WHO Initiative to Estimate the Global Burden of Foodborne Diseases

Fourth formal meeting of the Foodborne Disease Burden Epidemiology Reference Group (FERG)

Geneva, 8–12 November 2010
WHO Initiative
to Estimate the Global Burden
of Foodborne Diseases

Fourth formal meeting of the Foodborne Disease
Burden Epidemiology Reference Group (FERG)

Sharing New Results, Making Future Plans, and Preparing
Ground for the Countries

Geneva, 8–12 November 2010
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<th>Description</th>
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<tbody>
<tr>
<td>ADHD</td>
<td>Attention Deficit Hyperactivity Disorder</td>
</tr>
<tr>
<td>AFP</td>
<td>Acute Flaccid Paralysis</td>
</tr>
<tr>
<td>AFRO</td>
<td>WHO African Region</td>
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<tr>
<td>AMRO</td>
<td>WHO Region of the Americas</td>
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<tr>
<td>BB</td>
<td>Body Burden</td>
</tr>
<tr>
<td>BMD</td>
<td>Benchmark Dose</td>
</tr>
<tr>
<td>BMDL</td>
<td>Benchmark Dose Lower 5% confidence bound</td>
</tr>
<tr>
<td>BoD</td>
<td>Burden of Disease</td>
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<tr>
<td>BoDG</td>
<td>Burden of Disease Group</td>
</tr>
<tr>
<td>BW</td>
<td>Body Weight</td>
</tr>
<tr>
<td>CAB</td>
<td>Commonwealth Agricultural Bureau (now CAB International)</td>
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<tr>
<td>CAR</td>
<td>Central African Republic</td>
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<tr>
<td>Cd</td>
<td>Cadmium</td>
</tr>
<tr>
<td>CHERG</td>
<td>Child Health Epidemiology Reference Group</td>
</tr>
<tr>
<td>CE</td>
<td>Cystic Echinococcosis</td>
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<tr>
<td>CEA</td>
<td>Comparative Exposure Assessment</td>
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<tr>
<td>CI</td>
<td>Confidence Interval</td>
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<tr>
<td>CRA</td>
<td>Comparative Risk Assessment</td>
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<td>CSTF</td>
<td>Country Studies Task Force</td>
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<tr>
<td>CTTF</td>
<td>Chemicals and Toxins Task Force</td>
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<tr>
<td>DALY</td>
<td>Disability-Adjusted Life Year</td>
</tr>
<tr>
<td>DG</td>
<td>Director-General</td>
</tr>
<tr>
<td>DRC</td>
<td>Democratic Republic of Congo</td>
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<td>ECDC</td>
<td>European Centre for Disease Prevention and Control</td>
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<td>EDTF</td>
<td>Enteric Diseases Task Force</td>
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<tr>
<td>EE</td>
<td>Expert Elicitation</td>
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<td>EFSA</td>
<td>European Food Safety Authority</td>
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<tr>
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<td>Food and Agriculture Organization of the United Nations</td>
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<tr>
<td>FBD</td>
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<td>Foodborne Trematodiasis</td>
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<td>FDA</td>
<td>United States Food and Drug Administration</td>
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<td>FERG</td>
<td>Foodborne Disease Burden Epidemiology Reference Group</td>
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<tr>
<td>FERG 1</td>
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<td>FERG 2</td>
<td>Second formal meeting of the FERG (November 2008)</td>
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<td>Third formal meeting of the FERG (October 2009)</td>
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<td>Fourth formal meeting of the FERG (November 2010)</td>
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<td>FERG 5</td>
