

**European Food Safety Authority
Scientific Colloquium on Microorganisms in Food and Feed:
Qualified Presumption of Safety**

**Brussels, Belgium
13-14 December 2004**

**A Report to ISAPP by
Jim Heimbach
JHeimbach LLC
Washington DC, USA**

Background

The European Food Safety Authority (EFSA) is responsible for providing scientific advice and scientific and technical support to the European Commission with regard to the safety of foodstuffs, food ingredients, and procedures and substances used in the production of foods. A wide variety of bacteria and microfungi are used to produce fermented foods; in many cases, these are well-defined cultures, but many fermented foods are still produced either by spontaneous fermentation or by back-slopping, and the active cultures may be poorly defined.

EFSA notes that these uses of microorganisms are not subject to Community regulation, but rather are presumed to be safe based on their long history of use with no evident harm. However, there is no formal procedure for evaluating and operationalizing this “presumption of safety” such that it could be used as a basis for extrapolation to the likely safety of new applications of these strains and cultures or of closely related strains and cultures.

To this end, EFSA wishes to develop a qualified generic approval system based on the concept of “qualified presumption of safety” (QPS), defined as an assumption based on reasonable evidence and qualified to allow certain restrictions to apply. Such a system would improve the consistency of safety assessment and at the same time make better use of assessment resources by not requiring a full and arguably unnecessary safety review of organisms with a long history of safe use. Case-by-case safety assessments could be eliminated or restricted to only those aspects that are relevant for the organism in question.

EFSA convened a working group consisting of members of the Scientific Committee on Animal Nutrition, the Scientific Committee on Food, and the Scientific Committee on Plants, which prepared a working paper outlining this approach. This paper, *On a Generic Approach to the Safety Assessment of Microorganisms Used in Feed/Food and Feed/Food Production*, is available on the Commission website, http://europa.eu.int/comm/food/fs/sc/scf/out178_en.pdf.

The scientific colloquium was convened with the stated objective “to have an open scientific debate on the QPS approach and to explore options how to develop the concept of QPS into a proposal for the regulatory community that is based on sound scientific principles.” Further information about the objectives and structure of the colloquium may be found at EFSA’s website, http://www.efsa.eu.int/science/colloquium_series/no2_qps/610/colloq02_announcement_en1.pdf. Information regarding the results of the colloquium will also be placed on the website later this year.

Process

The colloquium was attended by about 80 scientists from all over Europe, as well as two Americans, Dr. Laura Tarantino of the Food and Drug Administration and me, representing ISAPP. Dr. Tarantino and I were selected to attend because EFSA regards the proposed QPS system as “similar in concept and purpose to the GRAS (Generally Recognized as Safe) definition used in the USA.” Incidentally, we have both concluded that QPS is not in any way similar to the American GRAS approach. While certain uses of substances may be determined to be GRAS based on safe history of use, such history is never regarded as an adequate basis to expand the uses of the substance significantly beyond those already existing.

After a plenary session with an introduction to EFSA and the QPS concept, as well as presentations on the French approach and the American GRAS concept, attendees were assigned to one of four discussion groups for the first afternoon and following morning. The discussion groups were:

Discussion Group 1: Traditional Uses of Microorganisms

Topics:

1. Is the safety evaluation of traditional uses necessary or desirable?
2. If yes, could the QPS approach be adapted to include natural fermentations?
3. If not, how could parameters like the presence of virulence factors and antibiotic resistances be considered?

Discussion Group 2: Taxonomy/Familiarity

Topics

1. What evidence of taxonomic status is needed?
2. What taxonomic level is appropriate for QPS?
3. What happens if a microorganism that has granted QPS would need to be reclassified? Will the QPS status be retained?
4. Is a history of apparent safe use sufficient evidence of safety (and for all purposes)?
5. Is lack of clinical data evidence of a lack of pathogenicity?
6. Should taxonomic units which include pathogenic strains be excluded from QPS?

Discussion Group 3: The Role of Molecular Tools in QPS

Topics

1. What is the role of molecular techniques in taxonomy and strain identification?
2. To what extent do the molecular tools define the risk of transmissible antibiotic resistance?
3. To what extent do the molecular tools define the risk of virulence?
4. What are the issues for the validation of results obtained by molecular techniques?
5. What is the potential of post-genomics tools?

