



Aspects of Risk-Benefit Assessment of Food Consumption

Directions for the future

Salomon Sand, Wulf Becker & Per Ola Darnerud

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Content

Preface.....	7
Summary	9
1. Introduction	11
2. Specific seminar topics.....	13
2.1 Nordic risk-benefit assessments of fish consumption.....	13
2.1.1 The Danish Assessment	13
2.1.2 The Finnish Assessment.....	15
2.1.3 The Norwegian Assessment	17
2.1.4 The Swedish Assessment	19
2.1.5 Summary of the risk-benefit approaches	21
2.2 Risk-benefit assessments of fish consumption in Belgium.....	22
2.3 A common scale for assessing risks and benefits; summary measures of population health.....	24
2.4 EFSA activities on risk-benefit assessment.....	26
2.5 Future advancements in toxicity testing and its possible implications	28
3. Discussion	31
4. Conclusion.....	37
Sammanfattning.....	39
Appendix I: Seminar programme	41
Appendix II:Seminar participants.....	43

Preface

Risk-benefit assessment in the food area has gained interest during recent years in Europe. In line with this development, the Swedish National Food Administration, with support from the Nordic Council of Ministers, arranged a seminar on this topic with the title "Aspects of Risk-Benefit Assessment of Food Consumption - Directions for the Future".

The purpose of the seminar was to provide an overview of methods that have been applied for risk-benefit analysis, and investigate the possibility to establish a common view, among the Nordic and Baltic countries, for how to proceed with work regarding risk-benefit assessment of food products. To this end, the idea was to gather representatives from each of the countries, together with internationally recognized experts. As a starting point, it was suggested that participating countries that have recently conducted risk-benefit assessments inform about the approaches they used, and the results of the analyses. The intention was also that invited experts are given the opportunity to present scientific work they have performed in the area of risk-benefit analysis. The focus lies on the conceptual and methodological level. Background information given in this respect provides a basis for discussions at the seminar that aim to result in conclusions regarding use of the risk-benefit approach in the food sector, and suggestions of future steps in the area.

The Uppsala seminar working group consisted of Salomon Sand, Wulf Becker, and Per Ola Darnerud, all from the National Food Administration, Sweden.

Summary

The National Food Administration arranged a seminar on risk-benefit analysis during the autumn of 2007. The seminar was held on October 18–19 in Uppsala, Sweden, and was funded by the Nordic Council of Ministers. The purpose was to provide an overview of methods that have been used for risk-benefit analysis, and to discuss the possibilities for future applications of this approach in the food area.

Experts from the National Food Administration and other Swedish organizations, the other Nordic countries, and the Baltic countries were present. At the seminar, invited speakers presented scientific work performed in the area. Risk-benefit activities in the Nordic countries concerning fish consumption were also summarised, and an organised discussions regarding risk-benefit analysis in the food area was held.

It was concluded that risk-benefit assessment requires collaboration between different areas, and an important aspect concerns the development of common scales according to which different types of positive and negative health effects can be compared. DALYs (disability-adjusted-life-years) is an example that has a history of use for calculations of Burden of Disease, but it was recognized that other measures should also be considered. EFSA has a leading role in Europe, and they have established a working group on risk-benefit analysis. It was discussed that risk-benefit analysis is useful in certain areas, and a number of suggestions were made in this respect, e.g. beneficial effects of fruit and vegetables versus intake of pesticides. Comparison of different cooking procedures was also suggested as a possible application.

1. Introduction

The National Food Administration organized a seminar on risk-benefit analysis in 2007. The two-day seminar was held on October 18–19 at Atrium Konferens in Uppsala, Sweden, and was funded by the Nordic Council of Ministers. The purpose was to provide an overview of methods that have been applied for risk-benefit assessment, and to discuss advantages, limitations, and future strategies for use of the risk-benefit approach in the food sector. In total, 60 experts from the National Food Administration and other Swedish organizations, the other Nordic countries, and the Baltic countries were present at the seminar. Invited speakers from Europe and Canada held presentations during the first day. On the second day, risk-benefit activities in the Nordic countries concerning fish consumption were presented. Participants also performed discussions in groups, which later were summarised in plenary and used as basis for establishing the conclusions of the seminar.

Risk-benefit activities in the food sector have so far mostly been directed to the analysis of positive and negative effects of fish consumption. Several scientific publications have been presented on this issue and assessments have been made by central institutions in the Nordic countries; the Danish Veterinary and Food Administration, the Finnish Food Safety Authority, the Norwegian Scientific Committee for Food Safety, and the Swedish National Food Administration. Efforts have also been made by other central organisations, including the Scientific Advisory Committee on Nutrition and the Committee on Toxicity in England. While the risk-benefit evaluations of fish consumption have been mostly qualitative in their nature, there are also some examples of quantitative approaches employed in the area, which for example has been conducted at the Harvard Centre for Risk Analysis. These latter investigations have made use of so-called summary measures of population health to compare risks and benefit on an integrated scale. The use of such measures was also discussed at the Uppsala seminar. Moreover, an overview of the activities conducted by the European Food Safety Authority (EFSA) was given, and initiatives in the U.S. regarding future strategies for toxicity testing were presented.

Below follows a summary of the specific activities and topics at the Uppsala seminar. A summary of the discussions at the meeting, and the conclusions of the seminar are also given. The seminar programme and the list of participants at the seminar can be found in Appendix 1 and 2, respectively.

2. Specific seminar topics

2.1 Nordic risk-benefit assessments of fish consumption.

During the seminar an overview of the Nordic risk-benefit assessments of fish consumption was given by Dr Sand. There are specific reports that summarize the investigations made in Denmark, Norway, and Sweden, and each of these reports can be retrieved from the website of the responsible authority. A common feature of the risk-benefit analyses made by the Nordic countries is that the positive and negative aspects of fish consumption are largely assessed in qualitative terms. Below follows a summary of the assessments made in Denmark, Finland, Norway and Sweden, and a comparison between the approaches used.

2.1.1 The Danish Assessment

The Danish report is from 2003, and it is an update of an earlier report from 1987. It is based on the recommendation in 1987 to eat around 30–40 grams fish per day, or 200–300 g/week, varied between fatty and lean fish. The updated report also includes an examination of fish oil as a dietary supplement and the microbiological aspects of fish as foodstuffs.

An overview of nutritional content in fish is made in the Danish report where the importance of fish as a source for vitamins (vitamin A, D), minerals (selenium, iodine), and certain fatty acids is stressed. The effects of n-3 fatty acid are discussed in more detail, and particularly its role in disease prevention. The beneficial effects of n-3 fatty acids on the cardiovascular system are considered to be of highest importance, and it is concluded that a risk reduction can be achieved with regard to fatal coronary heart disease while it is more uncertain whether or not increased fish consumption also reduces the risk for nonfatal outcomes. Reference is made to a number of studies which supports the Danish recommendation to eat 200–300 g fish per week in this regard; it is suggested that this is an appropriate level of consumption for achieving a risk reduction for heart disease. Other beneficial effects of n-3 fatty acids are discussed more briefly; a possible reduction in the risk for stroke, a risk reduction for pre-term birth, and beneficial developmental effects on the nervous system are mentioned. The Danish report also concludes that there are no clear result with regard to a risk reduction for the development of cancer, and that information is limited regarding the role of n-3 fatty acids in improving inflammatory disease (e.g. psoriasis, ulcerous colitis, Crohn's disease, rheumatoid arthritis), and other diseases (e.g. chronic lung disease, asthma, cystic fibrosis, and psychiatric disease).