<td>Fifth formal meeting of the FERG (to be held in November 2011)</td>
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<td>FOS</td>
<td>WHO Department of Food Safety and Zoonoses</td>
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<tr>
<td>GEMS</td>
<td>Global Environment Monitoring System</td>
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<td>GBD</td>
<td>Global Burden of Disease</td>
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<tr>
<td>GBS</td>
<td>Guillain-Barré Syndrome</td>
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<tr>
<td>HALE</td>
<td>Health-Adjusted Life Expectancy</td>
</tr>
<tr>
<td>Acronym</td>
<td>Description</td>
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<tr>
<td>HAV</td>
<td>Hepatitis A Virus</td>
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<tr>
<td>HBV</td>
<td>Hepatitis B Virus</td>
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<tr>
<td>HCC</td>
<td>Hepatocellular Carcinoma</td>
</tr>
<tr>
<td>IDD</td>
<td>Iodine Deficiency Disorder</td>
</tr>
<tr>
<td>JECFA</td>
<td>Joint FAO/WHO Expert Committee on Food Additives</td>
</tr>
<tr>
<td>KT</td>
<td>Knowledge Translation</td>
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<tr>
<td>KTPG</td>
<td>Knowledge Translation and Policy Group</td>
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<tr>
<td>LOS</td>
<td>Lipo-Oligosaccharides</td>
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<tr>
<td>M&amp;E</td>
<td>Monitoring and Evaluation Framework</td>
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<tr>
<td>NBD</td>
<td>National Burden of Disease</td>
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<td>NCC</td>
<td>Neurocysticercosis</td>
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<tr>
<td>PAHO</td>
<td>Pan American Health Organization</td>
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<tr>
<td>PCB</td>
<td>Polychlorinated Biphenyl</td>
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<tr>
<td>PDTF</td>
<td>Parasitic Diseases Task Force</td>
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<tr>
<td>PTWI</td>
<td>Provisional Tolerable Weekly Intake</td>
</tr>
<tr>
<td>PWE</td>
<td>People With Epilepsy</td>
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<tr>
<td>RIVM</td>
<td>The Dutch National Institute for Public Health and the Environment</td>
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<tr>
<td>SATF</td>
<td>Source Attribution Task Force</td>
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<tr>
<td>SIGLE</td>
<td>System for Information on Grey Literature in Europe</td>
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<tr>
<td>SEARO</td>
<td>WHO South-East Asian Region</td>
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<tr>
<td>SOP</td>
<td>Standard Operating Procedure</td>
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<tr>
<td>TEQ</td>
<td>Toxicity Equivalent</td>
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<tr>
<td>TF</td>
<td>Task Force</td>
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<tr>
<td>ToR</td>
<td>Terms of Reference</td>
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<tr>
<td>TT4</td>
<td>Total Thyroxine</td>
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<tr>
<td>TTO</td>
<td>Time Trade-Off</td>
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<tr>
<td>UN</td>
<td>United Nations</td>
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<tr>
<td>USA</td>
<td>United States of America</td>
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<tr>
<td>US EPA</td>
<td>United States Environmental Protection Agency</td>
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<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
<tr>
<td>WPRO</td>
<td>WHO Western Pacific Region</td>
</tr>
<tr>
<td>YLL</td>
<td>Years of Life Lost</td>
</tr>
<tr>
<td>YLD</td>
<td>Years Lived with Disability</td>
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</table>
Acknowledgments

