

QUALITY OF LIFE PROGRAMME – FOOD, NUTRITION, AND HEALTH – PROJECTS PROMOTION

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The EC Quality of Life Programme (QoL), Key Action 1 – Food, Nutrition & Health aims at providing a healthy, safe, and high-quality food supply leading to reinforced consumer's confidence in the safety of the European food.

Key Action 1 is currently supporting several European projects investigating analytical methods for food control including sensors, risk analysis, and food safety standardisation. Their objectives range from the development and validation of prevention strategies for mycotoxin formation via the development of a communication platform for Genetically Modified Organisms (GMO), validation and standardisation of diagnostic Polymerase Chain Reaction (PCR) for food-borne pathogens, up to the evaluation of the potential cancer-preventing activity of pro-and pre-biotic («SYNBIOTIC») combinations in human volunteers. This paper also informs on future research needs in food safety.

Key words:
analytical methods, European Research, food safety,
legislation, quality management, risk analysis,
standardisation

The general aim of Key Action 1 (KA1) within the EC Quality of Life Programme (QoL) is to better understand consumer's requirements and to provide a healthy, safe, and high quality food supply while improving the competitiveness of the European food industry (1). The overall objectives are: addressing consumer needs and enhancing the competitiveness of the European food industry; assuring the safety and integrity of the food supply; and understanding the role of nutrition in health and well

being. Furthermore, pre-and co-normative research objectives form specific and essential objectives of KA1.

These research objectives assume that the money being spent by every European household on food and drink, which is on average 20% of household's disposable income (2), is not leading to consumer's health damage, trade, economical and job losses. Namely, the European food and drink processing industries alone employ about 2.3 million people, and the 1996 consumption within the Community reached nearly Euro 500,000 million (2).

Furthermore, the »*problem solving research approach*« also aims at avoiding food-borne illnesses such as those reported in 1990 (120 cases per 100,000 population from 11 European countries) (3). Consequently, the Community research in the food domain grew in importance and budget during the nineties. This is shown by the fact that the budget allocated to food nearly doubled with subsequent programmes. The 19 gramme had the budget of Euro 123 million for food alone. The »Quality of Life and Management of Living Resources« programme of the 5th Framework Programme (5FP) has been going on since 1999. Its Key Action 1 on »Food, Nutrition and Health« has been allocated Euro 290 million to support the European food research over the period 1999–2002, out of which about Euro 35 million was already allocated to new food safety research projects.

The 15 projects briefly described in this article are related to the research areas of food safety which were opened in the first call for proposals in 1999 and contribute to the answers on the research priorities of KA1. These 15 projects are based on »problem solving« and aim at providing scientifically validated, reliable, and cost-effective and time-effective solutions to the specific area of food safety research to ensure consumer health and safety, preparation and updating of sound, scientifically based EU regulations, and strengthening of the competitive position of European food and food processing industry. The projects also have a collaborative character as different partners from various sectors such as food industry, official control laboratories, private and official research organisations, universities, and consumer organisations work together.

The following text is a brief overview of the objectives and the duration of the 15 projects grouped by objectives and priorities specified in the KA1's work programme:

DEVELOPMENT OF TESTS AND PROCESSES TO DETECT AND ELIMINATE INFECTIOUS AND TOXIC AGENTS THROUGHOUT THE FOOD CHAIN

Validation and standardisation of diagnostic PCR (Contract No. QLK1–1999–00226)

The project is seeking to validate and standardise the use of polymerase chain reaction (PCR) for detection of food-borne pathogens. Additional specific project objectives include validating a simple method for purifying DNA from bacterial cultures, establishing a central collection of certified DNA sample materials, establishing a databank containing key food-pathogen DNA sequence, listing strains for specificity testing,

developing standardised reagents, and validating pre-PCR sample treatment methods. To facilitate its routine use for diagnostic purposes, participants in this project are being asked to undertake a series of specific projects, such as to construct a DNA sample library and primer databank, validate the widely used thermocyclers and other automated equipment, and to develop uniform guidelines describing how tests should be conducted. Because much of the challenge in applying PCR to food-borne pathogens is technical, there is also a need to develop standardised training manuals and procedures for those who will conduct such tests.

