for developmental neurotoxicity (0.50 µg/kg bw/day) to assess health risks related to the dietary exposure to lead (EFSA 2010). In Boon, te Biesenbeek et al. (2017) this toxicity limit was used to calculate margins of exposure

(MOEs) related to the median (P50) and high (P95) intake of lead in the relevant population groups. At the MOEs for neurodevelopmental effects for both exposure estimates, the risk was considered to be low in young children, 'but not such that it could be dismissed as of no potential concern' (EFSA 2010) (see Table 19).

*Table 19: Estimated margins of exposure for the median and P95 long-term exposure to lead in children aged 2 to 6, children aged 7 and adults living in the Netherlands (Boon, te Biesenbeek et al. 2017).*

| **Population and endpoint**[a] | **Margin of exposure** | |
|---|---|---|
| | Median | High |
| *Children aged 2 to 6* | | |
| Developmental neurotoxicity | 0.57 [0.51-0.60] | 0.38 [0.33-0.42] |
| *Children aged 7* | | |
| Development neurotoxicity | 0.66 [0.61-0.68] | 0.38 [0.36-0.42] |

Note: Between brackets, the MOEs corresponding with the 2.5% lower and 97.5% upper confidence limit of the medium bound estimates of exposure are reported.
[a] For developmental neurotoxicity, the MOEs were calculated by dividing the $BMDL_{01}$ of 0.50 µg/kg bw per day by the dietary exposure estimates in children aged 2 to 6 (overall) and 7.

Identified relevant stakeholders are:

- Farmers (farmers are considered stakeholders as they produce crops containing certain levels of lead)
- Retail (retail is involved as downstream stakeholder in the supply chain of crops)
- Consumers (consumers are involved as they are the final stakeholders in the supply chain)
- Government: Inspection agencies (inspection agencies could intensify monitoring actions)

There is currently no scientific discussion or ambiguity about the toxicity of lead. Furthermore, there is a scientific consensus about the causal relationship between lead exposure and adverse developmental neurotoxic effects. No information was found about the specific stakeholders' concern regarding the health impact of lead, other than that all stakeholders consider lead to be a hazardous environmental contaminant. Therefore, a more thorough stakeholder assessment was not required.

*Description of potential policy scenarios*

Lead is found in crops grown on soil contaminated with lead. Soil plays a central role in food safety as it determines the composition of food and feed at the very start of the food chain. In 2015, concentrations of lead in soil of the first harmonised topsoil sampling and coherent analytical procedure of approximately 22,000 locations in Europe were published. This collection provides a reliable overview of the concentration of lead (and other heavy metals) in agricultural areas (Tóth, Hermann et al. 2016). The study showed that lead contamination is widespread with some relatively high concentrations in central Italy, France, Germany and the UK (from previous heavy industry or volcanic activity). Lead contamination of agricultural soil is widespread in the Netherlands too,

without high variability or 'hotspots' (not taking into account the high soil lead concentrations in urban areas).

To reduce lead levels in food items, two general policy options exist. In the first (hypothetical) option, crop growth and animal husbandry are limited to soil with low lead concentrations, or growth should only be allowed on sanitised soil. The other, more realistic option is to only allow food items with sufficiently low lead levels on the market.

Three policy scenarios could be considered to reduce the lead levels in food:

- Remediation of topsoil
- Setting/lowering maximal levels of lead in topsoil for agricultural land
- Lowering maximal levels of food and feed items

8.3.2 *Step 2: Identification of dominant risk type*

In this step, the Assessment Team selects a dominant risk type that is assumed to best suit the case at hand considering the information gathered in Step 1. There is scientific and societal consensus about the relationship between lead exposure and the hazardous effects, in particular neurodevelopmental neurotoxicity.

Considering the above, Type 1 risk is chosen as the dominant risk type.

8.3.3 *Step 3: Goal and scope definition of the assessment*

The purpose of this assessment is to show the effect of revising current EU MLs for lead on the development of neurodevelopmental toxicity in young children (increase in IQ score), their corresponding educational level later in life (increase in high school grade) and, ultimately, their expected yearly earnings at adult age.

*Definition of Business as usual scenario*

Currently, Dutch monitoring data in fruits, vegetables, milk and cereals showed lead concentrations as mentioned in Table 20.

*Table 20: Overview of the lead concentrations from Dutch monitoring data (Boon, te Biesenbeek et al. 2017).*

| **Food (group)** | **No. of samples (no. of non-detects)** | **Concentration (mg/kg)** | | |
|---|---|---|---|---|
| | | **LB** | **MB** | **UB** |
| *Dutch monitoring data* | | | | |
| *Grouped foods* | | | | |
| Fruiting vegetables | 172 (172) | 0 | 0.023 | 0.047 |
| Grain milling products | 39 (32) | 0.01 | 0.019 | 0.028 |
| Leaf vegetables | 216 (190) | 0.016 | 0.038 | 0.060 |
| Legume vegetables | 8 (5) | 0.005 | 0.009 | 0.013 |
| Legumes, beans, dried | 20 (1) | 0.030 | 0.031 | 0.032 |
| Miscellaneous fruits | 24 (7) | 0.022 | 0.022 | 0.023 |
| Pome fruits | 58 (33) | 0.006 | 0.020 | 0.034 |
| Root vegetable | 34 (29) | 0.018 | 0.039 | 0.06 |

