EFSA Journal 2012;10(10):s1001

SPECIAL ISSUE

Main achievements and challenges of the EFSA Scientific Committee since its inception

Vittorio Silano, Ada Knaap, David Lovell, Djien Liem[1, 2]

European Food Safety Authority (EFSA), Parma, Italy

Received: 07 June 2012

ABSTRACT

In about ten years of activity, the Scientific Committee of EFSA has been successful in addressing a number of challenging areas of increasingly complex nature related to scientific and procedural aspects of risk assessment in the food and feed chain. The scientific outputs adopted so far by the Scientific Committee are summarised and assigned to the three main areas of responsibility that the Scientific Committee covers: (i) opinions dealing with innovative risk assessment methodologies; (ii) opinions aiming at ensuring transparency and improving quality of specific components of risk assessment; and (iii) opinions addressing risk assessment of specific multisectoral issues. The main future challenge for the Scientific Committee will be in assisting EFSA to implement its 'Science Strategy' for the years 2012-2016, a recently developed and highly sophisticated approach: (i) to further develop EFSA's scientific excellence, and other core values, such as openness, transparency, independence and responsiveness; (ii) to optimise the use of European risk assessment capacity across the EU; (iii) to develop and harmonise methodologies and approaches to assess risks associated with the food/feed chain; and (iv) to strengthen the scientific basis for risk assessment and risk monitoring in the food/feed chain.

KEY WORDS

Risk, assessment, methodologies, transparency, quality, cloning, nanomaterials

[1] Correspondence: scientific.committee@efsa.europa.eu

[2] Acknowledgment: The authors wish to thank all the members of the Scientific Committee who contributed to the work that has been referred to in this article: Boris Antunovic, Susan Barlow, Andrew Chesson, John Daniel Collins†, Erik Dybing, Tito Fernandes, Albert Flynn, Claudia Fruijtier-Pölloth, Corrado Galli, Anthony Hardy, Bo Jansson, Klaus-Dieter Jany, Michael Jeger, Ada Knaap, Harry Kuiper, John Christian Larsen, David Lovell, Alicja Mortensen, Pierre Le Neindre, Birgit Noerrung, Iona Pratt, Ivonne Rietjens, Jan Schans, Josef Schlatter, Vittorio Silano, Staffan Skerfving, Frans Smulders, Philippe Vannier and Josep Vives-Rego. The authors also wish to thank the staff members of EFSA's Scientific Committee Unit for all support provided during the preparation of these scientific outputs.

Suggested citation: Silano V, Knaap A, Lovell D, Liem D; Special issue: Main achievements and challenges of the EFSA Scientific Committee since its inception. EFSA Journal 2012;10(10):s1001. [11 pp.]. doi:10.2903/j.efsa.2012.s1001. Available online: www.efsa.europa.eu/efsajournal

INTRODUCTION

The Scientific Committee of EFSA (SC), composed of the Chairs of the Scientific Panels and of six scientific experts who do not belong to any of the Scientific Panels, was established in mid-2003 by Article 24 of the Regulation (EC) No 178/2002[3] as one of the bodies of the European Food Safety Authority (EFSA). The SC has been responsible for the general coordination necessary to ensure consistency of scientific opinion procedures, in particular with regard to the adoption of working procedures and harmonisation of working methods. Moreover, it has provided opinions on multisectoral issues falling within the competence of more than one Scientific Panel, and on issues which do not fall within the competence of any of the Scientific Panels.

The work plan of the SC has been developed every three years through a priority setting procedure developed to take into account effectively the common needs of EFSA, and especially those of the Scientific Panels, in terms of innovative approaches to risk assessments as well as to respond to requests coming from the European Commission, the European Parliament, or from the EU Member States. Many working groups, mainly consisting of experts that are not Panel members or EFSA staff, have been established by the SC and their expertise has been very helpful when developing scientific opinions.

In addition to specific opinions dealing with multisectoral issues, the SC has been involved in developing innovative risk assessment methodologies and in harmonising risk assessment procedures and approaches in fields where EU-wide consensus had not already emerged. It is not surprising, therefore, that the SC's work has been focused on providing EFSA with essential tools needed to fulfil its mission in an optimal and coherent manner, by making use of the self-tasking procedure rather than providing opinions in reply to external requests, e.g. from the European Commission or European Parliament, which has been much more the case for EFSA's Scientific Panels.