While the discussion of the nutritional content in fish is focused towards beneficial effect, it is stipulated that pregnant women should not consume cod liver oil due to the high content of vitamin A. The main discussion in the Danish report regarding the risks associated with fish consumption concerns different contaminants and other undesirable substances in fish. The following substances were considered in the report:

- Mercury, cadmium, lead, arsenic
- Organotin compounds
- Dioxins and dioxin-like PCBs
- PCBs
- Persistent organochlorine pesticides
- Brominated flame retardants (PBDEs)
- Phenols and chlorophenols
- Polycyclic aromatic hydrocarbons (PAHs)
- Musk substances
- Mustard gas
- Algae toxins
- Residues of veterinary drugs
- Cleansing agents, disinfectants
- Other compounds (e.g. radioactive compounds)

For each group an overview is made with regard to occurrence, toxicity, and intake. To investigate the level of concern for each compound, estimated intakes (via fish) were compared with established tolerable intake limits, if applicable, or alternative reference points (e.g. for PBDEs “reference points” from animal studies were considered instead). In this analysis, cadmium, mercury, dioxins, and PAHs were highlighted and advise for risk reduction is here given in the Danish report. Special consideration is made with regard to certain fish products where the levels of these contaminants can be elevated; scallops (cadmium), large carnivorous fish (mercury), fatty fish from Baltic Sea or the Gulf of Bothnia (dioxins and dioxin-like PCBs), and grilled or smoked fish and the skin of such fish (polycyclic aromatic hydrocarbons, PAHs). The exposure via fish to the other substances or groups of substances overviewed was considered of low concern.

For mercury the recommendation in the Danish report is that pregnant and breast-feeding women should avoid meals with high mercury content. This recommendation is based on a worst case scenario where it is assumed that the woman has an intake of 200–300 g fish (with high mercury content) per week, and given this scenario the intake of mercury can exceed the tolerable intake level.

With regard to dioxins and dioxin-like PCBs the Danish report reasons that there is no basis for altering the general dietary recommendation for fish consumption on the basis of these substances. This applies both to

pregnant women and to the population generally. The report discusses that special recommendations to pregnant women could be misleading since “alteration of diet during pregnancy would have only a marginal influence on the total dioxin body load because of the long half-life involved, and no acute toxic effects of dioxin have been recorded”. It is however stated that women of childbearing age are recommended to eat a varied diet and they should not exclusively eat fatty fish from the Baltic Sea or the Gulf of Bothnia.

Besides the risks discussed above, special attention are also directed towards some other factors. Certain raw molluscs, e.g. oysters, may contain viruses or bacteria; mackerel and tuna can have high histamine content, which can give rise to poisoning; and escolar and snake mackerel have naturally high content of wax (non-triglyceride lipids), and should because of this be sufficiently cooked to avoid giving diarrhoea.

The general conclusion in the Danish assessment is that the intake of fish should be 200-300 g/week in total; including 1-2 meals and fish products put on bread several times a week. The intake should be varied between lean and fatty fish. Pregnant and breast-feeding women should not eat fish that can have elevated levels of methyl mercury (large carnivorous fish), and children below the age of 14 should also limit the intake of carnivorous fish. In addition, information is given of how risks can be minimized, as discussed previously (e.g. fish with high content of dioxins, cadmium, and PAH). The (maintenance of the) recommended fish intake is mainly motivated by findings of a decreased risk of fatal coronary heart disease; 200–300g/week is argued to be appropriate in this context. The reasoning behind the general conclusion is that pregnant and breast-feeding women are a risk group with regard to methyl mercury, but have a low risk with regard to cardiovascular disease. For the older part of the population, however, the beneficial cardiovascular effects outweigh risks associated with exposure to contaminants.

2.1.2 The Finnish Assessment

Recommendations regarding fish consumption were renewed in Finland during 2004. This was performed on the basis of results from new monitoring studies. The National Food Agency (now: the Finnish Food Safety Authority) set up a working group that was to assess the benefits and harmful effects of fish in the Finnish diet, based on new research results.

Fish analysis data and information on consumption was obtained from various sources. The EU-Fish project coordinated by the National Food Agency was being completed, which offered new data on the contents of environmental toxins in fish. Results of mercury analyses from the Finnish Environment Institute were also used. Information of catch volumes, and export and import of individual fish species, as well as the amounts of fish used for human nutrition and animal feed was provided by the

Finnish Game and Fisheries Research Institute. The working group also received reports from the most recent analyses made in the National Public Health Institutes, Finnutrition 2002 study, concerning the consumption of fish by age groups and regions, and the significance of fish as a source of nutrients. There were no major differences observed in fish consumption patterns with regard to region or level of education. Age, on the other hand, seemed to have a much greater effect on the consumption of fish.

The starting point in the assessment by the working group was; 1) that fish in general is a good and safe source of nutrition; 2) Finland complies with the risk assessment of methyl mercury by the WHO and that of dioxins and dioxin like PCBs by EU's Scientific Committee on Food and the WHO; and 3) new research results show that there are a few known fish species in the Finnish fishing regions that accumulate more environmental toxins than other species, which is why their intake should be restricted.

Regarding contaminants in fish, the working group decided that the dietary advice should be extended, and not only consider dioxins and dioxin-like PCBs. It was concluded that mercury should also be encompassed in the recommendations. This decision was to some extent influenced by the fact that the Joint FAO/WHO Expert Committee on Food Additives (JECFA) in their revision reduced the tolerable weekly intake for methyl mercury to 1.6 µg/kg body weight/week. Based on the new data the working group concluded that intake of metals other than mercury did not constitute a concern. The need to regulate exposure to radioactivity, or Cesium 137, in fish by means of eating recommendations was considered in consultation with the Radiation and Nuclear Safety Authority. It was here concluded that protection from excessive exposure to mercury via fish would also have the effect of protecting against high intake of Cesium 137.

It was decided that the recommendations should concern domestic fish only, since species specific data are not available for imported fish. However, previous studies of the National Food Agency have been conducted regarding content of heavy metals in canned fish, (e.g. tuna), and import control procedures also include control of such content continuously. Very few samples have shown to have elevated levels of cadmium and mercury. It was also pointed out that swordfish and shark may contain high levels of mercury, but that there is a low consumption of such fish in Finland.

In summary, the working group concluded that fish is an important part of the Finnish diet; fish is a good source for vitamin D and n-3 fatty acids. It was stressed that n-3 fatty have been shown to reduce the risk of cardiovascular diseases. Fish should be consumed at least twice a week (200 g), and consumption should be varied between different fish species in order to minimize the intake of any individual contaminant. This is in compliance with the previous recommendations issued by the National

Nutrition Council. However, the National Food Agency included certain restrictions to this advice. Due to the contaminant levels, children, young people, and persons at fertile age should only eat large Baltic herring (longer than 17 cm), or alternatively Baltic salmon, or pike caught from the sea or inland waters, once or twice a month. Pregnant and nursing mother are advised not to eat pike due to the mercury risk. Also, persons who eat inland water fish on a daily basis should decrease their consumption of other predatory fish that accumulate mercury. Such fish include large perch, pike-perch and burbot.