The Department of Food Safety and Zoonoses (FOS) of the World Health Organization (WHO), Geneva, Switzerland, wishes to express its sincere gratitude to all those who contributed towards the success of this meeting.

First and foremost we wish to thank all participants for their valuable technical input and their collegiality during the meeting. We are particularly grateful to Dr Arie Havelaar for his outstanding chairmanship of this fourth meeting of the FERG, as well as to the Chairs of the FERG Task Forces, Dr Nilanthi de Silva, Dr Herman Gibb, Dr Tine Hald, Mr Martyn Kirk, Dr Pierre Ongolo-Zogo and Dr Niko Speybroeck, for their excellent leadership. A final word of appreciation and special thanks goes to Ms Aden Asefa, Ms Linda Moloney and Dr Nicolas Praet for acting as meeting rapporteurs, and in particular to Mr Brecht Devleesschauwer for acting as main meeting rapporteur.

This report can be downloaded in electronic format from the following site: http://www.who.int/foodsafety/foodborne_disease/ferg/
Key Definitions

Food
According to the definition of the Codex Alimentarius Commission\(^1\), food means any substance, whether processed, semi-processed or raw, which is intended for human consumption, and includes all bottled drinks, chewing gum and any substance which has been used in the manufacture, preparation or treatment of “food”, but does not include cosmetics or tobacco or substances used only as drugs.

Foodborne diseases
Foodborne diseases (FBD) can be defined as diseases commonly transmitted through ingested food. FBD comprise a broad group of illnesses, caused by microbial pathogens, parasites, chemical contaminants or biotoxins.

Burden of disease
The term “Burden of Disease” in the context of this Initiative follows the principles of the Global Burden of Disease Study (Murray & Lopez, 1996; Lopez et al., 2006; WHO, 2008), and includes the quantification of morbidity, all disabling complications as well as mortality in a single summary measure (DALY).

DALY (Disability-adjusted life year)
The DALY measure combines the years of life lost due to premature death (YLL) and the years lived with disability (YLD) from a disease or condition, for varying degrees of severity, making time itself the common metric for death and disability. One DALY is a health gap measure, equating to one year of healthy life lost.

Source attribution
Source attribution (SA) is the partitioning of the human burden of a particular disease to specific sources. With regards to foodborne diseases, SA can be conducted at various points along the food distribution chain, from the animal reservoir to the point of consumption.

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The 194 Member States of the WHO are grouped into six regions. The six WHO regions and their constituents are visually presented in following map, which is an approximation of actual country borders, and are listed below.

**WHO African Region (AFRO)**

**WHO Region of the Americas (AMRO)**
Antigua and Barbuda, Argentina, Bahamas, Barbados, Belize, Bolivia, Brazil, Canada, Chile, Colombia, Costa Rica, Cuba, Dominica, Dominican Republic, Ecuador, El Salvador, Grenada, Guatemala, Guyana, Haiti, Honduras, Jamaica, Mexico, Nicaragua, Panama, Paraguay, Peru, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago, United States of America, Uruguay, Venezuela.

**WHO Eastern Mediterranean Region (EMRO)**
Afghanistan, Bahrain, Djibouti, Egypt, Islamic Republic of Iran, Iraq, Jordan, Kuwait, Lebanon, Libyan Arab Jamahiriya, Morocco, Oman, Pakistan, Qatar, Saudi Arabia, Somalia, Sudan, Syrian Arab Republic, Tunisia, United Arab Emirates, Yemen.

**WHO European Region (EURO)**
Albania, Andorra, Armenia, Austria, Azerbaijan, Belarus, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Geor-
gia, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Luxembourg, Malta, Monaco, Montenegro, Netherlands, Norway, Poland, Portugal, Republic of Moldova, Romania, Russian Federation, San Marino, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Tajikistan, The former Yugoslav Republic of Macedonia, Turkey, Turkmenistan, Ukraine, United Kingdom, Uzbekistan.

**WHO South-East Asian Region (SEARO)**
Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand, Timor-Leste.

**WHO Western Pacific Region (WPRO)**
Australia, Brunei Darussalam, Cambodia, China, Cook Islands, Fiji, Japan, Kiribati, Lao People's Democratic Republic, Malaysia, Marshall Islands, Micronesia (Federated States of), Mongolia, Nauru, New Zealand, Niue, Palau, Papua New Guinea, Philippines, Republic of Korea, Samoa, Singapore, Solomon Islands, Tonga, Tuvalu, Vanuatu, Viet Nam.
Foodborne diseases (FBD) pose a significant but often underrecognized threat to public health, worldwide. The World Health Organization (WHO) considers it its task to provide an objective quantification of the burden of disease arising from the ingestion of contaminated food and food products, and to this purpose it established the Initiative to Estimate the Global Burden of Foodborne Disease. The major goal of this Initiative is to create a comprehensive reference base of information that will allow decision-makers to rationally address food safety problems both nationally and globally.

In 2007, the WHO established the Foodborne Disease Burden Epidemiology Reference Group (FERG), a group of international experts who give recommendations to the WHO Director-General and to the Initiative. This report summarizes the outcomes of the fourth formal meeting of the FERG (FERG 4), which was organized by the WHO in November 2010.