1. INNOVATIVE RISK ASSESSMENT METHODOLOGIES

The SC has devoted most of its work to innovative risk assessment methodologies in the food/feed chain (Table 1). Some of these new methodologies have been developed by the SC; other work has focused on assessing and developing innovative methods originally devised by others.

Table 1: Innovative risk assessment procedures adopted by the EFSA Scientific Committee

Scientific output adopted by the SC	Summary of output
A. Risk assessment of genotoxic and carcinogenic substances (EFSA, 2005c; EFSA Scientific Committee (SC), 2012b)	The 'margin of exposure' (MOE) is recommended as a harmonised approach for assessing the risks posed in food and feed by unavoidable exposure to substances which are both genotoxic and carcinogenic. This approach can be applied to substances naturally occurring in foods, to environmental contaminants or to those resulting from food preparation or manufacturing processes, and impurities that find their ways into the food/feed chain. The advantage of this methodology is that it allows the comparison of risks posed by these substances based on their individual potency and on possible levels of exposure in the population, and thus is better suited to support risk managers in defining possible actions required to control exposure to such substances.

[3] Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety. OJ L 31, 1.2.2002, p. 1-24.

B. Identification of emerging risks (EFSA, 2006b; EFSA, 2007d)	The need to set up a system for identifying emerging risks, i.e. risks due to new hazards or to increased exposure or susceptibility to known hazards, was identified as a priority by the SC soon after the establishment of EFSA. Operational guidelines and recommendations for a practical implementation of such a system were then proposed in 2006 and an operational definition of 'emerging risks' was adopted by EFSA in 2007. Later on, the early identification of 'emerging risks' has been selected as one of the subjects for cooperation between EFSA and EU Member States. Currently, the work on emerging risks is continuing under the responsibility of the Emerging Risks Unit.
C. Qualified presumption of safety of microorganisms (QPS) (EFSA, 2005a; EFSA, 2007c)	QPS is a generic assessment system based on establishing the identity, body of knowledge, possible pathogenicity and end use of microorganisms. QPS status applies strictly to the safety of microorganisms and not to any traded product containing the organism or to a product of the microorganism. As the number of organisms considered suitable for QPS status is very large, the SC concluded that the introduction of a QPS system for microorganisms would meet the objectives of providing a practical tool for setting priorities and avoiding the need to carry out extensive investigations of organisms known not to cause concern.
D. Benchmark Dose (BMD) approach in risk assessment (EFSA, 2009d)	The BMD approach makes better use of the dose-response data from studies in experimental animals or from observational epidemiological studies to characterise and quantify potential risks. The SC concluded that the BMD approach is a scientifically more advanced method than the No-Observed-Adverse-Effect Level (NOAEL) for deriving a Reference Point for risk assessment, since it makes extended use of available dose-response data and provides a quantification of the uncertainties in the dose-response data. Using the BMD approach also results in a better defined Reference Point, as a consequence of using a specified magnitude for the benchmark response.
E. Risk/benefit assessment of food (EFSA Scientific Committee (SC), 2010)	The opinion addresses the increasing need to give advice on both the risks and benefits of foods. It gives guidance on performing risk-benefit assessments of food focused on human health risks and human health benefits. It is essential that the formulation of the problem precedes the risk-benefit assessment. A stepwise approach is recommended for the risk-benefit assessment consisting of several steps: (i) initial assessment, addressing the question whether the health risks clearly outweigh the health benefits or vice versa; (ii) refined assessment, aiming at providing semi-quantitative or quantitative estimates of risks and benefits at relevant exposure by using common metrics; and (iii) comparison of risks and benefits on a comparable scale.
F. 90-Day toxicity test on whole food and feed (EFSA, 2011d)	Guidance is provided on how to improve the performance and statistical analysis of 90-day toxicity tests on genetically modified (GM) whole food/feed and novel whole food/feed. A randomised block design is recommended when testing whole food/feed on socially-housed animals. Preparation of appropriate test diets is a key element of this test methodology. Fewer dose levels but more animals in control and top dose groups should be used to maximise the power of the study together with a power analysis to estimate a sample size capable of detecting a pre-specified biologically relevant effect size with a specified power and significance level.
G. Genotoxicity testing strategies (EFSA Scientific Committee (SC), 2011c)	The SC reviewed the current state-of-the-science on genotoxicity testing and provided a commentary and recommendations for a genotoxicity testing strategy, particularly aimed at harmonising testing requirements across EFSA Panels that assess food/feed products. A stepwise approach is recommended for the generation and evaluation of data on genotoxic potential, beginning with a basic battery of *in vitro* tests, comprising a bacterial reverse mutation assay and an *in vitro* micronucleus assay. Further recommendations are made on follow-up, where necessary, of the results of the basic battery.