2.1.3 The Norwegian Assessment

The Norwegian report from 2006 was prepared by an ad-hoc group of members of the Norwegian Scientific Committee for Food Safety (VKM) that also included some external experts. The work was made after a request from the Norwegian Food Safety Authority to assess nutritional benefits of consuming fish and other seafood in relation to health risks associated with intake of contaminants and other undesirable substances. The Norwegian assessment overview, as one part, the epidemiological findings regarding health effects of fish consumption. For effects on the cardiovascular system a review was made which included previous work by the Scientific Advisory Committee on Nutrition and the Committee on Toxicity in England¹ (SACN/COT) and The Danish Veterinary and Food Administration (the Danish report discussed previously). No additional new knowledge was regarded to have been acquired after the SANC/COT report, and it was concluded that a moderate change in food habits (an increase in fish consumption) could significantly reduce the risk for fatal cardiovascular disease in the population. In accordance with the Danish assessment it was considered not to be any clear results regarding the association between fish consumption and the development of cancer. Effects on growth and development that were highlighted in the Norwegian report included positive effects of n-3 fatty acids in terms of prolonged pregnancy (resulting in an increasing birth weight), and in terms of a positive effect on the visual function of premature babies. No negative effects were found after the use of n-3 fatty acids as a food supplement during pregnancy or as an addition to breast milk during the post-natal period. The negative developmental effects of PCB and mercury were also discussed. With regard to PCB, however, the intakes in Norway were presumed to be below critical levels.

In the overview of the nutritional content in fish it was stressed that intake of essential nutrients may be either too high or too low. A discussion is made with respect to recommended intakes according to the Nor-

¹ SACN/COT. Scientific Advisory Committee on Nutrition/Committee of Toxicity. Advice on fish consumption: benefits & risks. London:TSO, 2004

dic Nutrition Recommendations² and tolerable upper intake levels established by the Scientific Committee on Food. As a risk-benefit approach for nutrients, a comparison of the intake via fish with the two “reference points” were made for a number of nutrients; i.e. vitamin A, D, and B₁₂, selenium, iodine, and n-3 fatty acids. In this assessment, different intake scenarios were considered and defined; low intake (27 g/day), average intake (65 g/day), and high intake (119 g/day). Also, for each level of intake three combinations of lean to fatty fish were considered; exclusively lean fish, 2/3 lean fish and 1/3 fatty fish, and exclusively fatty fish. In general, the analysis indicated that a high consumption (119 g/day) does not result in adverse intakes of any of the nutrients; it may give an intake above the recommended intake, but it is still below tolerable upper intake levels.

In the Norwegian assessment a broad range of contaminants and other undesirable substances in fish were overviewed, which are summarised below:

- Mercury, Cadmium, Lead, Arsenic
- Organotin compounds
- Polycyclic aromatic hydrocarbons (PAHs)
- Dioxins, dioxin-like PCBs, and non-dioxin-like PCBs
- Brominated flame retardants (e.g. PBDEs)
- Chlorinated pesticides (e.g. toxaphene)
- Chlorinated paraffines, naphthalenes, and styrenes
- Perfluorinated compounds (PFOS)
- Algae toxins
- Infectious substances
- Disinfectants
- Residues of veterinary drugs (cultivated fish)
- Radioactivity

Similar to the Danish approach a general discussion of toxicity and intakes was performed for each compound group, and intakes via fish were compared with established tolerable intake limits, if applicable, or with other reference points. The analysis identified methyl mercury, and dioxins and dioxin-like PCBs to be of greatest concern, and these substances were further considered. It was pointed out that some other organic compounds (e.g. PAHs, and toxaphene) may also be of importance, and among the infectious substances *Listeria monocytogenes* was given the highest attention.

Different intake scenarios were evaluated for the important contaminants; methyl mercury, dioxins and dioxin-like PCBs. This was performed in a manner similar to that for nutrients (see above). The results

² NNR. Nordic Nutrition Recommendations 2004 – Integrating nutrition and physical activity. Nord 2004:13, Nordic Council of Ministers, Copenhagen, 2004.

from the analysis indicated that a high consumption (119 g/day) of fish with average mercury content will not result in that the tolerable intake level is exceeded (for adults as well as children). Fish with high mercury content was not included in the assessment discussed above. The consumption of such fish is low in the general population, and because of this it was not expected to change to overall picture. However, at the individual level the consumption of fish with high mercury content may lead to that the tolerable intake level is exceeded.

For dioxins and dioxin-like PCBs the intake scenario calculations indicated that a high consumption of fatty fish will result in that the tolerable intake is exceeded. Other calculations also indicated that that for a consumption of about two meals per week of farmed fish with an average dioxin and dioxin-like PCB content of 1.7 pg TE/g, the total exposure to dioxins and dioxin-like PCBs from the total diet will reach the same level as the tolerable intake. More generally, the Norwegian report points out that the tolerable intake is set to prevent accumulation in women before and during pregnancy, and it represents a safety level and not necessarily the level at which adverse effects will occur. Moreover, given young women's low consumption of fatty fish it is considered unlikely that a general recommendation of increased fish consumption will result in that fertile women will eat more than 2 meals/week.

In conclusion, given the median fish consumption of around 2 meals/week (65 g/day, 450 g/week), Norwegians are generally recommended eat more fish, which should be varied between lean and fatty fish. A higher consumption is primarily supported (qualitatively) in terms of beneficial cardiovascular effects in the older population, and also beneficial effects on pregnancy and foetus development. From a toxicological point of view there is no danger associated with a high consumption (4 meals/week or more) if consumption is varied and fatty fish does not exceed 2 meals/week.

2.1.4 The Swedish Assessment

The Swedish report is from 2007, and the project was initiated during 2004. The aim was to study methods for risk-benefit analysis, and also to perform an assessment based on Swedish data. The results are used in the ongoing revision of the dietary advice which will be finished in 2008.

The Swedish risk-benefit assessment of fish consumption focuses on a few selected contaminants (dioxin and dioxin-like PCBs, and methyl mercury), and nutrients (n-3 fatty acids, and vitamin D). Previous investigations have identified these factors to be most important, and intake and effect data was also available for these substances. Calculations were performed for how different intake scenarios influence the possibility to exceed the tolerable intake for dioxins/PCBs and methyl mercury. Com-

parisons were also made with regard to recommended intakes of n-3 fatty acids and vitamin D.

An extensive review of the health effects associated with the selected substances (n-3 fatty acids, dioxins/PCBs, and methyl mercury) was made. This included reproductive and developmental effects, effects on cognitive function and mental health, effects on immune response and inflammatory processes, effects on the cardiovascular system, cancer, acute effects, and combined effects of complex mixtures. On an overall level, the beneficial effects of n-3 fatty acids on the cardiovascular system and foetus development were considered of highest importance.

One type of intake calculation performed in the Swedish assessment considers "risk-benefit pairs"; mercury vs. vitamin D, and dioxins vs. n-3 fatty acids. For each pair it was assessed if a consumption resulting in a recommended intake of the nutrient, for the majority of the population, at the same time will result in an intake of the contaminant which is below the tolerable intake, for the majority of the population. A few of illustrations of this approach were given, and it was concluded that the type of fish considered is of importance. With regard to dioxins and n-3 fatty acids the desired requirement was according to the analysis fulfilled for farmed salmon but not for Baltic herring. Considering fresh water fish with an average mercury content of 0.5 mg/kg, a consumption corresponding to 2 times a month, in addition to habitual consumption of other fish, will provide a large part of the recommended intake of vitamin D, while the risk of exceeding the tolerable intake for methyl mercury is low. However, for fish with an average mercury concentration of 1 mg/kg the same consumption results in that the tolerable intake for methyl mercury is exceeded.