Rapid detection of transnational food-borne viral infections and elucidation of transmission routes through molecular tracing and development of a common database (Contract No. QLK1-1999-00594)

The project team has set the following overall objectives: to study the importance of enteric viruses as causes of illness across Europe with a special focus on multinational outbreaks of infection with Norwalk-like viruses and hepatitis A virus; to develop novel, standardised, rapid methods for virus detection and typing to be used in all participating laboratories; to establish the framework for a rapid, prepublication exchange of epidemiological, virological, and molecular diagnostic data; to determine which are the high-risk foods and major transmission routes of food-borne viral infections in the different countries and between countries; to describe the pattern of diversity within and between countries, and identify potential pandemic strains at the onset; and to investigate the mechanisms of emergence of these strains, including the possibility of spillover from animal reservoirs.

Reliable, standardised, specific, and quantitative detection of genetically modified food (Contract No. QLK1-1999-01301)

The primary objectives include the following: to develop reliable and transformation-event-specific tests for qualitative and quantitative detection of genetic modifications in food; to develop reliable and transformation-event-specific multiplex tests for determination of the diversity of genetic modifications in food; and to investigate how improved methods for detection of genetically modified foods will influence consumer confidence in food security and trust in science and risk regulators. Its specific goals are the following:

- to define the domain of application of a standard DNA extraction procedure for complex and processed food (quality and yield);
- to design species-specific reference-gene primer-probe sets for qualitative and quantitative PCR amplification and detection;
- to characterise the DNA sequence of the genetically modified organisms (GMOs) junction regions (insertion site and insert) for each of at least twelve GMOs;
- to design GMO-transformation-specific primer-probe sets for qualitative and quantitative PCR amplification and detection for each of at least twelve GMOs;
- to select the best primer-probe sets for multiplex qualitative and specific quantitative detection of genetic modifications in food and validate them in ring-trials;
- to investigate how improved methods for detection of genetically modified foods will influence consumer confidence in food security and trust in science and risk regulators;

- to identify of the domain of application and matrix-limitations for a standard DNA extraction protocol;
- to identify and characterise suitable taxon-specific reference genes, and the development of reference gene specific primer-probe sets for qualitative and quantitative PCR amplification and detection (that will define the 100% of the ingredient);
- to characterise the sequence of transformation events (obtain DNA sequence of junction regions);
- to develop, validate through ring-trials, and propose European standards for PCR-based transformation event-specific qualitative detection of at least 12 GMOs in single and multiplex assays.

IMPROVED UNDERSTANDING AND CONTROL OF CONTAMINATION CONDITIONS

Prevention of ochratoxin A in cereals (Contract No. QLK1-1999-00433)

This project aims at establishing methods to prevent ochratoxin A in cereal products by applying the Hazard Analysis Critical Control Point (HACCP) approach. It includes the whole food chain from the field to the final product. The objectives and expected achievements are divided in four important steps of the HACCP managing programme for ochratoxin A in cereals: identification of the critical control points (CCP); establishment of critical limits for the CCPs; development of rapid monitoring methods; and establishment of corrective action in the event of deviation of a critical limit. The outcome of all tasks will serve as a pool of knowledge and recommendations for HACCP-based ochratoxin management programmes, which will increase food safety and the marketability for the producer.

*Safe organic vegetables and vegetable products by reducing risk factors and sources of fungal contaminants throughout the production chain: the carrot – *Alternaria* model (Contract No. QLK1-1999-00986)*

The overall objective of this project is to develop strategies to ensure a safe supply of organic food by developing detection methods for future standardisation and by linking to the biotoxin working group CEN TC275/WG5, by anticipating mycotoxin risks, by tracing the sources of contaminants in the food production chain, and by eliminating the risk factors. The research will be done with the model carrot – *Alternaria*, the fungus being a known producer of harmful mycotoxins.

*Hazard analysis and control of food contamination: prevention of *Fusarium* mycotoxins entering the human and animal food chain (Control Mycotox Food) (Contract No. QLK1-1999-00996)*

The overall objectives of this project are to examine systems of pre-harvest crop treatment, and post-harvest control to remove contaminants and prevent fungal development in food. It will provide biological and chemical means of detoxifying mycotoxins. The best combinations of treatments in the chain will be identified by the

HACCP approach. The six key objectives to control and prevent contamination of food with *Fusarium* species and their mycotoxins are: development of critical control systems; preharvest biocontrol; post-harvest control; decontamination using microbial inoculants for prevention of entry into animal production systems; and decontamination using physical means.