H. Safety evaluation of traditional botanical food supplements and the Compendium (EFSA, 2004; EFSA Scientific Cooperation (ESCO) 2009, EFSA Scientific Committee (SC), 2009; EFSA, 2012a)	A two-tiered scientific approach on botanicals is suggested, depending on the existing level of knowledge on a given botanical and the substance(s) it contains. The guidance also provides a set of criteria to help in prioritising the safety assessment of botanical ingredients that are in use. A related report, produced in cooperation between EFSA and experts from national food safety authorities, gives a number of examples that illustrate how the proposed approach could be applied under different circumstances. Working together with EU Member States, EFSA has also compiled in 2008 and updated in 2012 the available information on a large number of botanicals which have been reported to contain substances that may be of health concern when used in food or food supplements and may require specific consideration.
I. Threshold of Toxicological Concern (TTC) as a screening tool for providing scientific advice (EFSA Scientific Committee (SC), 2012c)	The TTC approach is a probability-based screening tool that allows advice to be given on substances for which the chemical structure and exposure are known, but for which there are few or no relevant toxicity data. Many chemicals and types of toxicity have thresholds, i.e. a level of exposure below which adverse effects are not observed. Generic TTC values have been developed from existing data on many chemicals. Several TTC values to cover non-cancer effect are set at 18 to 1 800 micrograms per person per day, equivalent to 0.3 or 30 micrograms/kg body weight per day, depending on the structure of the chemical. The TTC value below which it is considered that consumers would be protected from cancer, with reasonable certainty of no harm, is set at the very low value of 0.15 micrograms per person per day, equivalent to 0.0025 micrograms/kg body weight per day. The Scientific Committee opinion concluded that the TTC approach is conservative and, as such, fit for purpose as a screening tool for setting priorities for assessing the safety of chemicals or for deciding whether exposure to a substance is so low that no further data are necessary.

Moreover, in 2009, the SC adopted the Opinion on 'alternative approaches for animal testing', which is an appraisal of the existing approaches for incorporating replacement, reduction and refinement methods ("three Rs") for toxicological animal tests that are relevant to the different areas of EFSA's activities.

The SC has not only developed many innovative risk assessment methodologies, but in some cases it has also undertaken initiatives to check a) whether the new risk assessment methodologies developed are (broadly) used or not; b) if yes, how they are used; c) if not, why they have not been used; and d) whether any needs have been identified for further improvements. A Compendium of traditional botanical products requested by EU Member States[4] was produced (EFSA, 2009f). It was therefore very encouraging for the SC that in 2012 its enquiry[5] indicated a high level of consensus on the usefulness of this methodology among the Member States.

[4] This was the outcome of a questionnaire completed by the Member States in relation to a Discussion Paper of the Scientific Committee on "Botanicals and Botanical Preparations widely used as food supplements and related products: Coherent and Comprehensive Risk Assessment and Consumer Information Approaches" (EFSA, 2004) which was presented to EFSA's Advisory Forum at its meeting in Rome on 1st October 2004 (available at http://www.efsa.europa.eu/en/af040930/docs/af040930-ax2.pdf)

[5] See: agenda item 10 of the Minutes of the 52nd Plenary Meeting of the EFSA Scientific Committee held on 5-6 December 2011, available at http://www.efsa.europa.eu/en/events/event/111205-m.pdf