For dioxins and methyl mercury other intake calculation were also performed, which are somewhat similar to those in the Norwegian assessment; a number of scenarios were defined and evaluated with regard to the possibility of exceeding tolerable intake limits. For dioxins it was concluded that a consumption of fish according to the general advise (lean fish twice a week, and fatty fish once a week), results in a low risk of exceeding the tolerable intake. A consumption of lean salt water fish once a week and fatty fish twice a week gives an intake that approximates to the tolerable intake. A similar situation is obtained for fatty fish from the Baltic Sea once a month, and varied consumption of lean and fatty fish twice a week. The general reasoning in the Swedish report with regard to dioxins is that it is not recommendable to generally increase consumption of fatty fish from the Baltic Sea, since this is not advisable for certain groups, while there is no reason to recommend not eating fatty fish from the Baltic Sea at all. It is stressed that for a women who eat according to the recommendation (2 meals lean fish a week, and 1 meal fatty fish a week; 375 g in total), the tolerable intake is not exceeded. Similar to the Norwegian assessment, it is also pointed out that the toler-

able intake represents a safety level and not necessarily the level at which adverse effects will occur.

For methyl mercury the intake calculations showed that the most common choice of lean and fatty fish according to surveys (2 meals lean fish a week, and 1 meal fatty fish a week) gives a methyl mercury intake corresponding to 20% of the tolerable intake, for a woman of child-bearing age, and 40% of the tolerable intake, for a child. However, for the other combinations of lean and fatty fish considered (adding up to 2–3 meals per week) the tolerable intake was always exceeded for a child, and sometimes also for a woman of child-bearing age. The general conclusion regarding methyl mercury is that the consumption of fresh water fish in the population is low, and for most consumers the intake does not exceed the tolerable intake. A limited consumption (1 meal/month; 125 g) of fish with a concentration of 1 mg/kg methyl mercury provides a low risk of exceeding the tolerable intake. It is also stressed that pregnant women constitute the most sensitive group.

The Swedish assessment concludes that an increased fish consumption in line with the general dietary advice of 2–3 meals a week (250–375 g/week), varied between different fish, is supported. It is probable that an increased consumption would reduce the risk for cardiovascular disease, particularly with regard to risk groups and among people who eat little or no fish. It is also probable that an increased consumption among women of child bearing age (who has a low consumption) is beneficial with regard to foetal development. An increased consumption among those who eat little fish would significantly increase the vitamin D intake. However, consumption of certain fish (e.g. fish from Baltic sea) with high contaminant levels could lead to that tolerable intake limits are exceeded; this primarily concern children and women of child bearing age (dioxins/PCBs), and pregnant women (methyl mercury).

2.1.5 Summary of the risk-benefit approaches

In all the Nordic assessments, contaminant risks are evaluated in terms of the possibility to exceed tolerable intake limits. In the Danish assessment, the overviewed contaminants are quite clearly categorised as of being of some or no concern. Special attention is given to certain fish where levels of the important contaminants can be high (methyl mercury is considered most important). Other risks are assessed more qualitatively (e.g. infectious substances). A similar approach is used in the Norwegian assessment where an even larger number of contaminants are overviewed (dioxins/PCBs and methyl mercury considered most important). In addition, different intake scenarios were evaluated for the important contaminants in the Norwegian assessment. Evaluation of consumption scenarios with regard to dioxins and methyl mercury is also performed in the Swedish assessment. In the Swedish assessment, however, there is no general

overview of all possible contaminants and undesirable substances in fish; it starts directly with the more important ones. The activities in Finland have also been directed more specifically towards certain contaminants (dioxins and dioxin-like PCBs, mercury and some other heavy metals, and cesium-137).

In both the Norwegian and Swedish assessments there are also approaches that simultaneously attempt to evaluate risks and benefits. In the Norwegian assessment this concerns the assessment for nutrients; intakes resulting from different consumption scenarios are calculated and compared to recommended intakes and tolerable upper intake levels. The Swedish assessment illustrated how “risk-benefit pairs” may be evaluated; dioxins vs. n-3 fatty acids, and methyl mercury vs. vitamin D. For each pair the intakes resulting from different consumption scenarios are calculated and compared to the recommended intake with regard to the nutrient, and the tolerable intake with regard to the contaminant.

All assessments considers the beneficial effect of n-3 fatty acid on the cardiovascular system to be most important, and probable beneficial effects on foetus development are also pointed out. These statements are based on qualitative overviews of the scientific literature, and the general conclusions made regarding how much fish should be consumed are mainly based on these factors. It should be noted that fish consumption differs between the countries; it is highest in Norway (median is 65 g/day), lowest in Denmark (median is 13 g/day), and intermediate in Finland (about 30-50 g/day) and Sweden (average is 30–35 g/day), and this appears to some extent to be reflected in the general conclusions.

2.2 Risk-benefit assessments of fish consumption in Belgium

Recent work regarding risk-benefit analysis of fish consumption in Belgium was also presented at the seminar by Dr Sioen, which was based on her thesis. Intake assessments of nutrients and contaminants were conducted using a probabilistic approach, taking into account the variability of seafood consumption data, body weight data, and nutrient and contaminant concentration data. The nutritional compounds studied were the long-chain n-3 polyunsaturated fatty acids (LC n-3 PUFAs, i.e. the sum of EPA and DHA), vitamin D, and iodine. These nutrients were chosen since they are present in seafood in a relatively high concentration compared to other food items. The contaminants considered were mercury and methyl mercury, seven indicator PCBs (iPCBs), dioxin-like PCBs (dl PCBs), sum of 7 polychlorinated dibenzo-*p*-dioxin congeners (PCDDs) and 10 polychlorinated dibenzofuran congeners (PCDFs), and total dioxin-like compounds (total TEQ).

An approach was established, including compilation of databases and the development of a software module, to calculate the simultaneous intake of the considered nutrients and contaminants. In this analysis, each consumption point is combined with a concentration point of multiple compounds, which gives information about correlations between the intakes of different compounds. To perform the necessary simulations a software module was developed; ProbIntake^{UG}.

To assess whether or not the nutritional recommendations were reached and to investigate if there were any toxicological concerns the dietary reference intakes for nutrients and the tolerable intake limits for contaminants were used as reference points. For the nutrients, intakes were divided by the corresponding dietary reference intakes (DRI); a ratio > 1 was considered favourable and indicating that the recommendation is reached. Similarly, for the contaminants the intakes were divided by the corresponding tolerable intake levels; a ratio > 1 was considered unfavourable and indicating that the toxicological reference value is exceeded. As previously discussed, the use of recommended and tolerable intake levels as reference points was illustrated in the Swedish risk-benefit report, but in this work the approach was used in a more systematic way that also considered several nutrients and contaminants using a probabilistic framework.

Under the considered approach two different situations were studied. First, the current situation was evaluated using consumption data observed in 341 adolescents (1997) and 821 adults (2004) in the Belgian population. According to the results from the simulation the studied population did not reach adequate intake of the three considered nutrients (LC n-3 PUFAs, vitamin D, iodine) on the basis fish consumption only. Fish consumption appeared not to be an issue of toxicological concern with regard to methyl mercury. On the contrary, for dioxin-like compounds the tolerable intake limit was exceeded in high consumers of fatty fish, and it was found that this could also be the case on the basis of their seafood consumption only.

As a second step, based on defined consumption scenarios, it was investigated whether the Belgian recommendation for LC n-3 PUFAs could be reached through fish consumption without toxicological concerns. The results indicated that the recommendation can be achieved by consuming fatty fish twice per week, or by a varied consumption of lean and fatty fish (on average 50% of each) at least three times a week. At this level of consumption the intake of methyl mercury was found not to be of toxicological concern. The intake of dioxin-like compounds from fish only approximated the tolerable intake in the case of a consumption of fatty fish three times a week or more. This was concluded to constitute a potential risk since other food products may also significantly contribute to the intake of such compounds.