| Food (group) | No. of samples (no. of non-detects) | Concentration (mg/kg) | | |
|---|---|---|---|---|
| | | LB | MB | UB |
| Stem vegetables | 11 (7) | 0.009 | 0.022 | 0.036 |
| Biscuits | 2(0) | 0 | 0.025 | 0.5 |
| Bread | 7(0) | 0 | 0.025 | 0.5 |
| Breakfast cereals | 2(1) | 0.179 | 0.179 | 0.179 |
| Macaroni/spaghetti/noodles | 2(0) | 0 | 0.025 | 0.5 |
| Muesli | 2(1) | 0 | 0.025 | 0.054 |
| Rice | 2(0) | 0 | 0.025 | 0.050 |
| Rye products | 1(0) | 0 | 0.025 | 0.050 |
| Milk | 66(66) | 0 | 0.053 | 0.011 |

As already mentioned, EU maximum limits (MLs) were set in Commission Regulation (EC) No. 1881/2006. Current lead exposure results in an intake of 0.5- 1.0 µg/kg bw/day Which is equal or 2x higher compared to the EFSA limit of 0.5 µg/kg bw/day. Lead is a common environmental contaminant and, with current policy and land use, lead exposures are not expected to decrease in the near future.

*Selection of policy scenario*
For this case study, the most practical, though hypothetical, policy scenario was chosen, i.e. a lowering of the MLs of lead in food and feed items in such a way that they lead to an exposure of young children which complies to EFSA's toxicity limit set for developmental neurotoxicity. This policy scenario has a direct relationship with the overall aim of the policy scenario, the reduction of lead exposure via food. Obviously, the lowering of Maximal Limits (MLs) will result in food items which cannot be marketed anymore. Note that this will lead to a decrease in the number of farmers who comply with the newly-set MLs and/or might have effects on food prices.

Lowering MLs will result in a higher number of lead-containing food items which cannot enter the market. Hence, this will lead to a decrease in exposure and, consequently, an increase in health. However, as the dietary lead exposure is diffuse, revising MLs anyway is complex. One possible scenario to reduce the exposure might be to selectively remove food items from the market which contribute most to the exposure. For example, taking the distribution of lead in fruits, vegetables, milk and cereals as the starting point, all items exceeding a set cut-off value would have to be removed from the market. The cut-off values then have to be chosen in such a way that the exposure of young children arrives at EFSA's toxicity limit for developmental neurotoxicity.

*Most suitable assessment methodology*
In this case study, the dominant risk type was considered to be a simple risk, as there seems to be both scientific as well as societal consensus about the adverse health effects of lead exposure. No indications of significant ambiguity have come forward and the data indicate a limited role for complexity and uncertainty surrounding the impacts, at least for the health impact.

An appropriate first tier framework would be to start with a qualitative investigation of the relevant impacts, although available quantitative information can be used in this arena as well. This will provide a first impression of the relevant multidisciplinary information that can serve as a basis for further policy as it increases transparency about the impacts considered.

The questions raised for the selection of a more extensive, second tier, assessment methodology are:

d) What level of scrutiny for the assessment is appropriate/proportionate for the case at hand?
e) What level of stakeholder involvement is required/appropriate?
f) What level of assessment is possible considering the available data?
    a. Is quantification of the most important positive and/or negative impacts possible?
    b. Is monetisation of the most important positive and/or negative impacts possible?

In this case study, we chose to limit the analysis to a semi-quantitative analysis because of data availability of the health effects on one side and the resource constraints of this project on the other. Data was already available about the dietary lead intake of young children in the Netherlands and its relationship with IQ development and income loss in later life. Therefore, the societal benefits of the policy measure to lower the MLs to comply with EFSA's toxicity limit were calculated for children currently in the age range from 0-9 years. Resource and time constraints of this project did not allow quantification and monetisation of the main costs.

It is anticipated that if sufficient resources are available, the main costs can be calculated and a full societal cost-benefit analysis could be considered, including appropriate discounting of costs and benefits.

A less resource intense break-even analysis could also be considered as a second tier. In that case, the current approach would only need some small modifications to allow for discounting of the benefits and to include the benefits for the next generation of children as well as the current 0-9 year old children (see uncertainty). Such a break-even analysis would give an order of magnitude of the costs that are permissible for the policy measure to still be beneficiary for society as a whole.

*Clarification of scope of the assessment*
MLs are set in at the European level, however, monitoring and intake calculations refer to the Dutch situation. The scope of this assessment is, therefore, the Netherlands only. In this impact analysis, timing and discount issues have not been taken into account.

8.3.4 *Step 4: Impact assessment*
In this case study the benefits are calculated for a situation in which the dietary lead exposure of young children complies with EFSA's toxicity limit for neurodevelopmental toxicity.

In order to quantify the effect of setting EU MLs for lead as low as possible (detection limit), the following sequential steps were quantified for young children in the Netherlands:

1. The dietary intake of lead
2. The effect of dietary lead on lead in the blood (dietary lead ↓ => lead in blood↓).
3. The effect of a decrease in lead in blood on the IQ score (lead in blood ↓ => IQ ↑).
4. The effect of an increase of the IQ score on the educational level later in life (IQ ↑=> educational level ↑)
5. The relationship between an increase of the educational level and the expected yearly earnings at adult age (educational level ↑=> yearly earnings ↑).