2. ENSURING TRANSPARENCY AND IMPROVING QUALITY OF SPECIFIC COMPONENTS OF RISK ASSESSMENT

At the EFSA inception, there was a strong need for the SC to develop guidance on how to ensure transparency and quality of the scientific opinions adopted by EFSA's Scientific Committee and Panels. Therefore, during its first 3-year mandate, the SC focussed on advising EFSA on how to meet those objectives. Initial opinions of the SC were on approaches dealing with exposure assessment (EFSA, 2005b) and uncertainties in exposure assessment (EFSA, 2006c). In the opinion on exposure assessment, the SC provided guidance on harmonised methods for exposure assessments to be carried out by EFSA's Panels together with advice on a suitable strategy for the collection of e.g. food consumption and occurrence data. In its opinion on uncertainties in exposure assessment, the SC recommended a systematic examination of potential sources and types of uncertainty, to maximise the likelihood that important uncertainties are recognised. A tiered approach to analysing uncertainties was also recommended. Each uncertainty in an assessment may be analysed at one of three tiers: initially, all important uncertainties may be analysed qualitatively; those uncertainties that appear critical to the outcome may be analysed deterministically or probabilistically.

In 2007, the SC also delivered its proposal on how to handle urgent questions to EFSA and how to carry out INternal and EXternal (INEX) review of EFSA's scientific work to give a continuing feedback about the quality of its work (EFSA, 2007b). The INEX guidance developed by the SC consists of four components: (i) self-review: during the development of an opinion or any other scientific document the compliance with best scientific practice should be checked; (ii) internal scientific review: before adoption by the relevant Scientific Panel(s) or Committee a sample of EFSA draft opinions or other scientific documents should be reviewed by senior scientific staff not previously involved in the preparation or adoption of the opinion; (iii) external scientific review: a number of EFSA adopted opinions, or other scientific documents should be reviewed by independent scientists; and (iv) the appreciation of EFSA's scientific work by the intended users should also be assessed.

Issues related to the transparency of the process and science in risk assessment were addressed with two separate SC opinions in 2006 (EFSA, 2006a) and 2009 (EFSA, 2009b), providing, respectively, a broad set of procedural and substantial suggestions and recommendations. The opinion of 2006 dealt with process-related transparency, addressed many aspects including: (i) handling of requests for scientific opinions; (ii) selection of qualified independent scientists; (iii) adequate exchange of information between risk assessors and risk managers; (iv) involvement of stakeholders prior and during the risk assessment; (v) adoption of opinions; (vi) dissemination of opinions; (vii) confidentiality and access to documents; and (viii) procedure for revising/updating scientific opinions. The 2009 opinion, dealing with the scientific principles of risk assessment, addressed: (i) data and data sources; (ii) inclusion and exclusion of data; (iii) confidential data; (iv) assumptions; (v) assessment; (vi) variability; (vii) uncertainties; and (viii) conclusions of the risk assessment.

The SC returned to this procedural type of opinion during its third mandate (2009-2012) when it became evident that working approaches of different EFSA Panels on specific subjects (e.g. endocrine active substances (EFSA, 2010b), anti-microbial resistance (EFSA, 2011a), and environmental (ecological) risk assessment (EFSA, 2011b)) needed to be further harmonised. Consequently, task forces composed of EFSA scientific staff and external experts were created, which prepared reports that were then used as a starting point for further discussions by the SC.

Similarly, in order to harmonise further the approaches for handling issues common to different Panels, the SC adopted four additional scientific opinions. They deal with:

- statistical approaches (EFSA Scientific Committee (SC), 2011b) with the aim of clarifying the concepts and definitions of biologically-relevant and/or statistically-significant effects and reviewing statistical approaches relevant for risk assessment;

- default assumptions (EFSA Scientific Committee (SC), 2012a) describing the scientific rationale for a number of default values to be used in a harmonised way across EFSA's Scientific Committee, Scientific Panels and Units in the absence of empirical data;
- terminology in risk assessment (EFSA Scientific Committee (SC), 2012d) to improve harmonisation and consistency of risk assessment terminology used by experts in EFSA.

3. RISK ASSESSMENT ON MULTISECTORAL ISSUES

A few requests for opinions on truly multisectoral issues have been received by the SC.