It was concluded that a regular seafood consumption (twice a week), with important contribution of fatty fish (at least 50%), in combination with regular consumption of EPA and DHA enriched margarine, can be advised to maximize LC n-3 PUFAs intake without exceeding the tolerable intake for dioxin-like compounds. It is however stressed that this conclusion is conditional upon the compliance of existing rules and regulations that helps to prevent highly contaminated food products to become available on the market.

2.3 A common scale for assessing risks and benefits; summary measures of population health

One of the challenges in making risk-benefit analysis more quantitative concerns the development of a common scale for comparison of positive and negative health effects associated with consumption of food products, or more specifically, with regard to individual chemical and microbiological constituents in food products. The use of recommended and tolerable intake limits as the nutritional and toxicological reference value is a starting point in this sense, but the problem needs further development. There are a few examples where so-called summary measures of population health have been used in the context of risk-benefit analysis of food products. Summary measures of population health measure the health of a population by combining data on mortality and non-fatal health outcomes into a single number. According to the WHO these measures are classified in two categories; *health expectancies*, and *health gaps*. These two classes of measures are complementary. Health expectancies are population indicators that estimate the average time (in years) that a person could expect to live in a defined state of health. Health gaps measure the difference between actual population health and some specified norm or goal. Examples of health gaps and health expectancies are disability-adjusted life years (DALYs) and quality-adjusted life years (QALYs), respectively. An overview of these types of measures, and in particular DALYs, was given at the seminar by Dr. Moradi.

DALY is the best known health gap and summary measure of population health. This metric was chosen in the Global Burden of Disease (GBD) study initiated in 1992, which is a collaborative effort between the WHO, the Harvard School of Public Health, and the World Bank. The DALY measures the difference between a current situation and an ideal situation where everyone lives up to the age of the standard life expectancy, and is in perfect health. DALY combines both time lost due to premature mortality and non-fatal conditions; it is the sum of the years of life lost due to premature mortality (YLL) in the population and the years lost due to disability (YLD). One DALY represents the loss of one year of equivalent full health.

QALY measure the total number of years of perfect health in a population. A year in perfect health is considered equal to 1.0 QALY, and the value of a year in ill health would be discounted (be less than one). QALYs have been used to assess the risks and benefits of fish consumption. These studies considered two of the identified important risk-benefit constituents in fish; methyl mercury and n-3 fatty acids, but not dioxin-like compounds. More specifically, risks in terms of developmental effects (reduced IQ, and delayed ability to speak), associated with methyl mercury, were weighed against benefits in terms of reduced risk for cardiovascular disease (stroke and coronary heart disease) and increased IQ in children, associated with n-3 fatty acids³.

Efforts made in the Netherlands where the DALY was chosen as an integrated measure of health impact was presented at the seminar by Dr. Baars. The report "Our food, our health - healthy diet and safe food in the Netherlands", compiled by the National Institute for Public Health and the Environment (RIVM) in 2004, addressed a number of questions regarding risks and benefits of food consumption⁴; How healthy is the Dutch diet? How safe is Dutch food? What health gains can be achieved through better diet, better eating habits and by reducing overweight? What is the appropriate balance between the desire for a healthy diet and the need to ensure safe food? And how will this affect the various parties involved in food production, distribution and consumption?

With regard to the Dutch diet, the five most important dietary health determinants were investigated; i.e. saturated fatty acids, trans-fatty acids, fish, fruits, and vegetables. In the analysis, two reference scenarios were defined. In one scenario it was assumed that all Dutch people follow the dietary recommendations with regard to the five factors considered. This situation was considered to be associated with the maximum theoretical health gain. Since this may not be achieved in practice another scenario was also investigated in which the dietary habits are partially improved towards the recommendations. Interventions resulting in the defined improvement, called "middle scenario", was considered practically achiev-

³ Cohen JT, Bellinger DC, Connor WE, Kris-Etherton PM, Lawrence RS, Savitz DA, Shaywitz BA, Teutsch SM, Gray GM. A quantitative risk-benefit analysis of changes in population fish consumption. *Am J Prev Med.* 2005; 29:325-34.

Cohen JT, Bellinger DC, Shaywitz BA. A quantitative analysis of prenatal methyl mercury exposure and cognitive development. *Am J Prev Med.* 2005; 29:353-65.

Cohen JT, Bellinger DC, Connor WE, Shaywitz BA. A quantitative analysis of prenatal intake of n-3 polyunsaturated fatty acids and cognitive development. *Am J Prev Med.* 2005; 29:366-74.

König A, Bouzan C, Cohen JT, Connor WE, Kris-Etherton PM, Gray GM, Lawrence RS, Savitz DA, Teutsch SM. A quantitative analysis of fish consumption and coronary heart disease mortality. *Am J Prev Med.* 2005; 29:335-46.

Bouzan C, Cohen JT, Connor WE, Kris-Etherton PM, Gray GM, König A, Lawrence RS, Savitz DA, Teutsch SM. A quantitative analysis of fish consumption and stroke. *Am J Prev Med.* 2005; 29:347-52.

Ponce RA, Bartell SM, Wong EY, LaFlamme D, Carrington C, Lee RC, Patrick DL, Faustman EM, Bolger M. Use of quality-adjusted life year weights with dose-response models for public health decisions: a case study of the risks and benefits of fish consumption. *Risk Anal.* 2000; 20:529-42.

⁴ RIVM report 270555009, Our Food, Our Health - Healthy Diet and Safe Food in the Netherlands, can be derived from www.rivm.nl

able. The reduction in health loss, in terms of disease incidence and mortality, DALYs, and life expectancies associated with the “maximum” and “middle” scenarios were estimated; the DALY for the middle scenario was approximately half the size of that for the maximum scenario indicating that a practically achievable intervention will reduce the burden of disease attributable to the dietary composition (with regard to the five factors stated) by approximately fifty per cent. The burden of disease, in terms of DALYs, associated with food borne infections, and chemical constituents in food, including various proteins, mycotoxins, phycotoxins, phytotoxins, nitrate/nitrite, growth promoters, and process contaminants, was also estimated.

In summary, the estimated health loss or potential health gain following improved diet and avoidance of exposure were as follows: 130,000–250,000 DALYs for unfavourable diet, in terms of the five health determinants considered (the range is the difference for the “middle” and “maximum” scenarios); 1,000–4,000 DALYs for food borne infections; and 1,500–2,000 DALYs for chemical contamination. From this it was concluded that Dutch people are less healthy than they could be due to an unhealthy diet; dietary interventions can reverse a substantial proportion of the estimated health loss; and much greater health gains can be made by encouraging a healthy diet compared to improving food safety.

2.4 EFSA activities on risk-benefit assessment

The European Food Safety Authority (EFSA) arranged a science colloquium on “Risk-Benefit Analysis of Foods” in 2006⁵. The outcome of this colloquium was presented at the seminar by Dr. Carlander. Also, information was given regarding the current status of the EFSA Working group on Human Health Risk-Benefit Assessment, and their objectives. About 100 participants with expertise in toxicology, microbiology, exposure, epidemiology, and nutrition, from 26 European Countries, Australia, Canada and USA were present at the 2006 colloquium, and the private, academic and regulatory sectors were represented. The participants were divided up in groups, and a number of specific questions were discussed. A brief summary of the outcome and conclusions from the colloquium and the group discussions are given below.

There was a general consensus that a risk-benefit analysis should mirror the paradigm already well established for risk analysis, consisting of a risk-benefit assessment part, a risk-benefit management part, and a risk-benefit communication part. Consequently, the benefit assessment part of the risk-benefit assessment should mirror that for the risk assessment part; i.e. include benefit identification, benefit characterisation (dose-

⁵ The EFSA’s 6th Scientific Colloquium Report, Risk-Benefit Analysis of Foods: Methods and Approaches, can be derived from www.efsa.europa.eu

response assessment), exposure assessment, and benefit characterisation. Also, the risk-benefit analysis should contain a means, quantitative if possible, to weigh the potential risk against the potential benefit.