Age dependent intake data for 0-7 year olds were taken from Boon, te Biesenbeek et al. (2017). These data were converted to lead in blood by means of the US-EPA Integrated Exposure Uptake Biokinetic model (US-EPA 1994a; US-EPA 1994b), resulting in an aggregated uncertainty distribution of lead in blood concentration of 0-7 year olds. In turn the simulated blood levels were converted to IQ using dose-response modelling as proposed by (EFSA 2010). Overall this resulted in a decrease of the IQ score of 1.7 points in 0-7 year olds. In exposed children the uncertainty of the IQ score therefore was characterised as normal ($\mu$=100-1.7; $\sigma$ = 15) and in non-exposed children as normal ($\mu$=100; $\sigma$ = 15). Both these distributions were used to calculate the fraction of the population corresponding with one of the following educational levels later in life:

*Table 21: The stratification of the Dutch elementary, secondary or higher educational level to IQ-range*

| **Level of Education** | **IQ - range** |
|---|---|
| Special Education (ZML)[1] | ≤75 |
| PraktijkOnderwijs (PO) | (75-85) |
| VMBO | (85 - 95) |
| VMBO/MBO | (95 - 105) |
| Bachelor | (105 - 115) |
| MSc/PhD | >115 |

[1]without certificate

As shown in Figure 11, the decrease in exposure of young children to dietary lead will, as expected, lead to a higher educational level.

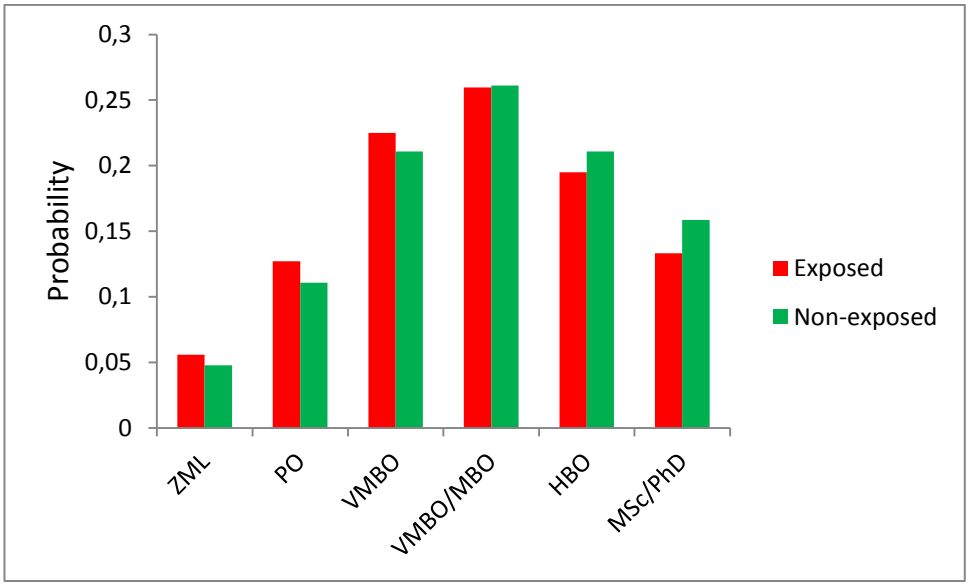



*Figure 11: The probability distribution of the educational level after exposure to dietary lead during childhood (exposed) or in the absence of such exposure (non-exposed).*

The probabilities shown in Figure 11 were combined with the expected yearly earnings corresponding to each educational level (see Table 22), resulting in the expected yearly earnings at adult age.

*Table 22: Expected yearly earnings of the Dutch educational levels (CBS 2011)*

| Level of Education | Expected Yearly Earnings (€) |
|---|---|
| ZML | 9,600 |
| PO | 11,400 |
| VMBO | 13,200 |
| VMBO/MBO | 16,200 |
| HBO | 25,200 |
| MSc/PhD | 30,000 |

Given a population size of 1.43 million young children in the Netherlands in 2016 this resulted in € 26.0 billion of yearly earnings in the case of childhood exposure to dietary lead and € 27.0 billion in the absence of such exposure. Overall the removal of the dietary exposure of young children to lead is expected to lead to an annual increase of yearly earnings of € 1 billion.

The calculated increase in earnings refers to an IQ loss of -1.7 points whereas the SEA focuses on an exposure which leads to an IQ loss of -1 point, i.e. EFSA's Point of Departure for neurodevelopmental toxicity in young children. The increase in yearly earnings corresponding with the latter is € 0.4 billion.

Clearly, the calculated increase in yearly earnings does not immediately occur when the decrease of the exposure to lead is enforced. This, of course, stems from the fact that the latter enforcement is effective during early childhood whereas the corresponding monetary effect occurs during the active working period, i.e. the time period of active income generation. Bounding the latter period by ages of 25 and 65

years and enforcing the decrease in the dietary exposure to early 2017 implies that the first monetary effect will become visible in 2035. From there on this effect will gradually increase until it reaches its full potency around 2075, i.e. an increase in yearly earnings of € 0.4 billion.