3.1. Animal cloning (EFSA, 2008, EFSA, 2009e, EFSA, 2010a and EFSA, 2012b)

The SC opinion (EFSA, 2008) indicated that death and disease rates of clones are significantly higher than those observed in conventionally reproduced animals. However, Somatic Cell Nucleus Transfer (the most common technique used to clone animals) has also resulted in the production of healthy cattle and pig clones, and healthy offspring that are similar to their conventional counterparts based on parameters such as physiological characteristics, behaviour and clinical status. There is no indication that differences exist in terms of food safety for meat and milk from clones and their progeny compared with those from conventionally bred animals. However, such a conclusion is based on the assumption that meat and milk are derived from healthy animals, which are subject to relevant food safety regulations and controls. Only pigs and cattle were addressed in this opinion, because adequate data were only available for these two species. No environmental impact is expected but there are only limited data available. In 2009, 2010 and 2012, EFSA received further requests from the European Commission for updates on scientific developments on the issue of cloning of farmed animals for food production purposes. Based on the literature searches and data provided, it was concluded that information available on species other than cattle and pigs, which would allow for assessment of food safety and animal health and welfare aspects, is still limited.

3.2. Nanomaterials and nanotechnologies (EFSA, 2009a, EFSA Scientific Committee (SC), 2011a)

The European Commission has asked EFSA to provide advice on potential risks arising from the use of nanoscience and nanotechnologies in food and feed (EFSA, 2009a). The risk assessment paradigm (hazard identification, hazard characterization, exposure assessment and risk characterization) was considered applicable for engineered nanomaterials (ENMs). It became evident that the majority of the available information on toxicity of ENMs is from *in vitro* studies or *in vivo* studies using routes of exposure other than food. The risk assessment of ENMs has to be performed on a case-by-case basis. The SC made a series of recommendations, for example to develop methods to detect and measure ENMs in food/feed and biological tissues, to survey the use of ENMs in the food/feed area, to assess the exposure in consumers and livestock, and to generate information on the potential for oral toxicity of different ENMs.

In 2011, a practical approach for assessing potential risks arising from applications of nanoscience and nanotechnologies in the food and feed chain was produced by the SC (EFSA Scientific Committee (SC), 2011a). In the opinion the SC provided guidance on: (i) requirements for the physico-chemical characterisation of ENMs used e.g. as food additives, enzymes, flavourings, food contact materials, novel foods, feed additives and pesticides, and; (ii) testing approaches to identify and characterise hazards arising from the nanoproperties which, in general, should include information from *in vitro* genotoxicity studies, absorption, distribution, metabolism and excretion studies, and repeated-dose 90-day oral toxicity studies in rodents.

4. FUTURE CHALLENGES FOR THE EFSA SCIENTIFIC COMMITTEE

The main challenge for the SC in the future will be to support EFSA in the implementation of the Science Strategy for 2012-2016[6], adopted by the EFSA Management Board in December 2011, including the: (i) implementation of the Integrated Quality Management System by 2016; (ii) organisation of a multi-annual data collection work program; (iii) identification of research priorities for the European Commission and Member States; (iv) further development of the EU Menu to evaluate food consumption in different countries; (v) further work on scientific transparency in risk assessment (RA) especially when dealing with uncertainties and with RA terminology; and (vi) development of a harmonised risk assessment approach applicable, although with some specificities, throughout the food/feed sector. In such a framework, the SC is also expected to contribute to the systematic identification of priority areas for the promotion of scientific cooperation between EFSA and Member States. Moreover, the results achieved by the SC during the first ten years of EFSA clearly lead on to some specific future priorities to develop risk assessment methodologies in areas already addressed in the past, while completely new priority areas have also emerged in the mean time (for some examples see Table 2).