The colloquium regarded that the human health risks and benefits that should be considered represent effects that can be clearly identified and casually related with food or food components. Also, high quality data on exposure and dose-response is needed, and for effects under consideration a clear problem formulation should also exist.

Concerning the tools and data needed, it was concluded that, on the risk side, information on incidence of outbreaks could be used and the impact of disease could be quantified (burden of disease). On the benefit side, nutritional status in population could be quantified. The use of recommended and tolerable intake limits was not considered appropriate for quantitative risk-benefit analysis, but was considered useful for identifying whether or not an assessment is needed. It was suggested that probabilistic exposure and effect modelling tools could be useful in the area, and also interspecies scaling approaches (e.g. physiologically based pharmacokinetic modelling). Regarding data requirements, a present limitation is that dose-response data on humans are mostly not available for foods and scarce for single nutrients.

Risk-benefit analysis was regarded not to be a routine procedure, and it should only be used when an impact on public health is expected; e.g. when the margin between beneficial and detrimental intake levels is small. A clear problem formulation is needed, and assumptions and uncertainties should be clearly addressed. The possibility of a tiered risk-benefit approach was considered; qualitative, semi-quantitative, and quantitative. What is most feasible in specific cases depends on the availability of data. It was considered essential to evaluate risks and benefits in the appropriate population groups. Different life stages for the manifestation of risks and benefits should also be considered. However, the weighing of one population group against another should be avoided.

The important question of how to evaluate risks and benefits quantitatively on a common scale was addressed. A number of possible measures were here identified; mortality and morbidity, days of work lost, disability-adjusted life years (DALYs), quality-adjusted life years (QALYs), and cost of illness/willingness to pay approaches. It may be pointed out that the measures suggested above are all quite related. The colloquium concluded that there is no generally applicable measure, and regarded that the use of DALYs or QALYs is most suitable for complex, societal-wide situations.

The borderline between risk assessment and risk management was discussed. This borderline is not fixed and may shift with the nature of the outcome. As scientific tools become available that allow the assessor to quantify risks and benefits, the task of risk-benefit comparison will move from risk management into risk assessment. A continuous iterative inter-

action between assessors and managers with possible input from stakeholders was considered essential throughout this process.

The colloquium recommended that a guidance document should be developed by EFSA to address the problem formulation, definitions and language to be used, conversion of animal data to human situations, methods and approaches, and the potential pitfalls. The meeting considered that it was premature to formulate guidelines on good risk-benefit analysis practice, but there was agreement that some preliminary guidance could be derived in line with the conclusions from the meeting.

Information was also provided at the Uppsala seminar regarding the established Working Group on Human Health Risk-Benefit Assessment of Foods under the Scientific Committee of EFSA. The terms of reference of the working group is to prepare a guidance document for performing risk-benefit assessments of food related to human health risks and human health benefits. More specifically, the tasks include; the scope and objective; common language; identification of situations for risk-benefit analysis; guidance on problem formulation; consideration of methods and approaches needed to assess risks and benefits and how to compare them (common scale of measurement); consideration of how animal and other data can be extrapolated; identification of potential limitations of any risk-benefit analysis; review of ongoing activities; and recommendations on future initiatives.

2.5 Future advancements in toxicity testing and its possible implications

The National Research Council (NCR) Committee on Toxicity Testing and Assessment of Environmental Agents was requested by the U.S. Environmental Protection Agency (EPA) to conduct a review of toxicity testing methods and to develop a long-range vision for toxicity testing and a strategic plan for its implementation⁶. The NCR committee's vision was presented at the Uppsala seminar by Dr Krewski, and it was discussed how this vision compares against initiatives in risk-benefit analysis undertaken in Europe.

Currently, the approach to toxicity testing relies primarily on studies that evaluate outcomes in whole animals. The NCR committee discussed possibilities for improving the current system but concluded that a paradigm shift is needed to achieve the criteria set out in the committee's 2006 interim report; 1) to provide broad coverage of chemicals, chemical mixtures, outcomes, and life stages, 2) to reduce the cost and time of testing, 3) to use fewer animals and cause minimal suffering in the animals used, and 4) to develop a more robust scientific basis for assessing

⁶ The NCR report, *Toxicity Testing in the 21 Century: A Vision and a Strategy*, is available at the National Academies Press, www.nap.edu

health effects of environmental agents. As a result, the committee envisions a new toxicity-testing system that evaluates perturbations in key toxicity pathways by using new methods in computational biology and a broad array of *in vitro* tests based on human biology.

There are three major components of the committee's vision: chemical characterization, toxicity testing, and dose-response and extrapolation modelling. The components are considered to be interrelated, and some evaluations may proceed in a stepwise manner; from chemical characterization, to toxicity testing, to dose-response and extrapolation modelling. An important feature of the vision is consideration of the risk context (described as the decision-making context that creates the need for toxicity-testing information) at each step and the ability to exit the strategy at any point when information is sufficient for decision-making.

Pathway based assays constitute the central component of the vision for toxicity-testing. Cellular response pathways that, when sufficiently perturbed, are expected to result in adverse health effects are termed *toxicity pathways*. The consequences of a biologic perturbation depend on its magnitude, which is related to the dose, the timing and duration of the perturbation, and the susceptibility of the host. At low doses, many biologic systems may function normally within their homeostatic limits. At higher doses biological responses occur, which may be successfully handled by adaptation although some susceptible people may be affected. More intense or persistent perturbations may overwhelm the capacity of the system to adapt and lead to tissue injury and possible adverse health effects. Thus, development of predictive assays that use cells or cell lines, preferably of human origin, to evaluate relevant perturbations in key toxicity pathways constitutes a crucial part of the vision. Emphasis is placed on tests using high-throughput methods, but medium-throughput assays could be used for more integrated cellular responses, such as cytotoxicity, cell proliferation, and apoptosis. It is expected that the need for traditional animal testing over time should be greatly reduced and possibly even eliminated. An apparent challenge in the development of suitable *in vitro* test system concerns how to mirror the metabolism in the whole animal. The committee concluded that for the foreseeable future, any *in vitro* strategy will need to investigate likely metabolites by *in vivo* testing.

The question was raised at the Uppsala seminar whether or not the NCR committee's vision for toxicity testing could be in line with the present risk-benefit initiatives in the food area. Some of the participants argued that in principal a similar strategy could also be envisioned for nutrients; nutrition testing. In resemblance to the proposition by the NCR committee that would require the exploration and advancement of knowledge regarding *nutrition pathways*. It is not clear though whether this would need to be done under a completely different scheme or if the concept of nutrition testing partly might be encompassed within the vision already proposed; i.e. will much of the undertakings necessary for ad-

vancing our knowledge regarding perturbation in pathways relate to chemical response in general, or is there a strict division between toxicity and nutrition in this respect? On the level of the risk-benefit problem an additional step would also be the integration of toxicity and nutrition testing. An interesting question in this respect concerns the common scale problem discussed in the risk-benefit area; how to compare negative and positive health effects quantitatively, and whether or not such comparisons are better facilitated on the level of biological pathways.