Early detection of toxigenic Fusarium species and ochratoxigenic fungi in plant products (Contract No. QLK1-1999-01380)

The aim of this project is to prevent and reduce the consumer health risk from mycotoxin contamination in food and feed. This will be achieved through the development of molecular diagnostic methods for an early detection of toxigenic *Fusarium* species and ochratoxigenic fungi in plant products, new and more sensitive immunological tests for detection of mycotoxins in food, and biochemical and molecular studies to characterise genes responsible for ochratoxin A synthesis. In addition, this project aims at providing tools to reduce and control the risk of mycotoxins in plant products and in the food chain obtaining agro-industrial products of greater market value, which leads to enhanced economic development of rural areas (farmers, animal breeders, etc.).

NEW METHODOLOGIES FOR ASSESSING MICROBIAL, CHEMICAL, AND ALLERGENIC RISKS AND EXPOSURES

Development, validation, and application of stochastic modelling of human exposure to food chemicals and nutrients (Contract No. QLK1-1999-00155)

The objectives of this project are:

- to develop a comprehensive set of mathematical purpose-built algorithms to take account of all the necessary components for stochastic modelling of a variety of food chemicals and to develop appropriate computer software;
- to conduct a multi-centre study using existing national data and explore the influence of input distributions on the model output for the key components of the stochastic model of food chemical intake (i.e. food intake, chemical occurrence, chemical concentration, market share, brand loyalty, and correlated foods);
- to generate databases of true intakes of (i) food additives, based on brand level food consumption and ingredient composition, (ii) pesticide residues, based on duplicate diets, and (iii) nutrients, based on biomarker studies;
- to assess the validity of the developed stochastic modelling software against true intakes, to conduct a comprehensive sensitivity analysis of validated models, and to compare these intakes against those derived using current approaches to exposure assessment;
- to provide a comprehensive set of practical guidelines for the appropriate use of stochastic modelling of food chemical intake and to provide guidelines for correct interpretation of the output of stochastic modelling; and
- to actively communicate all research findings to national authorities and scientific bodies as well as standardisation bodies involved in food chemical exposure as-

assessment at regular stages throughout the project and, furthermore, to incorporate their feedback in the development of the software and the guidelines.

Food Safety in Europe: Risk assessment of chemicals in food and diet (FOSIE)
(Contract No. QLK1-1999-00156)

The project will focus on the following objectives:

- to carry out a detailed state-of-the-art appraisal of all stages involved in risk assessment and seek to integrate these in the most relevant manner for assessing risk using the matrix approach;
- to explore the means of improving the principles applied to, and the scientific basis of, risk assessment with respect to natural toxicants, food additives, and contaminants in the food chain, including possible interactions between individual chemicals and effects of the food matrix;
- to identify gaps in knowledge that might lead to differences in interpretation of toxicological and exposure data and the research need to reduce these;
- to determine the nature and the level of testing needed for safety evaluation relevant to the nature of the chemical, level of use/occurrence in the diet and human exposure (including novel foods and processes and nutritional supplements);
- to add a European contribution to international initiatives to harmonise principles, terminology and methodology for risk assessment;
- to move toward a scientifically transparent and justifiable consensus on risk assessment issues;
- to assist risk managers in developing appropriate defensible food standards that adequately protect the safety of the consumer whilst allowing for innovation in food production and processing.

Risk assessment of Cryptosporidium parvum, an emerging pathogen in the food and water chain in Europe (Contract No. QLK1-1999-00775)

This project will investigate *Cryptosporidium parvum*, an emerging pathogen and will establish the risk that *C. parvum* poses to the food and water industry. The objectives of the project are:

- development of routine procedures for the isolation and detection of oocysts from test samples (food and water);
- determination of the survival and infectivity of *C. parvum* in the food and water;
- development of procedures for control of *C. parvum* in the food and water industry;
- development of a risk assessment model for *C. parvum* for the food and water industry.

European network safety of genetically modified food (Contract No. QLK1-1999-01182)

The objectives of this network are:

- to identify key issues of the safety evaluation of genetically modified food crops, and to examine whether current research methods are adequate to characterise specific safety hazards;

- to co-ordinate ongoing research regarding safety testing of transgenic foods within the European research framework program 5 (FP5);
- to design new sufficiently sensitive and specific (*in vitro*) test methodologies for safety and nutritional evaluation of whole complex foods;
- to address the risks of gene transfer from genetically modified organisms to the gut micro-flora of humans and animals;
- to examine new strategies for the detection of genetically modified food (GMF), which enable detection at specific threshold levels for raw materials, processed products, and food ingredients;
- to examine the fate of genetically modified raw materials and processed products throughout food production chains (tracking and tracing);
- to develop criteria for quality assurance systems to guarantee »non-GMO-containing« materials throughout food chains;
- to develop a communication platform of GMO producers, scientists involved in research and safety evaluation of GMOs, retailers, regulatory authorities, and consumer groups with the scope to improve safety assessment procedures, risk management strategies, and risk communication.