Table 2: Some specific priority issues identified by EFSA's Scientific Committee in 2012 for future work

- Identification of emerging risks by a standing *ad hoc* Working Group under the umbrella of the SC composed of representatives of the SC and Panels.
- Identifying/implementing new approaches for hazard characterisation (e.g. mode of action, mixture toxicity, omics, Quantitative structure-activity relationships (QSAR), *in vitro/in silico* approaches).
- Hazard characterisation of botanicals and botanical preparations to work out the third version of the Compendium and developing a safety assessment approach through a QPS methodology.
- Consideration of overall exposure estimates (including non-food sources) for the safety assessment of carcinogenic, genotoxic and other highly-toxic substances in food/feed.
- Risk assessment of chemical mixtures in the area of plant protection products and the possible extension of this approach to other sectors.
- Developing a joint project between EFSA, the European Commission (Directorate Generals (DGs) Research, Environment and Health and Consumers) and competent agencies in Member States to ensure a systematic and early identification of data that would require an updating of opinions already adopted by EFSA.
- Collaboration of the Scientific Committee with the relevant Panels (Pesticides (PPR), Plant health (PLH), Genetically modified organisms (GMO), Feed (FEEDAP), Biological Hazards (BIOHAZ), Contaminants (CONTAM)) on harmonising environmental risk assessment methodologies and developing test methodologies in the area of ecotoxicology.
- Developing a guidance on a practical methodology for risk ranking comparing the positive and negative health impact of chemical, biological and nutritional components in food; and advising EFSA on how to conduct a multi-agency project on risk ranking in cooperation with key organisations within and outside the EU.
- Updating SC's guidance document on the risk assessment of engineered nanomaterials released in 2011 taking into account developments occurring at international (i.e. Organisation for Economic Co-operation and Development (OECD)) and third country (i.e. U.S. Food and Drug Administration (FDA)) level and by specifically considering the issues related to the definition of nanomaterials being worked out at European level.
- Systematic updating of SC's opinion on the risk assessment of animal cloning taking into account the results of fast developing scientific investigations in this sector.
- Preparation of a scientific opinion on the theory of low dose non-monotonic dose-response in toxicology.

[6] Available from http://www.efsa.europa.eu/en/corporate/doc/sciencestrategy12.pdf

- Possible collaboration with the World Health Organization (WHO) and other risk assessment bodies in the development of international consensus on a harmonised approach for the application of the concept of TTC in the area of food and feed safety.
- Reviewing the current use of human data in risk assessments and preparing a guidance document for its use in EFSA's risk assessment practices.
- Systematic review of the implementation of risk assessment methodologies as developed by the Scientific Committee and Panels in the routine work of relevant Panels to promote the adoption of a more integrated scientific evaluation approach across EFSA.

CONCLUSIONS

In the last ten years, through more than 50 plenary sessions and 400 working group sessions, the SC has addressed many challenging areas of an increasingly complex science. It has made an important contribution to one of EFSA's main tasks: ensuring the safety of food and feed across the EU. The work of the SC has been at the forefront of scientific thinking and at times controversial. In recognition of this, the SC has, since its inception, been fully engaged in public consultations on its work.

The SC has also taken on a leadership role in providing guidance on good risk assessment practices applicable across EFSA as well as worldwide. Horizontal guidance has been developed that is applicable across sectors on generic issues, such as on how to address consistency, transparency and uncertainties in risk assessment. The SC has also developed more specific vertical guidance on methodological issues within a sector such as in the area of botanicals and nanomaterials.

A further important achievement of the SC has been its ability to provide an effective platform which has allowed open and systematic internal consultation on most of the different issues addressed by EFSA. Through this, the SC has proven to be able to initiate and achieve highly effective consensus building procedures.

In the first ten years of the Scientific Committee's existence, it has helped to introduce important changes in the risk assessment process within the European Union. The future will be of continuing innovation in many of the technical areas, with rapid developments expected in many areas of the biological sciences. One of the challenges for EFSA will be to continue to maximize the effectiveness of the many experts who volunteer to contribute to its Scientific Committee, Panels and Working Groups to ensure that EFSA as a whole continues to receive the independent, relevant and the highest quality advice that it has been fortunate to have had for the first ten years of its existence. The importance of maintaining such a group of independent experts, who are selected on scientific expertise and experience rather than to represent narrow interest groups, cannot be over-emphasized and will be the key to maintaining this successful beginning.