3. Discussion

On the second day of the seminar participants were divided into four discussion groups. A chair and a secretary were appointed to each group. A number of questions had been compiled beforehand by the organizers which were used in the group discussions. The groups did not need to answer all questions, but could optionally focus their discussions towards some of the specific topics included. The questions that were given are presented below:

1. Main lessons and conclusions from work in the risk-benefit assessment area so far?
2. Give examples of areas within the food sector that could take advantage of including a risk-benefit assessment. Should it be used generally or in specific cases?
3. Is the DALY concept a proper scale to use in risk-benefit analyses, or do we need to come up with something else? Do different problems demand different scales?
4. EFSA and/or national (Nordic, Baltic) efforts in improving risk-benefit analysis; the balance?
5. How to look on aggregated risks in a risk-benefit perspective? Should or could several risk assessment endpoints be summarised?
6. Could risk assessment and “benefit assessment” be performed according to parallel modes or schemes?
7. How to proceed with risk-benefit assessment activities in practice; what are the next steps?

Each group presented the outcome of their respective discussion, and thereafter a general discussion was held. The results from these activities are summarized below:

1. Main lessons and conclusions from work in the risk-benefit assessment area so far?

The risk-benefit concept could be an important tool for decision making and policy development. However, there are presently no established procedures, tools, or methods available for risk-benefit assessment of food products. To make advancements in this area it is of importance to increase interactions and understanding between toxicologists and nutritionists. These two areas of expertise need to develop a common language on the scientific level, which is a challenge. Use of a risk-benefit approach may result in that consumers receive a single message, or ad-

vice from one source/group, instead of information regarding risks and benefits separately, the latter which potentially can be more contradictory.

Presently, the availability of necessary scientific data is a general problem. Risk-benefit analysis also requires that data regarding positive and negative effects of food consumption is comparable. For example, there is in general more information available on dose-response for toxicants relative to nutrients. On the other hand, dose-response information on nutrients are typically in dose intervals relevant to humans while the same type of data for toxicants are in dose intervals that generally are higher compared to the exposure experienced by the majority of the human population. Data need also to be applicable to different groups in the population. At the general level a question is also how broad the scope of risk-benefit should be, for example from a risk management point of view we may look broader than the health for the consumer, e.g. economical issues.

2. Give examples of areas within the food sector that could take advantage of including a risk-benefit assessment. Should it be used generally or in specific cases?

It was discussed that a risk-benefit approach is not a routine procedure, and should be used when there are small margins between the risks and benefits. Also, at what level of detail a risk-benefit analysis can be made, e.g. quantitative vs. qualitative analysis, may vary on a case by case basis. As previously pointed out risk-benefit initiatives in the food area has so far mainly focused on fish consumption and it was agreed that much is now known in this respect, and it is time to explore other applications. A number of areas were taken up for discussion, namely:

- Fortification of foods and supplementation
- Food additives
- Fruits and vegetables
- Processed foods
- Wine and chocolate

Of course in many cases the risk-benefit problem can be approached from different angles, and the areas mentioned above are more or less specific. In the case of food fortification and supplementation the risk-benefit analysis may be specific and concern the characteristics of a certain substance; e.g. folic acid and its negative and positive health effects, but it is also complicated by the fact the risks and benefits for example may differ between different life stages.

It should be noted that what is regarded as a benefit (and risk) was not discussed and defined explicitly at the Uppsala seminar, and this may of

course affect the specification of the problem. For example in the case of food additives a question would be whether or not aspects like flavouring, colouring, other things related to the appetizing, and maintenance of product consistency should be included in the risk-benefit framework, besides the potential negative health effects associated with the additive/s vs. its preservative functions that retards spoilage and prevents bacterial contamination, as well as possible nutritional roles.

In the case of vegetables and fruits there are several specifications of a risk-benefit problem that can be made; e.g. the harmful effects of pesticides vs. beneficial effects of nutrients or bioactive substances, the risks and benefits of nitrate in vegetables, or the harmful effects of pesticides vs. their protection against microbial contamination. Depending on the purpose of the analysis, an option would also be to assess the risks and benefits with regard to fruits and vegetables on an overall basis.

Processed foods are also a complex area where several aspects may be considered; e.g. how different cooking procedures affect formation or modification of certain food constituents which may modulate the risks and benefits. A few other examples were also suggested, such as wine and chocolate, which are special since the consumption of such products mainly relates to social and quality aspects of life.

3. Is the DALY concept a proper scale to use in risk-benefit analyses, or do we need to come up with something else? Do different problems demand different scales?

One of the more highlighted questions regarding risk-benefit analysis has concerned the problem of how to compare different positive and negative health effects on the same quantitative scale. The use of summary measures of population health, and in particular DALYs, was debated at the seminar. This measure has for example been used by the WHO to compare different risk factors globally. While the DALY represents a measure that under defined situations could be used in a risk-benefit framework (and in fact it has already been used for such purposes), there is a need to consider and develop other alternatives as well. The DALY appears most suitable to use in broader settings since it is generally regarded as political or economical instrument for prioritizing future interventions and preventions. More advanced applications of the DALY concept are also data demanding which does not make it a routine procedure. The DALY equation is rather complicated and relies on a number of parameters that need consideration; e.g. disability weights, and age weighting. A high transparency is here of importance. For example, a question that was brought up in this respect was whether both national and international figures are required for disability weights; e.g. the severity of an effect in relation to another may for example be perceived differently in different countries.

In general it appears that depending on the data availability and the particular risk-benefit problem to be solved, different approaches for comparing risks and benefits quantitatively needs to be considered. It was also pointed out that while it is of interest to make advancements beyond the use of recommended intake limits and tolerable intake levels as quantitative reference point, these may be used as rough instruments in a tiered approach, that as a first step identifies the more important (risk and benefit) factors. Emerging approaches in risk assessment that place more emphasis on uncertainty analysis and a better characterization of the effects (e.g. benchmark dose concept) and the exposure were also considered to be useful elements in the development of procedures for the risk-benefit assessment.

5. How to look on aggregated risks in a risk-benefit perspective? Should or could several risk assessment endpoints be summarised?

6. Could risk assessment and “benefit assessment” be performed according to parallel modes or schemes?

Some participants pointed out that major risks and benefits need to be identified first, and then any possibilities for aggregation of the effects can be considered. This question also relates to the “common currency” problem discussed above, which does not only concern how to weigh positive effects against negative effects but also how to compare different effects in either category. The seminar participants pointed out the importance to develop general guidance regarding the effects to be considered in a risk-benefit framework. The meeting agreed on the principle to conduct a benefit assessment according to a scheme similar to that for risk assessment, which is in line with previous suggestions in the area. Also, it was pointed out that evaluation of risks and benefits in parallel was also employed in the Nordic risk-benefit assessments on fish consumption.

4. EFSA and/or national (Nordic, Baltic) efforts in improving risk-benefit analysis; the balance?

7. How to proceed with risk-benefit assessment activities in practice; what are the next steps?

It was suggested that EFSA should have a coordinating and leading role. Presently, conduction of risk-benefit analysis is not included in the EFSA’s remit, but it was suggested at the 2006 colloquium that a guidance document on this issue should be developed. Also, it was considered that EFSA plays an important role with regard to harmonization of tools in the area of food safety in general, and therefore also concerning emerging

approaches in the area of risk-benefit analysis. Currently, this would be on the level of a general framework for risk-benefit analysis, which is already in progress (the EFSA Working Group on Risk-Benefit Analysis). International initiatives were considered important for reaching consensus on several critical aspects of risk-benefit analysis. Further, an example of specific tasks where it may be of importance to have centralized organization concern database issues; it was suggested that there may be a need for an extensive and detailed database of occurrence data that can be shared, and this may be an important task for EFSA to coordinate. However, a need to conduct risk-benefit initiatives on national levels was also recognised. National activities are important for starting practical work in the area in timely manner, which seems as the most effective way of increasing the knowledge base and experience in the field.