Continuing on the path taken during the previous FERG meeting, a large number of new foodborne disease morbidity, mortality and burden estimates were presented and discussed at FERG 4:

- The global burden of diarrheal diseases;
- The global burden of foodborne trematodiasis;
- The global burden of cystic echinococcosis;
- The global burden of neurocysticercosis;
- The global burden of aflatoxicosis; and
- The global burden of cassava cyanide ingestion.

In addition, the FERG experts appraised the progress made on the commissioned systematic reviews for other enterics, parasites and chemicals, and on the protocols to be used in the source attribution expert elicitation process and in the national FBD burden assessments and policy situation analyses. Each task force (TF) also made recommendations for new commissioned work.

As the Initiative is moving forward, the FERG and its TFs are updating their work plans:

- A pilot evaluation of the source attribution expert elicitation protocol will be performed;
- Both health and economic impact will be considered as criteria for selecting diseases for future burden assessment studies; and
- Economic burden assessment studies will be initiated.

The various task forces adopted their work plans for 2011 and beyond, which cover the continuation of the systematic reviews, the finalization of the pathogen priority lists, and the further strengthening of the interfaces between the different TFs. The Country Studies TF made the final preparations for initiating the pilot country studies in 2011. Four countries have been selected for these studies: Albania, Japan, Thailand and Uganda.
The WHO Secretariat appreciated the large number of recommendations made during the fourth FERG meeting, and is now working on executing these. Finally, during the FERG mid-term evaluation, Dr Maged Younes, director of the WHO Department of Food Safety and Zoonoses (FOS), lauded the results already achieved by the FERG, and re-confirmed the high level commitment of the WHO to this Initiative.
1. Introduction

The Foodborne Disease Burden Epidemiology Reference Group (FERG) is a multidisciplinary and multisectoral expert group established as the advisory body of the World Health Organization’s (WHO) Initiative to Estimate the Global Burden of Foodborne Diseases (hereafter referred to as the Initiative). This report summarizes the proceedings and discussions stemming from the fourth formal meeting of the FERG (FERG 4), held from 8 to 12 November 2010 in Geneva, Switzerland.

In conjunction with FERG 4, a stakeholder meeting was held on 11 November 2010. The stakeholder meeting was designed as a forum for dialogue, exchange and collaboration, open to all those sectors of society interested in the work of the Initiative, including WHO Member States, bi- and multilateral donors, foundations, consumer groups, NGOs, academia, scientific and public media as well as agricultural and food industry. More information on this event is available at: http://www.who.int/foodsafety/foodborne_disease/ferg4_stakeholder/en/.

1.1 Meeting objectives

The third meeting of FERG had identified the following specific areas for follow-up at the fourth meeting:

1. The appraisal of the progress of the commissioned work and the implementation of the adopted work plans for all TFs; and
2. The formal evaluation of the first half term of the Initiative and FERG.

The main objectives of FERG 4 were therefore to:

1. Provide an opportunity for all FERG members to meet and discuss the progress made since FERG 3;
2. Review, revise or finalize the commissioned work of all TFs, including the formulation of next steps;
3. Go public with draft morbidity, mortality and burden of disease estimates;
4. Evaluate and revise work plans for 2011 for all TS;
5. Provide inputs into the Country Studies protocol for launch of pilot studies in near future;
6. Discuss the progress of the Knowledge Translation and Policy Group (KTPG), established in March 2010 as the second subgroup of the Country Studies Task Force (CSTF); and
7. Appraise and discuss the mid-term evaluation of the Initiative and FERG.