About the authors

Vittorio Silano, Chair of the Scientific Committee from 2003 to 2012, Chair of the Editorial Board of the EFSA Journal from 2009 to 2012, **Ada Knaap,** Vice-Chair of the Scientific Committee from 2003 to 2012, Member of the Editorial Board of the EFSA Journal from 2009 to 2012, **David Lovell,** Vice-Chair of the Scientific Committee from 2009 to 2012, Member of the Editorial Board of the EFSA Journal from 2009 to 2012, and **Djien Liem,** Head of the Scientific Committee Unit.

REFERENCES

EFSA (European Food Safety Authority), 2004. Discussion Paper on "Botanicals and Botanical Preparations widely used as food supplements and related products: Coherent and Comprehensive Risk Assessment and Consumer Information Approaches". Document of the Scientific Committee with reference EFSA/SC/26 Final, 25 June 2004.

EFSA (European Food Safety Authority), 2005a. Opinion of the Scientific Committee on a request from EFSA related to a generic approach to the safety assessment by EFSA of microorganisms used in food/feed and the production of food/feed additives. The EFSA Journal (2005) 226, 1-12.

EFSA (European Food Safety Authority), 2005b. Opinion of the Scientific Committee on a request from EFSA related to Exposure Assessments. The EFSA Journal (2005) 249, 1-26.

EFSA (European Food Safety Authority), 2005c. Opinion of the Scientific Committee on a request from EFSA related to A Harmonised Approach for Risk Assessment of Substances Which are both Genotoxic and Carcinogenic. The EFSA Journal (2005) 282, 1-31.

EFSA (European Food Safety Authority), 2006a. Transparency in risk assessment carried out by EFSA: Guidance Document on procedural aspects. The EFSA Journal (2006) 353, 1 – 16.

EFSA (European Food Safety Authority), 2006b. Opinion of the Scientific Committee on a request from EFSA related to the early identification of emerging risks. The EFSA Journal (2006) 375, 1-14.

EFSA (European Food Safety Authority), 2006c. Guidance of the Scientific Committee on a request from EFSA related to Uncertainties in Dietary Exposure Assessment. The EFSA Journal (2006) 438, 1-54.

EFSA (European Food Safety Authority), 2007a. Scientific advice by the Scientific Committee. EFSA's Responsiveness to Urgent Questions. Approaches to enhance EFSA's responsiveness to Urgent Questions. The EFSA Journal (2007) 525, 1-4.

EFSA (European Food Safety Authority), 2007b. Scientific Advice by the Scientific Committee. Internal and External Review. Proposal for a Review System for EFSA's Scientific Activities. The EFSA Journal (2007) 526, 1-15.

EFSA (European Food Safety Authority), 2007c. Opinion of the Scientific Committee on a request from EFSA on the introduction of a Qualified Presumption of Safety (QPS) approach for assessment of selected microorganisms referred to EFSA. The EFSA Journal (2007) 587, 1-16.

EFSA (European Food Safety Authority), 2007d. Definition and description of "emerging risks" within EFSA (European Food Safety Authority), 2007. Definition and description of "emerging

risks" within the EFSA's mandate. Document of the Scientific Committee & Advisory Forum Unit with reference EFSA/SC/415 final, 10 July 2007.

EFSA (European Food Safety Authority), 2008. Scientific Opinion of the Scientific Committee on a request from the European Commission on Food Safety, Animal Health and Welfare and Environmental Impact of Animals derived from Cloning by Somatic Cell Nucleus Transfer (SCNT) and their Offspring and Products Obtained from those Animals. The EFSA Journal (2008) 767, 1-49.

EFSA (European Food Safety Authority), 2009a. Scientific Opinion of the Scientific Committee on a request from the European Commission on the Potential Risks Arising from Nanoscience and Nanotechnologies on Food and Feed Safety. The EFSA Journal (2009) 958, 1-39.

EFSA (European Food Safety Authority), 2009b. Guidance of the Scientific Committee on transparency in the scientific aspects of risk assessment carried out by EFSA. Part 2: general principles. The EFSA Journal (2009) 1051, 1-22.

EFSA (European Food Safety Authority), 2009c. Opinion of the Scientific Committee on a request from EFSA on existing approaches incorporating replacement, reduction and refinement of animal testing: applicability in food and feed risk assessment. The EFSA Journal (2009) 1052, 1-77.