Furthermore, note that to guarantee a reduction of the dietary exposure of young children to the level of EFSA's toxicity limit for neurodevelopmental development, i.e. 0.5 µg/kg bw/day, needs EU MLs for lead in fruits, vegetables, milk and cereals to be lowered, which are the highest contributors to the total dietary exposure (together responsible for 64% of the exposure). To reduce the total dietary intake with MLs on raw milk, fruits, vegetables and cereals, MLs need to decrease by a factor 5 (see Table 23).

*Table 23: EU maximum limits (MLs) and proposed MLs*

| Food category | Current ML (mg/kg) | Proposed ML (mg/kg) |
|---|---|---|
| Raw milk products | 0.2 | 0.04 |
| Fruit/vegetables | 0.1 | 0.02 |
| Cereals | 0.3 | 0.06 |

The costs for lowering food lead levels are not quantified in this case study. However, the qualitative impacts on costs are considered in the following table:

*Table 24: Qualitative description of cost impacts of the proposed policy measure*

| Impact category | Description of impact |
|---|---|
| Economy | **Farmers and retail**<br>• Potential loss of profit within the supply chain (farmers and retail, crop losses). Most of these costs are passed on to the consumers, however some might be borne by the farmers<br>• Potential increase in import of crops from outside the Netherlands with low lead levels<br>• Potential increase of export of crops that cannot be sold in the EU to outside the EU<br><br>**Food Consumers**<br>• Increased cost for food consumption<br><br>**Government: Inspection Agencies**<br>• Potential increased inspection costs as a larger amount of food items are potentially not allowed on the market (it is unclear whether this leads to just a shift in inspection budget or to an increase in these costs) |
| Society | **Farmers**<br>• Loss of market share and increase in import of crops from outside the NL could lead to job losses in the agricultural sector in the NL. A |

| Impact category | Description of impact |
|---|---|
| | change in employment rate will affect social security and pensions.<br>• Increased emotional impact for economic impact based on reduced profit<br><br>**Food Consumers**<br>• Increased societal concern regarding food prices and available choices, economic impact on society |
| Environmental | **Farmers**<br>• Increased use of area for agriculture to compensate for the loss of food items on the market because of the stricter ML. |

Finally, the total benefits for reducing the lead exposure of young children would result 0.4 billion euros annually from 2035 and onwards. To realise this level of exposure, reduction costs are expected for farmers, retail, government inspections and subsequently consumers.

8.3.5 *Step 5: Uncertainty*

In the foregoing, the increase of the yearly earnings due to the decrease in dietary exposure to lead during early childhood was calculated at € 0.4 billion (point-estimate). Here it should be realised that this calculation refers to a reduction of the dietary intake in young Dutch children *currently* aged 0-7 years. Clearly if such decrease is applied permanently, i.e. is continued for about 2-3 decades, the entire adult population will consist of individuals who have all had a reduced exposure to dietary lead during early childhood. Given an estimated adult population size at that time to range from 15 to 20 million, the increase of the early earnings is expected to be at least one order of magnitude higher than € 0.4 billion.

Furthermore the calculation of the increase of the yearly earnings is prone to the following uncertainties:

1) Dietary intake of lead during early childhood
The dietary intake of lead during childhood was characterised by the median intake of 2-7 year olds. The uncertainty adhering to this intake is rather low, i.e. the P95/median intake ratio being 1.4 (Boon, te Biesenbeek et al. 2017).

2. Dietary lead and lead in blood
To convert the dietary intake to blood levels the US-EPA Integrated Exposure Uptake Biokinetic model (US-EPA 1994a; US-EPA 1994b) was used. This resulted in a log-normal uncertainty distribution of lead in the blood of 0-7 your olds (see Figure 12). Given that cut-off values for lead in blood correspond with IQ loss (see below) this distribution was used to calculate the fraction of blood values exceeding the set cut-off values. For example, as shown in Figure 12, 80.6% of the blood values exceeded the blood cut-off of 1.2 µg/dL, i.e. the EFSA cut-off corresponding with an IQ loss of 1 point. In a similar way fractions

corresponding to IQ losses of 2, 3, 4, 5 and 6 points were calculated. In all the expected IQ loss was calculated at -1.7 points (point-estimate).