Timelines discussed and agreed at the FERG 4 meeting have in large parts been delayed due to budgetary and leadership challenges the Initiative faced in the first semester of 2011. A revised roadmap including updated timelines of the work of FERG can be found in the report of the 2011 FERG Strategic Planning Meeting held in late 2011 in Durrës, Albania.
1.2 Structure of the report

This report starts by giving the reader insights into the background of the WHO Initiative to Estimate the Global Burden of Foodborne Diseases and the FERG. An overview is given of the importance of FBD and the current efforts to quantify their global and national burden. The FERG’s newest task force, the Country Studies Task Force, is then highlighted by elaborating on its two main tasks, the support for national FBD Burden studies and the development of tools for translating knowledge into policy.

The report continues with a comprehensive outline of the plenary sessions held by the FERG members, where the progress of the different task forces was presented, appraised and discussed. This chapter is structured per thematic task force, and gives an overview of each task force’s progress so far, the presentations and subsequent discussions, and the specific agreements and action points. Finally, a summary is given of the commissioned evaluation of the overall progress of the Initiative, followed by an overview of the recommendations made by the experts for the future directions of the FERG as a whole.

The report concludes with the conclusions drawn during FERG 4 and a summary of the meeting outputs. Three appendices are added to the report, including an overview of FERG memberships and roles, the list of participants, and the final FERG 4 agenda.
2. Background

2.1 The Foodborne Disease Burden Epidemiology Reference Group (FERG)

If countries are to effectively address the health needs of their populations, the threats to health need to be identified and quantified. A large number of diseases can be transmitted through ingested food. These so-called foodborne diseases (FBD) are caused by a variety of agents, including bacteria, viruses, parasites, chemical and toxins, and give rise to a variety of clinical presentations. In order to rationally address these threats, countries have to make best use of their limited recourses, and decision-makers need high-quality scientific information to guide their priority setting.

Burden of disease is the morbidity and mortality associated with the acute and chronic manifestations of disease. In order to estimate the burden of disease, composite measures of population health may be used, such as the disability-adjusted life year or DALY. This metric has been extensively used by WHO and others to describe global, regional and national burden of disease.

Although some countries have recently started to quantify their national burden of FBD, the global burden of these diseases has not yet been fully described. WHO’s Initiative to Estimate the Global Burden of FBD, launched in 2006, aims to compile and publish the first quantitative description of the global burden of FBD, expressed in terms of DALYs, and stratified by age groups, sex, and WHO regions. In 2007, WHO established the Foodborne Disease Burden Epidemiology Reference Group (FERG) to act as the technical advisory body to the Initiative. The FERG is made up of experts from different fields, including risk assessment, epidemiology, bacteriology, virology, parasitology, toxicology, source attribution, expert elicitation, knowledge translation and policy. The composition and structure of the FERG, and its interaction with the WHO Secretariat, is visualized in Figure 2.

More details on the rationale for estimating the global burden of FBD and for establishing the FERG can be found in the previous FERG meeting reports (available at www.who.int/foodborne_disease/burden/en/).

Figure 2:
Composition and structure of the FERG
2.2 Country studies task force (CSTF)

2.2.1 Role and structure of the CSTF – Introducing the Knowledge Translation and Policy Group

In order to get a full picture of the global burden of FBD, national-level data on the health burden of contaminated food are essential. For many countries, however, these data are currently not available. To this purpose, the WHO established the Country Studies Task Force (CSTF) as the fifth thematic task force of the FERG. The CSTF is mandated to address this data gap by advising the WHO on support strategies and tools to enable countries to conduct their own FBD burden studies. This specific task of the CSTF is being taken on by the CSTF Burden of Disease Group (BoDG), which is composed of epidemiological experts from different task forces, and complemented by external advisers (Figure 3).

The final aim of the Initiative is to enable decision-makers and other stakeholders to set appropriate, evidence-informed priorities in the area of food safety. Key to the fulfillment of this goal is “knowledge translation”, a term which describes the exchange, synthesis, and effective communication of reliable and relevant research results. The focus is on promoting interaction among the producers and users of research to remove the barriers to research use, and tailoring information to different target audiences so that the epidemiological results of the Initiative are used more widely in food safety decision-making and practice.