4. Conclusion

In conclusion, the meeting agreed that since risk-benefit analysis considers the whole picture, it will help to avoid making sub-optimized decisions. Also, use of risk-benefit analysis promotes the communication of a coherent message, and helps to avoid the communication of several messages from different sources that potentially may appear conflicting. Risk-benefit analysis is not a routine procedure; it is useful in the case of small margins between risks and benefits. There is currently a lack of data for risk-benefit analysis in many respects. A tiered approach may be necessary; the availability and type of data determine how to approach the problem, e.g. whether the analysis is qualitative, quantitative, or both. While an overview of all potential risks and benefits needs to be conducted for a given problem, the final analysis may be directed towards the more important ones. In general, the scheme for risk assessment also appears appropriate for assessing the benefits.

An increased cooperation between different expert fields was considered crucial, and how to compare positive and negative effects quantitatively represents an important issue. Summary measures of population health, like DALYs, can be used for complex questions, but other approaches should also be developed. In general, which quantitative approach is suitable may differ on a case by case basis; this may be related to the problem formulation and objective of the analysis, and the type of data available. Developments discussed in the area of risk assessment, i.e. probabilistic methods, may also be useful in the context of risk-benefit analysis. On the international level EFSA was considered to have a leading and coordinating role, but national initiatives are also important for making advancements in the field.

Sammanfattning

Livsmedelsverket anordnade under hösten 2007 ett seminarium om risk och nytta med titeln "Aspects of Risk-Benefit Assessment of Food Consumption - Directions for the Future". Seminariet hölls den 18-19 oktober i Uppsala och finansierades inom ramen för Nordiska Ministerrådets livsmedelssamarbete. Syftet var att ge en översyn om metoder för risk-nytta-analys samt diskutera möjligheter för framtida tillämpningar inom livsmedelsområdet.

Experter från Livsmedelsverket, andra svenska organisationer, övriga nordiska länder samt de baltiska länderna var närvarande. Inbjudna föreläsare presenterade vetenskapligt arbete på området. En summering av de nordiska ländernas risk-nytta-arbete med fisk gjordes även, och avslutningsvis hölls en organiserad diskussion om risk-nytta-analys inom livsmedelsområdet.

Seminariet konkluderade att risk-nytta-analys kräver samarbete mellan olika områden och att ett viktigt mål är framtagandet av en gemensam skala för att kunna värdera och jämföra olika typer av positiva och negativa hälsoeffekter. DALYs (disability-adjusted-life-years) är ett exempel som tidigare använts vid t.ex. beräkning av sjukdomsburden ("Burden of disease"), men alternativa mått bör även beaktas. EFSA har en ledande roll i arbetet inom Europa och har etablerat en arbetsgrupp där risk-nytta-analys diskuteras. Det konstaterades att risk-nyttavärdering är tillämpligt särskilt inom vissa områden, t.ex. nyttoeffekter med frukt och grönt vägt mot intag av bekämpningsmedel. Jämförelser av olika tillagningssätt togs även upp som ett möjligt område för risk-nytta analys.

Appendix I: Seminar programme

Seminar on aspects of risk-benefit assessment of food consumption – directions for the future

The seminar is supported by a grant from the Nordic Council of Ministers, Nordic Working Group for Diet, Food & Toxicology (NKMT)

October 18–19, 2007, Uppsala, Sweden

Locality: Atrium (Folkets Hus), Dragarbrunnsgatan 46, Uppsala

Day 1 (Thursday, Oct. 18)

10.00–10.30 *Registration, coffee/tea served*

10.30–10.45 Introduction by the organisers

Chairman: Leif Busk, NFA, Uppsala, Sweden

10.45–11.15 DALY and QALY – an introduction

Tahereh Moradi, Karolinska Institutet, Stockholm, Sweden

11.15–12.00 Our food, Our health: Healthy diet and safe food in the Netherlands

Bert-Jan Baars, National Institute of Public Health and the Environment, The Netherlands

12.00–13.10 *Lunch*

13.10–13.40 *After-lunch divertissement*

13.45–14.30 Toxicity testing in the 21st century

Daniel Krewski, McLaughlin Centre for Population Health Risk Assessment, University of Ottawa, Canada

14.30–15.15 Risk-benefit analysis of seafood consumption using probabilistic modelling

Isabelle Sioen, University of Ghent, Belgium

15.15–15.45 *Coffee/tea*

15.45–16.30 Update on EFSA's activities in the area of risk-benefit assessment

David Carlander, EFSA

16.30–17.00 Summing up, speakers in panel

19.30 Dinner at Restaurang Trean, Hamnesplanen 3.

Day 2 (Friday, Oct 19)

Chairman: Leif Busk, NFA, Uppsala, Sweden

09.00–09.10 Information and introduction

09.10–10.10 Review of risk-benefit activities on fish in the Nordic countries

Salomon Sand, NFA, Uppsala, Sweden

Remarks and questions from Nordic and other delegates.

- 10.10–11.10 Group discussion (4-5 groups), including *coffee/tea* (smaller rooms are available)
- 11.10–12.10 Reports from the groups
- 12.10–13.20 *Lunch*
- 13.20–14.00 Conclusions from the seminar

Appendix II: Seminar participants

Participants	Organisation	Country
Abramsson Zetterberg Lillianne	National Food Administration	Sweden
Ankarberg Emma	National Food Administration	Sweden
Baars Bert-Jan	National Institute for Public Health and the Environment	Netherlands
Becker Wulf	National Food Administration	Sweden
Berglund Marika	Institute of Environmental Medicine, Karolinska Institutet	Sweden
Bjerselius Rickard	National Food Administration	Sweden
Briem Brynhildur	Environment and Food Agency	Iceland
Busk Leif	National Food Administration	Sweden
Carlander David	EFSA Scientific Committee and Advisory Forum Support Unit	Italy
Dadadóttir Sigurborg	Environment and Food Agency of Iceland	Iceland
Darnerud Per Ola	National Food Administration	Sweden
Dimitrovskaja Maja	National Food Administration	Sweden
Fotland Tor Øystein	Norwegian Scientific Committee for Food Safety	Norway
Frey Margus	Veterinary and Food Board	Estonia
Hallikainen Anja	Finnish Food Safety Authority	Finland
Hallström Helena	National Food Administration	Sweden
Haugen Margaretha	Norwegian Public Health Institute	Norway
Hedlund Britta	Swedish Environmental Protection Agency	Sweden
Herlin Maria	Institute of Environmental Medicine, Karolinska Institutet	Sweden
Hörnfeldt-Olson Katarina	National Food Administration	Sweden
Ilbäck Nils-Gunnar	National Food Administration	Sweden
Ilevicius Zilvinas	State Food and Veterinary Service	Lithuania
Johansson Gunnar	Swedish National Institute of Public Health	Sweden
Johansson Lars	Directorate for Health and Social Affairs, Department for Nutrition	Norway
Johnsson Pernilla	National Food Administration	Sweden
Karlsson Pernilla	The Swedish Chemical Agency	Sweden
Kāzocina Aija	Food Center of Food and Veterinary Service	Latvia
Kranauskas Almantas	National Nutrition Center Ministry of Health	Lithuania
Krewski Daniel	McLaughlin Centre for Population Health Risk Assessment, University of Ottawa	Canada
Larsen Jens-Jørgen	The National Food Institute	Denmark
Leino Olli	Department of Environmental Health	Finland
Licht Cederberg Dorthe	Danish Veterinary and Food Administration	Denmark
Lind Monica	Institute of Environmental Medicine, Karolinska Institutet	Sweden
Lindblad Mats	National Food Administration	Sweden
Lindqvist Roland	National Food Administration	Sweden
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