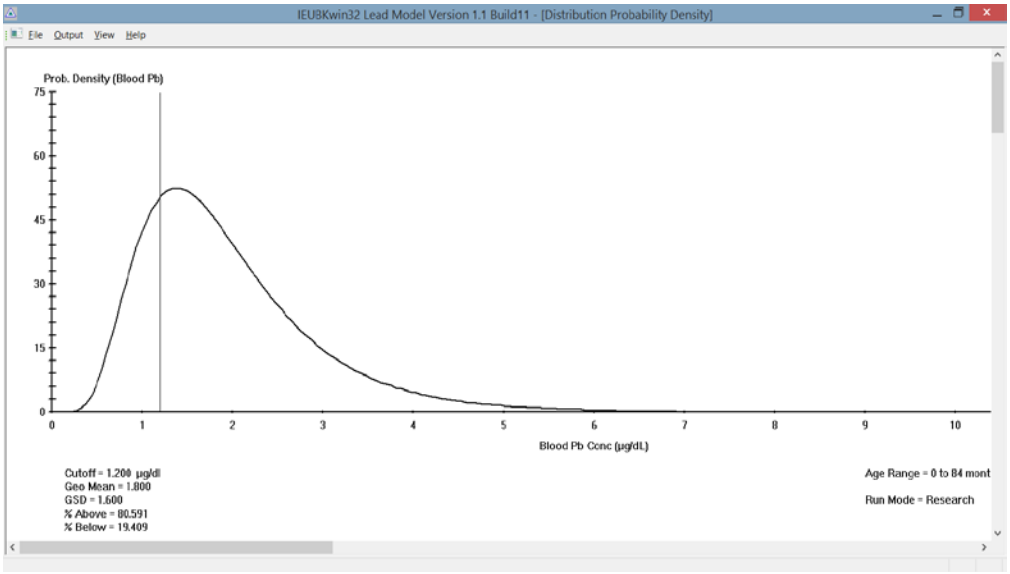



*Figure 11: The probability distribution of the educational level after exposure to dietary lead during childhood (exposed) or in the absence of such exposure (non-exposed).*

3. Lead in blood and IQ score

Lanphear, Hornung et al. (2005) found a quantitative relationship between lead in blood and the IQ score in young children (see Figure 13). The EFSA (2010; 2012) reanalysed this relationship and concluded that, up to a lead in blood concentration of 7 µg/dL, this relationship may be approximated by a linear relationship, with 1.2 µg lead/dL blood leading to a decrease in IQ of 1 point, i.e. a linear relationship with a slope factor -1/1.2 ≈-0.83 (point-estimate). The uncertainty adhering to this approach however is rather low, i.e. the P05/median and P95/median IQ ratios in the Lanphear analysis being smaller than 1.1.

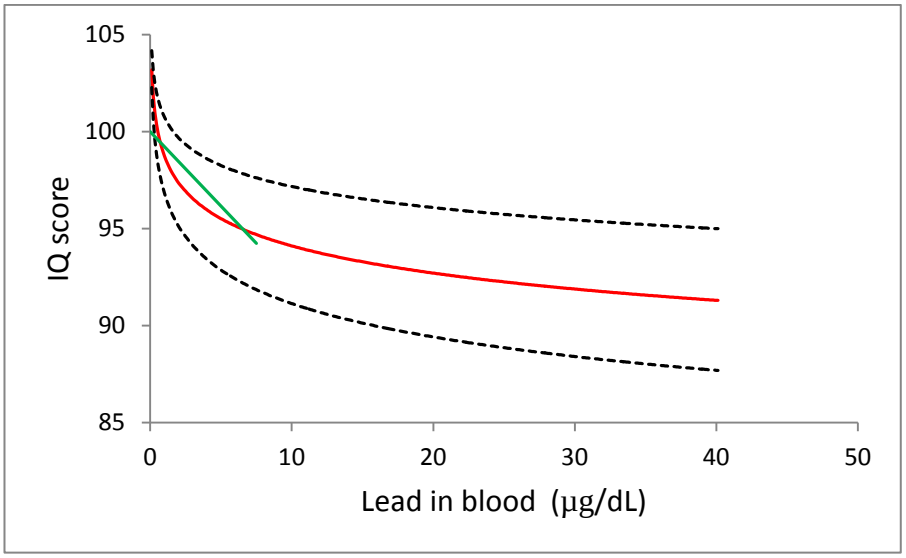



*Figure 13: The relationship between lead in blood and the IQ score of young children described by (Lanphear, Hornung et al. 2005). Median: red line, 95% confidence limits: black dotted lines, EFSA: green line.*

4. IQ score, educational level, yearly earnings and population dynamics. The present SEA used, as a default, Dutch 2017 data for the relationships between the IQ score, the educational level, yearly earnings and the (absolute) population size of young children. In this context the future time-trends of these entities were ignored.

8.3.6 *Step 6: Comparison of impacts*

The final assessment can compare the health impact with the economic impact of the policy measure. This step was not quantitatively performed in this case study due to time and budget restraints.

# 9 Conclusion and reflection

Policy measures related to chemical substances in food (e.g. food safety standards) are usually set based on a toxicological risk assessment. On some occasions, however, the proposed measure is questioned. This can be the case where there is a substantial economic impact expected for specific stakeholders, for example, if farmers cannot grow their crops in an economic efficient way. The food safety measure can also be questioned in cases where there is concern about proposed safety standard based on uncertainties in the risk assessment. Issues like combination toxicology, endocrine disruption and representativeness of animal toxicity studies for humans can create discussion among the stakeholders about the appropriateness of a limit value. Finally, there are situations in which there is no safe limit (non-threshold effects) value for a chemical present in food products (e.g. genotoxic carcinogens). In the above examples, the food safety standard can be questioned and lower or higher values can be proposed. In such cases, pure risk assessment might not provide all the relevant information for policy makers to make a well-founded decision. A socio-economic evaluation can be useful as it provides a broader basis of information to make well-informed and transparent policy decisions, incorporating various impacts of the proposed measure for society as a whole. The aim of this project was to develop an SEA framework to assess the impacts of food safety measures to serve (next to the more regular risk assessment) as underpinning for policy decisions. Our proposal for an assessment framework should be ambitious enough to instigate a discussion on the potential value of SEA in this field with the various actors involved, however, it should not be too ambitious as that might be too far away from current practice and could be too complicated to understand in terms of benefit for the field.