Discussion Group 4: Advantages and Disadvantages of the QPS Approach

Topics

1. What are the strengths and weaknesses of the QPS approach?
2. Are there better alternatives to the QPS approach? If so, what are the advantages and disadvantages of these alternatives when compared to QPS.
3. Should it be a requirement for QPS to deposit the given strain in a culture collection?
4. Could the QPS approach be extended to enzymes and other products of micro-organisms?
5. Identify putative consequences of implementing the QPS or any suggested alternatives for e.g. consumers, industry, risk assessors, risk managers.

I requested and received assignment to Discussion Group 4. Incidentally, this discussion group also included two other ISAPP members, Colette Shortt (Yakult) and Eamonn Connolly (BioGaia). The conclusions and recommendations from each discussion group were reported back to a final plenary session for general discussion and conclusions, and the colloquium adjourned.

The plan is for a report of the colloquium to be prepared by the rapporteurs from the four discussion groups. This report will be considered by a newly established EFSA QPS working group charged with revising the QPS working paper, taking into account the comments made and considering how the QPS approach could be applied by EFSA for the safety assessment of microorganisms within the framework of current and proposed Community legislation.

Issues Discussed

There was considerable confusion among those most familiar with the EU regulatory environment for microorganisms about the objective of the entire QPS process. As I understand it, there is currently no Community-wide regulation of microorganisms used in the production of food for humans or as probiotic organisms, while microorganisms used in the production of animal feeds are tightly regulated at the individual country level. Many individuals asked—with a fair level of concern—whether the QPS initiative presaged a change in this regulatory environment. The EFSA representatives insisted that it did not, but I admit that the potential application of the system is not clear to me.

Putting aside this question, most attendees agreed that it is appropriate to develop a harmonized approach to the assessment of the safety of microorganisms. A number of contentious scientific issues emerged.

1. Where will the boundaries be drawn? Will it encompass “traditional fermentations” in which the culture(s) used is(are) ill-defined or spontaneously derived? I was surprised to learn that many large production facilities use cultures that are only partially defined or not defined at all.

2. Antibiotic resistance determinants, particularly in relation to those organisms commonly used in the preparation of human foods, was seen as an extremely difficult area, partly because of the limited available data regarding patterns of antibiotic resistance and lack of standardization, and partly because some level of antibiotic resistance is known or suspected to be common among bacterial strains in common use. It was argued that antibiotic resistance has not been recognized as a problem in foods and there is no evidence to suggest that this form of human exposure has led to any measurable increase in resistance to antibiotics of clinical importance. Consequently the continuing use of existing strains should not be placed in jeopardy.

3. The need for an unequivocal identification of strains, and questions regarding the appropriate taxonomic level (genus, species, subspecies, strain) needed in order to make valid generic statements regarding safety. There was uncertainty whether identity should always reflect the state of the art or whether identity based on phenotypic criteria would be sufficient. There were some concerns that smaller companies may not have the facilities to undertake extensive taxonomic studies. In addition, it was pointed out that several microbial groups which might be eligible for QPS status are poorly understood and their taxonomy is undergoing almost continuous revision. There was extensive discussion of the potential impact of redefining a strain’s taxonomic classification upon its QPS status.

Many participants argued that it should never be necessary to characterize bacterial strains beyond the species level. I disagree, and so did the Discussion Group 2 recommendation, which suggested the subspecies level for lactic acid bacteria and the species level for most yeasts.

4. The question of whether taxonomic units that include pathogenic strains are appropriate for inclusion in QPS. The consensus is that it should depend on the gene transfer potential—similar in some ways to issues regarding transference of antibiotic resistance; most individuals were reluctant to rule out the possibility of some *Staphylococcus* or *Enterococcus* strains, for example, being regarded as generally safe based on history of past use.

5. Finally, I feel strongly that any strain that is to be regarded as safe based on history of use must be deposited in a recognized culture collection, but this was far from universally agreed to. Many individuals argued on the basis of confidentiality or economics that such deposit should not be required.

Next Steps

As noted above, a new EFSA working group is considering the recommendations and conclusions of the colloquium and revising the working paper on QPS. It is expected that a final report on the QPS approach will be available by summer of 2005.