

Foreword

Introduction

This supplement builds on the achievements of the European Commission-funded Concerted Action on Biomarkers of Exposure and Effect in Relation to Quality of Life and Human Risk Assessment supported within the FAIR RTD programme (ERB FAIR CT 961178). The Concerted Action, which involved 16 institutions throughout Europe, was coordinated by the Central Science Laboratory (CSL), an Agency of the UK Ministry of Agriculture, Fisheries and Food.

Aims of the project

The goal of this Concerted Action was to review biomarker approaches which provide information on beneficial and deleterious dietary combinations in relation to human health and to consider the important implications for scientists, industry, legislators and the consumer. In order to achieve this objective, it was necessary to:

- determine which biomarker approaches were presently being used;
- decide which were the major health-related issues and endpoints which needed to be considered;
- consider the relative merits of approaches based on biomarkers of exposure and of biological effect;
- delineate the interplay of deleterious and beneficial dietary components;
- carry out cooperative trials where possible to prioritise and assess the area;
- identify and prioritise research areas in the field of biomarkers which might be suitable for future shared cost research.

Within the CSL there were already groups whose research interests focused upon biomarkers of exposure and of effect. This enabled the CSL coordinators to identify emerging researchers in the area of biomarkers from throughout Europe who were then invited to participate in the Action. In addition, the multifaceted nature of biomarker research encouraged the establishment of links to other EC-funded research projects including those on functional foods (FUFOSE) and diet (NEODIET).

Deliverables

The key deliverables of this Action were the production of a register of experimental methods used in biomarker research and a critical review of research in the area of biomarkers. The register of methods was designed to contain experimental information which was tried and tested in the participants' own laboratories whilst the review concentrated on a number of key themes. Five groups were set up within the project to focus on these

deliverables and to try and ensure a consistency of approach.

Group 1: Information technology for biomarker methods

The group dealing with information technology and biomarker methods were presented with the task of developing a common method for collecting biomarker information in a way that could be easily assimilated and was sufficiently generic to be applicable to biomarkers from a range of disciplines. Key criteria were as follows: Author, Keywords, Biomarker evaluated, Qualitative/quantitative, Invasiveness, Reproducibility/transferability, Validity, Specificity/sensitivity, Cost, Ease of use/duration of assay, Sample type, State of development, Comparison with other methods, Other information/comments, Laboratories using the method and short bibliography

Forty methods for the measurement of biomarkers of exposure and effect were collated based on the use of these criteria. During the course of assembling the register of methods, it was quickly appreciated that an electronic version of the database would be particularly valuable. In a separately funded project a Web-based database was set up and loaded with a small number of methods to show proof of principle. This database can be found at <http://biomarkw.csl.gov.uk>

Group 2: Nutrients in the diet

Group 3: Non-nutrients in the diet

These two groups initially met independently but later had joint meetings. The key aspects dealt with included the following points which provided the basis for the structure of the review entitled 'A critical assessment of some biomarker approaches linked with dietary intake'. In each case the intention was not to provide a definitive view of all aspects in each area but rather to use examples to illustrate key questions and points.

- (1) Introduction.
- (2) What are the factors influencing the use of biomarkers of exposure and effect for nutrients and non-nutrients?
- (3) What are the effects and/or limitations of the analytical method?
- (4) What are the effects of metabolism?
- (5) How consistent is the information from several biomarkers for one component?
- (6) How do individual life-styles influence the appropriateness of a biomarker?
- (7) Biological effect monitoring.
- (8) What effects do interactions have on biomarker use and interpretation?

- (9) Case study – biomarkers for aflatoxin exposure and effect.
- (10) Development of biomarkers – what are the gaps and why is the information needed?

Group 4: Epidemiology

This group was set up after the initial meeting of the Concerted Action when it was realised that epidemiological considerations were inadequately represented but were of great importance. For this reason, an additional member of the Action was recruited. Once again key themes were identified and specific examples were used to illustrate the most important points resulting in the paper ‘A critical evaluation of the application of biomarkers in epidemiological studies on diet and health’ which contains the following sections.

- (1) Introduction.
- (2) Sample collection, processing and storage.
- (3) Relationship of biomarker to dietary intake.
- (4) Relationship of biomarker to natural history of disease.
- (5) Examples of integration of biomarkers into studies of diet and health
- (6) Conclusions.

Group 5: Health and disease

This group met to consider the key aspects of biomarker research in relation to health and disease. The most important factors to be considered were as follows.