EFSA (European Food Safety Authority), 2009d. Guidance of the Scientific Committee on a request from EFSA on the use of the benchmark dose approach in risk assessment. The EFSA Journal (2009) 1150, 1-72.

EFSA (European Food Safety Authority), 2009e. Statement of EFSA prepared by the Scientific Committee and Advisory Forum Unit on Further Advice on the Implications of Animal Cloning (SCNT). The EFSA Journal (2009) RN 319, 1-15.

EFSA (European Food Safety Authority), 2009f. Compendium of botanicals that have been reported to contain toxic, addictive, psychotropic or other substances of concern on request of EFSA. EFSA Journal 2009;7(9):281. [100 pp.].

EFSA (European Food Safety Authority), 2010a. Update on the state of play of animal cloning. EFSA Journal 2010;8(9):1784. [21 pp.].

EFSA (European Food Safety Authority), 2010b. Scientific report of the Endocrine Active Substances Task Force. EFSA Journal 2010;8(11):1932. [59 pp.].

EFSA (European Food Safety Authority), 2011a. EFSA approaches to risk assessment in the area of antimicrobial resistance, with an emphasis on commensal microorganisms. EFSA Journal 2011;9(10):196. [29 pp.].

EFSA (European Food Safety Authority), 2011b. Review of current practices of environmental risk assessment within EFSA. Supporting Publication: 2011:116. [39 pp.].

EFSA (European Food Safety Authority), 2012a. Compendium of botanicals reported to contain naturally occurring substances of possible concern for human health when used in food and food supplements. EFSA Journal 2012;10(5):2663. [60 pp.].

EFSA (European Food Safety Authority), 2012b. Statement of EFSA prepared by the Scientific Committee Unit on Further Advice on the Implications of Animal Cloning (SCNT). In preparation.

EFSA Scientific Committee (SC), 2009. Guidance on Safety assessment of botanicals* and botanical preparations** intended for use as ingredients in food supplements. EFSA Journal 2009; 7(9):1249. [25 pp.].

EFSA Scientific Committee (SC), 2010. Guidance on human health risk-benefit assessment of foods. EFSA Journal 2010; 8(7)1673. [41 pp.].

EFSA Scientific Committee (SC), 2011a. Guidance on the risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain. EFSA Journal 2011;9(5):2140. [36 pp.].

EFSA Scientific Committee (SC), 2011b. Statistical Significance and Biological Relevance. EFSA Journal 2011;9(9):2372. [17 pp.].

EFSA Scientific Committee (SC), 2011c. Scientific opinion on genotoxicity testing strategies applicable to food and feed safety assessment. EFSA Journal 2011;9(9):2379. [68 pp.].

EFSA Scientific Committee (SC), 2011d. Guidance on conducting repeated-dose 90-day oral toxicity study in rodents on whole food/feed. EFSA Journal 2011;9(12):2438. [21 pp.].

EFSA Scientific Committee (SC), 2012a. Guidance on selected default values to be used by the EFSA Scientific Committee, Scientific Panels and Units in the absence of actual measured data. EFSA Journal 2012;10(3):2579. [32 pp.].

EFSA Scientific Committee (SC), 2012b. Statement on the applicability of the Margin of Exposure approach for the safety assessment of impurities which are both genotoxic and carcinogenic in substances added to food/feed. EFSA Journal 2012;10(3):2578. [5 pp.].

EFSA Scientific Committee (SC), 2012c. Scientific Opinion on Exploring options for providing advice about possible human health risks based on the concept of Threshold of Toxicological Concern (TTC). EFSA Journal 2012;10(7):2750. [103 pp.].

EFSA Scientific Committee (SC), 2012d. Scientific Opinion on Risk Assessment Terminology. EFSA Journal 2012;10(5):2664. [43 pp.].

EFSA Scientific Cooperation (ESCO) Working Group on Botanicals and Botanical Preparations, (2009); Advice on the EFSA guidance document for the safety assessment of botanicals and botanical preparations intended for use as food supplements, based on real case studies on request of EFSA. EFSA Journal 2009;7(9):280. [104 pp.].