In this context, the Knowledge Translation and Policy Group (KTPG) of the FERG was established in 2010 as the second subgroup of the CSTF (Figure 3). This group works closely with the Burden of Disease subgroup (BoDG) of the CSTF to address the task force’s dual mandate of advising the Initiative on country-level burden of disease assessments and on strategies to ensure that future food safety decision-making is based on solid epidemiological evidence.

The KTPG aims to overcome the frequently observed research-policy and practice gap. Furthermore, it attempts to ensure that the efforts of the Initiative will not be merely an academic exercise. Its ambition is to catalyze real change in public health decision-making and practice by ensuring the evidence generated is usable by decision-makers and other end-users to help make food safer.

More specifically, the objectives of the KTPG are to:

- ensure that the work of FERG and in particular of the CSTF is policy-relevant and responds to decision-makers’ needs with regard to research;
- understand the contextual factors at global and country levels which may enhance or impede food safety research up-take and develop appropriate strategies and methods to address them;
- foster institutionalized interaction and communities of practice between food
safety researchers and decision-makers throughout the research process at country level;
• strengthen food safety researchers’ and decision-makers’ capacity to overcome the research-policy gap at country level through the provision of conceptual frameworks, tools and training modules;
• provide WHO with advice on additional multisectoral, policy-relevant food safety research needs at global and country levels; and
• build strong relationships with relevant global, regional and national networks and other key stakeholders involved in promoting research utilization in food safety policy-making.

The KTPG is composed of experts from a variety of disciplines, among them political science, social science, public health, training and education, economics, and communications and advocacy.

**Figure 3:**
The double-pillared mandate of the CSTF

2.2.2 National burden of foodborne disease studies

The dual mandate of the CSTF is concretized in the national FBD burden studies. These studies are integrated national-level disease burden and policy situation analyses, which will be conducted by WHO member states and methodologically supported by the two CSTF subgroups. They are intended to take place in two phases: a preliminary pilot study and a full country study.

Pilot studies are designed as pre-assessments for the full country studies. Their goal is to test the feasibility of the full country studies and to adapt the CSTF protocols to country-specific needs. It is hoped that countries conducting the pilot studies will proceed
to the next stage of conducting a full study. This full study will then conduct the actual data collection and FBD burden assessment, quantified in terms of disability-adjusted life years.

The proposed CSTF working frame for the national FBD burden studies is as follows:

1. The development of protocols that can be used by countries to estimate their national burden of FBD, including the appropriate uptake and use of FBD burden data into policy decisions and practice;
2. The development of training materials to assist countries in building capacity to undertake a national FBD burden study;
3. The initiation, conducting, and completion of an agreed number of pilot national FBD burden studies and policy context mapping;
4. The evaluation of country study protocols and training tools after the pilot studies are completed and the recommendation of necessary revisions; and
5. The initiation, conducting, and completion of national FBD burden studies and policy context mapping in each WHO region.
3. Progress since the establishment of the WHO Initiative

3.1 Publication and communication of FERG results

The progress of the Initiative and the FERG is reflected in the FERG’s summary documents, which have been appearing annually since its launch in 2007. These documents reflect the flavor and strategic outlook of the major consultations and meetings that have marked and guided FERG activities. These documents can be accessed online at www.who.int/foodborne_disease/burden/en/.

In addition to the meeting reports, several commissioned systematic reviews have formed the basis for peer-reviewed articles in scientific journals:


3.2 GBD 2010: update on progress

The Initiative follows the Global Burden of Disease (GBD) approach, a broader and long-standing enterprise to estimate the global burden of more than 100 diseases, disabilities, and risk factors (Murray & Lopez, 1996; Lopez et al., 2006; WHO, 2008). In order to align the work of the FERG with the GBD approach, an update was given on the GBD 2010 study and on the establishment of new disability weights. In addition, a presentation was given on the new national burden of disease (NBD) toolkit, developed by the GBD group.