New methods for the safety testing of transgenic food (Contract No. QLK1-1999-00651)

The overall objective of this project is to develop and validate the scientific methodology which is necessary for assessing the safety of food from genetically modified plants in accordance with the EU Regulation 258/97 of 27 January 1997 concerning novel foods and novel food ingredients. The specific objectives are:

- to improve the sensitivity and specificity of standard OECD guideline toxicity tests towards detection of specific chemical entities in the genetically modified food matrix by the measurement of additional biological endpoints based on prior knowledge;
- to improve knowledge through precise information regarding the gene construct, its site of insertion and the chemical and toxicological characteristics of the gene product based on chemical analytical studies and short-term *in vivo* and *in vitro* studies;
- to improve knowledge through precise information regarding unintended secondary changes in the genetically modified food item, which may alter the nutritional-toxicological properties of that food. The project will examine a two-step safety testing procedure for genetically modified plant food, having chemical analysis and short term *in vivo* and *in vitro* testing in the first step and the core 90-day rat study in the second step. The test design will be evaluated through the testing of 3 transgenic rice varieties (gene inserts: GNA lectin, PHA-E lectin, Bt-toxin) measured against the testing of spiked rice.

ROLE OF FOOD IN PROMOTING AND SUSTAINING HEALTH WITH RESPECT TO DIET AND NUTRITION, TOXICOLOGY, EPIDEMIOLOGY, ENVIRONMENTAL INTERACTION, CONSUMER CHOICE, AND PUBLIC HEALTH

Evaluation of the safety and efficacy of iron supplementation in pregnant women (Contract No. QLK1-1999-00337)

Iron deficiency during pregnancy is common and can have harmful effects on the mother and child. Supplementation with iron is desirable even if the mother's iron levels are only slightly lower than recommended. The amount prescribed, however, varies widely and there is a growing concern about the risks associated with excessive iron accumulation. This project will examine the effect of two doses of iron supplements, given within the clinical range, on a variety of indicators of health and well being in pregnant women. Concurrently, it will study the effects of supplementation directly in humans and will test the involved mechanisms using cell culture and animal models. In addition, it will identify the optimum levels of supplementation during pregnancy and will also determine the maximum safe level. Iron supplements have unpleasant side effects and our data will provide information why this should be the case. Supplementation will have effects on the metabolism of other nutrients in addition to iron, and our experiments will seek to show which nutrients are affected and what are the mechanisms of interaction. A further aim will be to provide rational guidelines for supplementation strategies and recommendations for safe levels of supplementation.

Synbiotics and cancer prevention in humans (Contract No. QLK1-1999-00346)

The overall aim of the proposal is to evaluate the potential cancer-preventing activity of pro-biotic and prebiotic («SYNBIOTIC») combinations in human volunteers. The strategy that will be followed to attain this target consists out of 5 major points:

- to identify synbiotic combinations offering the greatest competitive advantages in the colonic ecosystem, using *in vitro* fermentation techniques;
- to confirm the anti-carcinogenic effect of the most promising synbiotic combination in a well-established animal model for colon carcinogenesis;
- to refine the range of biomarkers suitable for use in the human intervention study on synbiotics and CRC risk and to establish conditions for sample storage and transport for the study;
- to gain insight into the underlying mechanisms involved in the anticancer effects in the rat model by the use of biomarkers reflecting different stages of the carcinogenic process (initiation, promotion, and metastasis) and immunological parameters;
- to evaluate the potential of a synbiotic combination in human subjects (adenoma patients) using the biomarkers as above to prevent colorectal cancer.

ESCODD – European Standards Committee on Oxidative DNA Damage (Contract No. QLK1-1999-00568)

The principal objectives of this Concerted Action are the following:

- to validate HPLC, GC-MS, and LC-MS-MS methods used for the measurement of 8-oxo-7,8-dihydroguanine (8-oxo-gua) and 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxo-dG) using reference standard DNA samples analysed in parallel in different laboratories, including heavy labelled standards for mass spectrometry;
- to increase the sensitivity and reliability of these »conventional« methods;
- to measure DNA oxidation in parallel on identical samples using »conventional« methods and repair endonuclease-based methods;
- to reach a consensus on the average level of oxidation in normal human DNA.