*Investigation part*
As part of the project an investigation was made of available SEA(-like) methodologies within the field of food and beyond, to see what is already available and what experiences could be used as the basis for the framework to be developed. In the field of food research, no experience with SEAs was found via a literature search or in response to a questionnaire sent to international scientists and scientific agencies dealing with chemical food safety. Actors, however, did express interest in the development of such a framework. The OECD organised a workshop on the Socioeconomic Impact Assessment of Chemicals Management in July 2016 aimed at identifying the current status of practice and methodologies for cost-benefit analysis of risk management measures and frameworks addressing the human health and environmental impacts of chemicals in OECD Member Countries (OECD 2016). This workshop confirmed the impression that an SEA in the field of chemicals in food is not yet under development and that experiences with SEAs mainly comes from other policy fields.

*Proposed SEATS framework*
The framework developed in this report has been based predominantly on experiences with SEAs in other fields. SEA methods and tools that

RIVM already had hands-on experience with provided the most important basis for the development and offered the possibility of incorporating lessons learned from SEA practice in other fields in the development of this new framework. These experiences show that, in the practice of SEA, there is a large focus on quantifiable impacts, although the importance of non-quantifiable impacts is also recognised. Cases that address uncertain or ambiguous risks could benefit most from less quantitative approaches, addressing issues such as social concern and risk perception and involving stakeholders in the assessment set up. It was recognised that risk issues in the context of food that could benefit from a broader SEA might very well be uncertain and/or ambiguous. SEATS is developed for food and therefore incorporates both the more quantitative SEA assessment methods and tools available, and the 'softer' aspects like social concern and risk perception by using the concept of risk governance defined by the IRGC.

*Case studies*
SEATS was tested on two cases studies, one on lead and one on the fungicides Triazoles. One case was categorised as a 'simple' risk issue (lead) and the other as an 'uncertain' risk issue (Triazoles). In this way, both the more quantitative and the more qualitative assessment routes were tested. The case studies revealed that SEATS is very helpful for setting up a structured SEA and arriving at a 'fit for purpose' analysis. The framework gives hands-on guidance and asks practical questions that help the actual analysis to be performed. The case studies done for this project were carried out with a limited level of detail, providing a first tier testing of the usefulness of SEATS.

*General remarks*
It is recognised that SEATS incorporates many steps and that a substantial amount of input data and decisions are required to come to a proper assessment. This is typical for an SEA, especially when an SCBA is chosen as the assessment tool. This might give problems in situations where data availability is limited. From the work in other fields, discussed in the OECD workshop in July 2016, it is clear that quantification and monetisation of health and environmental impacts can be particularly difficult as the data required is often not available. Within SEATS, other methods and tools are also incorporated that require lower data input (and resources) to come to an assessment. This gives rise to the question about what level of detail should be provided for the SEA and, in connection with this, what level of required resources is proportionate to the case at hand. This question is incorporated within SEATS to make sure that the assessment performed is fit for purpose. Besides that, it will be a case-by-case decision as to what level of resources and detail of the analysis is found appropriate for the case at hand, it can also depend on the policy context and what is deemed valuable and acceptable there. As SEA is new in the context of chemical food safety policies, there is currently no common opinion on when an SEA would be beneficial and at what level of detail.

# 10 Recommendations for further work

As a first step for follow up, SEAs could be performed for the more complex/uncertain/ambiguous cases that would benefit most from an SEA, for example for endocrine disruptive substances or substances with uncertain risks (glyphosate). Whether an SEA could also be beneficial for the more simple cases within chemical food safety can be left for later discussion. More elaborated testing of SEATS would be required to get better idea of its usefulness for performing SEA in the context of food regulation and to be able to further refine SEATS based on the experiences from case study practice. Furthermore, the idea of stakeholder involvement would require further testing to get better impression of what this would mean in practice and how and when this could be helpful for the decision-making process. Good practice examples of stakeholder involvement in the policymaking processes could be very helpful in this respect as well as having experts on stakeholder involvement available in the project team to develop a more extensive case study.

As said, currently, SEA has no basis in any chemical food safety legislation. Experiences from other fields show that a legal basis for SEA is very important to get SEA implemented in policy practice. It might even be a precondition for the implementation and further development of SEA. The start-up of a discussion among scientists, policy makers and other stakeholders in the field of chemical food safety would be required if we are get a better idea of how and when SEA could be helpful within this policy context. In such a discussion the pros and cons of SEA could be further clarified as well as providing a more solid, broad and transparent basis for decision-making. Performing SEAs also can require substantial resources and it can sometimes be questioned whether such resources are proportionate for the case at hand. Furthermore, performing an SEA takes time and could in, practice, also be used to delay and frustrate the policy making process. The current report could help to start such a discussion as it provides an impression of what an SEA in the context of chemical food safety regulation could look like in practice. Availability of more elaborated case studies however, could further help to start-up this discussion.