- (1) What are the most important disease/health issues which have a link with diet?
- (2) How strong is that link?
- (3) Which of these are most important in the context of human exposure to them?
- (4) What biomarkers are available?

The subgroup focused on three key diseases – cancer, coronary heart disease and osteoporosis – for their review on ‘Biomarkers in health and disease’. During the course of this Action, a separately funded project which addressed the question of biomarkers as predictive tools in toxicity testing was initiated by the coordinators and this resulted in a workshop and a publication (Benford *et al.* (2000) *Alternatives to Laboratory Animals* **28**, 119–131).

Structure of this supplement

This supplement is split into two sections. In the first, the review of biomarkers is presented as three papers based on the themes presented above. This critical evaluation of biomarkers is followed by peer reviewed research papers which were presented at the final open meeting of the Concerted Action in Jena, Germany. The research papers reflect the wide nature of the final meeting and the breadth of interests of the participants.

Some conclusions

As a result of this Concerted Action an extensive amount of information has been generated only some of which is presented here. There are important questions which arise from the deliberations of the participants over a period of three years. Biomarker research has an impact on a number of areas including a better understanding of what constitutes a healthy diet, development and validation of new ‘functional’ foods, chronic illness and the elderly, quality of life and prevention of disease. The development of **validated** and **predictive** biomarkers is an essential research objective. This means that the biomarkers must be both analytically and biologically valid and should reflect a future health outcome at a stage when dietary intervention will be effective. This is an important **European Research Area** with the potential to develop consensus methods and policies throughout Europe which will help legislators, assist European industry and competitiveness, stimulate scientific research and, most of all, benefit the consumer through improving the flow of information and enhancing proven health benefits.

Acknowledgements

The coordinators, Dr Helen Crews and Dr Bryan Hanley, would like to thank the participants and our EC colleagues, for all their hard work and support, and also for their patience with us during our laboratory relocation from Norwich to York which took place during the last year of the project. The participants tackled a difficult and ambitious project with enthusiasm and good humour. They can be proud of their work and should be congratulated on the subsequent successes in gaining funding for new biomarker projects.

Coordinators:	Dr Helen Crews and Dr Bryan Hanley, CSL, Sand Hutton, York YO41 1LZ, UK
Administrative support:	Tracy Farrington and Lesley Wilson, CSL, Sand Hutton, York YO41 1LZ, UK
EC Coordinator:	Dr Laurent Bochereau, European Commission, Directorate-General Research, Science, Research and Development, Rue de le Loi 200, B-1049, Brussels, Belgium
Project Management Team:	Dr Helen Crews, Dr Bryan Hanley Dr Nora O’Brien, Department of Nutrition, University College Cork, Ireland Dr Hans Verhagen, Unilever Research, Vlaardingen, Netherlands

Participants in the
Concerted Action:

Dr Gerrit Alink, Wageningen
Agricultural University,
Wageningen,
The Netherlands
Dr Christer Andersson,
National Food
Administration, Uppsala,
Sweden
Dr Krys Bottrill, FRAME,
Nottingham, UK
Dr Veronique Braesco,
INRA, Clermont-Ferrand,
France
Dr Francesco Branca,
Dr Giuseppe Maiani, Istituto
Nazionale di Ricerca per
gli Alimenti e la
Nutrizione, Rome, Italy
Dr Anastassios Kovatsis,
Aristotelian University of
Thessaloniki, Greece
Dr Nora O'Brien,
Dr Julie Woods, University
College, Cork, Ireland
Dr Lars Ovesen,
Rikke Andersen, Danish
Veterinary and Food
Administration, Denmark

Prof. Beatrice Pool-Zobel,
Friedrich-Schiller-
University, Jena, Germany
Dr Mike Scotter,
Lesley Wilson,
Dr Bert Popping, CSL, York,
UK
Dr Michele Solfrizzo,
Consiglio Nazionale delle
Ricerche, Bari, Italy
Dr Stefan Vieths,
Paul-Ehrlich-Institut,
Langen, Germany
Dr Robin van den Berg,
TNO, Nutritional Food
Research Institute, Zeist,
The Netherlands
Dr Hans Verhagen, Unilever
Health Institute,
Vlaardingen,
The Netherlands
Prof. Chris Wild, School of
Medicine, University of
Leeds, UK
Prof. Gary Williamson,
Dr Birgit Holst, Institute of
Food Research, Norwich,
UK