It is clear that oxidation of guanosine during sample preparation for GC-MS and HPLC is a serious problem. It is essential that it is eliminated, that the protocols are standardised, and that the variability and errors in different assays are reduced if we are to achieve a sound judgment of the amount of damage present – a prerequisite for assessing the importance of oxidative DNA damage in the aetiology of diseases such as cancer, Down's syndrome, cystic fibrosis and premature ageing syndromes such as the Werner's syndrome, as well as its role in normal ageing. This Concerted Action will provide for the systematic exchange of standards and samples between participants with regular meetings to discuss the results and to optimise methodology. In addition, scientists will take part in exchanges between laboratories to facilitate the adoption of improvements in technique.

IDENTIFIED FUTURE RESEARCH NEEDS IN THE FOOD SAFETY AREA BASED ON THE WORK PROGRAMME COVERAGE ANALYSIS AND ALL SUPPORTED PROJECTS UP TO NOW

Based on the currently supported projects a work programme coverage analysis has been made which revealed a number of research needs in the food safety area, most of which is covered by food safety and technology proposals submitted in the year 2000 such as economic impacts of HACCP on food industry, slaughterhouses, and so on; processes for inactivating non-conventional agents; safety assessment of convenience foods and catering systems including lifestyles; consolidation of databases taking into account risk groups, link nutrients and hazards, and regional differences; assessment of effects of long-term exposure and mixtures of known hazards; quantitative risk assessment including validation of methodologies; allergenic risk and exposure assessment; epidemiological studies and their links to food consumption data; microbial ecology of food-borne pathogens; transfer mechanisms of antibiotic resistance between animal, microbial, and human reservoirs via food ingestion; optimisation of sampling protocols, specifically retail sampling; rapid detection tests and multi-residue procedures in areas such as migration, prions, phytotoxins, and so on; determination of infectivity levels of non-conventional agents in animal tissues and products; risk communication including risk perception by increasing understanding based

on breaking down barriers and networking; and performance written standards (i.e. criteria-based pre-normative research), not restricted only to descriptive written standards for analytical methods and tests.

CONCLUSIONS

In view of these broad implications and important roles of the 15 KA1 projects, it can be concluded that they substantially contribute to the objectives of KA1, to the Community food legislation (2), and to the following overall aims:

- ensuring a high level of protection of public health, safety, and the consumer as well as restoring consumer's confidence;
- supporting European legislation as well as pre-and co-normative research in the area of food safety and technology;
- ensuring the free movement of goods within the internal market by actively using the standardisation type approach;
- ensuring that the legislation is primarily based on scientific evidence, and science based risk analysis;
- ensuring the competitiveness of the European industry;
- providing support to the use of the HACCP approach.

Further information on the work programme, guides for proposers, evaluation approach and forms, additional details on supported QoL-KA1-research projects can be found on the internet: <http://www.cordis.lu/life>. The Web page also provides hyperlinks to other Web pages showing results of various supported EC-research projects in the food safety area under the previous EC-Framework Programme 4.

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Sažetak

PROGRAM KVALITETE ŽIVLJENJA: HRANA, PREHRANA I ZDRAVLJE – PROMOCIJA PROJEKATA

Program kvalitete življenja (QoL) Europske zajednice, Ključna akcija 1 (KA1) – Hrana, prehrana i zdravlje ima svrhu pružanja zdrave, sigurne i visokokvalitetne opskrbe hranom sa svrhom jačanja povjerenja potrošača u sigurnost europske hrane. Ključna akcija trenutno podupire nekoliko različitih europskih projekata ispitivanjem analitičkih metoda za kontrolu hrane uključivši senzore, procjenu rizika i standardizaciju sigurnosti hrane. Njihov cilj polazi od razvoja i vrednovanja strategije prevencije za stvaranje mikotoksina preko razvoja komunikacijskih platforma za genetički modificirane organizme (GMO), validacije i standardizacije dijagnostičke metode lančane reakcije polimerazom (PCR) za patogene nastale u hrani, do evaluacije potencijalne aktivnosti sprečavanja karcinoma probiotičkih i pre-biotičkih ("sinbiotskih") kombinacija u humanih dobrovoljaca. U ovom radu navedene su također potrebe za daljnjim istraživanjima u području sigurnosti hrane.

Ključne riječi:

analitičke metode, europska istraživanja, sigurnost hrane, GMO, HACCP, zakonodavstvo, PCR, upravljanje kakvoćom, analiza rizika, standardizacija

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