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# 12 List of Abbreviations

| | |
|---|---|
| ADI | Allowable Daily Intake |
| ALARA | As Low As Reasonably Achievable |
| Bw or b.w. | Body weight |
| BAU | Business as Usual scenario |
| BEA | Break-Even Analysis |
| BMD | Benchmark dose |
| BMDL | Benchmark dose lower bound level |
| BPR | Biocidal Product Regulation |
| CAC | Codex Alimentarius Commission |
| CARMA | Risk assessment of Campylobacter in the Netherlands via broiler meat and other routes |
| CEA | Cost Effectiveness Analysis |
| CPB/PBL | Economic Policy Analysis/Netherlands Environmental Assessment Agency |
| CUR | Cost-Utility Ratio |
| DALY | Disability-Adjusted Life Years |
| ECHA | European Chemical Agency |
| EFSA | European Food Safety Authority |
| EU | European Union |
| FAO | Food and Agricultural Organization |
| GM | Genetically modified |
| FRAC | Fungicide Resistance Action Committee |
| GMO | Genetically modified organism |
| IA | Impact Assessment |
| IP | Identity Preserved |
| IRGC | International Risk Governance Council |
| IVM | Institute for Environmental Studies |
| JRC | Joint Research Centre |
| LB, MB, UB | Lower bound, Medium bound, Upper bound |
| MCA | Multi-Criteria Analysis |
| ML | Maximum Limit |
| MOE | Margin of Exposure |
| MRL | Maximum Residue Limit |
| NGO | Non-governmental organisation |
| OCW | Ministry of Education, Culture and Science |
| OECD | The Organisation for Economic Co-operation and Development |
| PBT | Persistent, Bioaccumulative and Toxic |
| PPP | Plant Protection Products |
| PPPR | Plant Protection Products Regulation |
| PS | Policy Scenario |
| QMRA | Quantitative Microbiological Risk Assessment |
| REACH | Registration Evaluation, Authorisation and Restriction of Chemicals |
| SCBA | Social Cost-Benefit Analysis |
| SEA | Socio-Economic Assessment |
| SEAC | Socio-Economic Analyses Committee |
| SZW | Ministry of Social Affairs and Employment |
| TDI | Tolerable Daily Intake |
| US EPA | United States Environmental Protection Agency |

| | |
|---|---|
| VWS | Ministry of Health, Welfare and Sports |
| WHO | World Health Organization |
| WRR | Dutch Scientific Council for Governmental Policy |
| WTP | Willingness to Pay |

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# 14 Appendices

## 14.1 Appendix 1 Literature search

Details about the literature search
Database: MEDLINE 1950 to present, MEDLINE In-Process & Other Non-Indexed Citations
Search Strategy:

1 (pesticide* or herbicide* or insecticide* or fungicide* or rodenticide* or biocide* or plant protection products or insect repellents or pesticide* residues or pesticide synergists or chemosterilants).ti. (34105)
2 (food contact materials or (materials and contact and food) or additives or food additives or food preservatives or feed additives or flavors or food enzymes or stabilizers or food packaging materials or e-numbers).ti. (4627)
3 (veterinary medicines or veterinary drugs or drug residues or antimicrobial residues or natural toxins or feed contaminants or food contaminants).ti. (812)
4 exp *pesticides/ or *pesticide residues/ or *pesticide synergists/ or *herbicides/ or *insecticides/ or *fungicides/ or *rodenticides/ or *disinfectants/ or exp *food additives/ or *food preservatives/ or *food packaging/ or *flavoring agents/ or *food contaminants/ or *food contamination/ or *veterinary drugs/ or *drug residues/ or *toxins, biological/ or exp *mycotoxins/ (260809)
5 1 or 2 or 3 or 4 (269458)
6 (policy or standards or limits or norms or regulatory or regulation* or legislative or legislation or (valuation and risk*) or banning or bans or ban or (reduc* and risk*) or measures).ti. (371137)
7 (food safety standards or residue limit* or ((maximal or maximum) and (limit* or level*)) or migration limit* or allowable concentration*).ti. or (food safety standards or residue limit* or ((maximal or maximum) and (limit* or level*)) or migration limit* or allowable concentration*).kw. or maximum allowable concentration/ (9240)
8 public policy/ or policy/ or health policy/ or public health/ or public health practice/ or government regulation/ or environmental pollution/lj or environmental exposure/lj or food safety/lj or consumer product safety/lj or food contamination/lj or food packing/lj or legislation, food/ or food industry/lj or food industry/st or guidelines as topic/ (195137)
9 risk assessment/ or pest control/me, st or weed control/me, st or exp pesticides/st or food safety/st or food additives/st or flavoring agents/st or drug residues/st or pesticide residues/st (193479)
10 5 and (6 or 7 or 8 or 9) (11799)
11 (cost benefit* or benefit-cost* or cost beneficial or cost effect* or cost utilit* or cost efficien* or cost efficac* or econom* or pharmacoeconomic*).ti. (62810)
12 (cost benefit* or benefit-cost* or cost beneficial or cost effect* or cost utilit* or cost efficien* or cost efficac* or econom* or pharmacoeconomic*).kw. (25773)

13 (cost* and (effect* or benefit* or beneficial or quality or efficien*)).ti. (29351)
14 (economic evaluation* or economical evaluation* or economic analysis or economic study or economic studies).tw. (11386)
15 cost-benefit analysis/ or costs-and-cost analysis/ (105961)
16 models, econometric/ or models, economic/ (11117)
17 (socio-economic* or socioeconomic* or societal cost or societal costs or (costs and society) or multicriteria analysis or multi-criteria analysis or health impact or impact assessment or public health evaluation or impact).ti. (150294)
18 socioeconomic factors/ or multicriteria analysis.tw. or multicriteria analysis.kw. (123450)
19 pest control/ec or weed control/ec or exp pesticides/ec or legislation, food/ec (645)
20 10 and (11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19) (304)
21 20 and (english or dutch).lg. (289)
22 (detection or screening or chrormatography or spectrometry or hplc or fluorescence or column).ti. (438826)
23 21 not 22 (286)
24 remove duplicates from 23 (274)

## 14.2 Appendix 2 Questionnaire

14.2.1 *Questions*

In addition to the literature, there could be initiatives and experiences in the working field that have not been published in peer-reviewed journals and that, as a consequence, were not retrieved in the literature search. A questionnaire was therefore prepared to ask contacts in the field of food safety to share any information on initiatives regarding SEA in the area of chemical food safety. The questionnaire was sent by email in the period February to June 2016 to 41 (inter)national scientists from 21 institutes over the world (see table A1). The contact persons were asked if they knew about initiatives and if so to provide information on:

- Aim and the Scope of the assessment method
  - *Please describe the aim and the scope of the method and in which framework the method is used.*
- General description of the assessment method
  - *Which general parts are assessed in the method (e.g. human health, impact on applicants, impact on consumers)?*
  - *Please describe the steps of the process, which data is needed and where does it come from.*
  - *What conclusions can be drawn from the assessment method?*
- Recommendations for development of a new method.
- What recommendations could you give us for the development of a new method?

A short summary of the responses is shown in Table A2.

*Table A1: List of reactions received from the institutes*

| | Country | Institute | Reaction received (Y/N) | Valuable for project (Y/N/Partially) |
|---|---|---|---|---|
| 1 | DE | BfR | N | - |
| 2 | DE | BVL | Y | N |
| 3 | FR | ANSES | Y | P |
| 4 | UK | HSE/CRD | N | - |
| 5 | UK | Imperial College London | N | - |
| 6 | UK | Loughborough University | Y | N |
| 7 | UK | Independent consultant | N | - |
| 8 | IT | University of Milano | N | - |
| 9 | DK | Danish EPA | Y | P |
| 10 | DK | DTU | Y | N |
| 11 | USA | EPA | Y | P |
| 12 | CAN | Health Canada | N | - |
| 13 | AUS | APVMA | Y | P |
| 14 | - | WHO | Y | P |
| 15 | - | FAO | Y | N |
| 16 | EU | EFSA | Y | N |
| 17 | NL | NVWA | N | - |
| 18 | NL | University of Utrecht | Y | N |
| 19 | EU | ECHA | Y | N |
| 20 | EU | ECPA | N | - |
| 21 | - | OECD | Y | P |

*Table A2. Short summary of literature, websites, presentation and initiatives offered from (inter) national scientists via the questionnaire.*

| | Title | Date |
|---|---|---|
| 1 | Food Standards Application Handbook 2016 | March 2016 |
| 2 | Consumer's awareness, attitudes and behaviours towards food fortification in Australia and New Zealand. | December 2013 |
| 3 | Griffiths et al. What to do at low doses: A bounding approach for economic analysis | 2002 |
| 4 | Olsson et al. The Cost of Inaction – A socioeconomic analysis of costs linked to effects of endocrine disrupting substances on male reproductive health. | 2014 |
| 5 | Guide for costing illnesses and valuing health outcomes. – A guide by the Centre for Health Economics Research and Evaluation for Food standards Australia New Zealand. | 2015 |
| 6 | Ter Burg et al. A first exploration of health impact assessment of chemical exposure: | June 2014 |

| | | |
|---|---|---|
| | Assigning weights to subclinical effects based on animal studies. | |
| 7 | SEAC background document Bisphenol A. | December 2015 |
| 8 | Presentation: Benefit-Cost Analysis and Risk assessment. Chris Dockins US EPA | - |
| 9 | Presentation: The use of socio-economic analysis (SEA) within the REACH regulation. Rob Jongeneel RIVM | March 2013 |
| 10 | RIVM Report: Health impact assessment in REACH restriction dossiers – Development of a structured HIA format. Jongeneel et al. | 2014 |
| 11 | OECD report: The cost of air pollution – Health impacts of road transport. Roy et al. | 2014 |
| 12 | ECHA – Guidance on Socio-Economic Analysis – Restrictions | May 2008 |
| 13 | Final assessment report RED 3 Erythrosine in food colouring preparations. | May 2010 |
| 14 | Anses report: Improving effectiveness of consumer information and prevention of microbiological risks in food. | 2015 |
| 15 | Website: The social at ANSES. https://www.anses.fr/en/content/social-sciences-anses | - |
| 16 | EPA Report: Benefits and costs of the clean air act, 1970 to 1990, 1990 to 2010 and 1990 to 2020 | 2011 |

**RIVM**
*De zorg voor morgen* begint vandaag