3.2.1 GBD 2010 disability weights, age weighting, discount rate and co-morbidity

The GBD 2010 study is a three-year project, funded by the Bill & Melinda Gates Foundation, and led by a core team of researchers from the Institute for Health Metrics and Evaluation at the University of Washington, Harvard University, Johns Hopkins University, the University of Queensland, and WHO. A first draft of the estimates is expected by May 2011. Some diseases such as leptospirosis and other low-burden diseases will be dropped from the GBD list. As compared to the first GBD study (Murray & Lopez, 1996),
the GBD 2010 study will entail some new methodological choices, which are summarized in the following sub-sections.

**New disability weights**

The new disability weights are based on valuations of lay people from six countries. Five of these countries are developing countries (by mail survey), one is a developed country (USA; by telephone survey).

Approximately 200 conditions (sequelae) are included in the valuations. Each participant valued approximately 20 conditions (randomly selected).

Pairwise comparison was the valuation technique used to assess the values of the disability. Pairwise comparison entails that a participant is shown two health states and the participant is asked to choose which of the two is worse. If there are many reversals, the health states are close together on the scale 0 to 1. If there are few reversals, the health states are far apart on this scale.

For calibration purposes a smaller sample has also valued some conditions with the time trade-off (TTO) technique. The TTO asks participants to give up time in order to be restored to full health; the more time they want to give up, the worse the condition is.

For more complex diseases, an internet survey will be performed. With the internet survey, a random sample of conditions is selected and valued. So if the internet survey is taken twice, most probably a new set of conditions will be presented.

At this moment there are not yet enough responses to the survey. Therefore, no preliminary disability weights are available. Approximately 50,000 responses are aimed for. Currently, approximately 14,000 responses have been collected.

A problem with the health state descriptions is that they are sometimes described poorly. For instance, paraplegia was valued as more severe compared with quadriplegia, because many of the symptoms incorporated in the description of paraplegia were also symptoms of quadriplegia (for instance inability to walk), but were not included in the description of quadriplegia.

**Subdivision of health states**

Overall, with a few exceptions, the health states will be subdivided into mild, moderate and severe.

Missing FBD disability weights

The list of conditions included by the GBD group in the health state valuation surveys will be forwarded to FERG. With this list, FERG can evaluate if disability weights for particular health states are missing. In case of missing disability weights, it was advised to use a similar methodology (paired comparison; derived from a small sample of judges).
to assess disability weights for these health outcomes or to derive them from the new
disability weights.

**Age weighting and discount rate**

It is very likely that age weighting and time discounting will not be used in the GBD 2010 study.

**Co-morbidity**

There is an intention to adjust for co-morbidity in the GBD 2010 study. This adjustment will only involve conditions that often occur together, e.g., conditions co-occurring in elderly.

### 3.2.2 National burden of disease tools

The NBD toolkit contains a set of spreadsheet templates for carrying out Years Lost due to Disability (YLD), Years of Life Lost (YLL), Disability-Adjusted Life Year (DALY) and Comparative Risk Assessment (CRA) calculations. The NBD toolkit is currently in beta test mode and is being made available to selected research groups in Member States for experimental use.

The NBD templates contain WHO “prior” estimates of mortality and burden of disease for WHO Member States for the year 2004. These estimates are based on the global burden of disease: 2004 update as published in October 2008. Mortality estimates are based on analysis of latest available national information on levels of mortality and cause distributions. YLD estimates are based on the GBD 2004 analyses of incidence, prevalence, duration and severity of conditions for the relevant epidemiological sub-region, together with national and sub-national level information available to WHO. The GBD 2004 uses the population estimates for WHO Member States for 2004 prepared by the UN Population Division in its 2006 revision.

The NBD toolkit currently comprises the following:

1. A DALY summary file containing WHO estimates of deaths, YLL, YLD and DALYs by age, sex and cause for a given Member State and its region, with the option of incorporating locally derived estimates and comparing these with WHO figures;
2. A cause-specific YLD template containing WHO estimates of mortality, incidence, prevalence, duration and severity for any given cause for a given Member State and its region, with the option of incorporating locally derived estimates and comparing these with WHO figures. Locally derived YLD calculated using this template can easily be inserted into the above DALY summary file;
3. A life expectancy and health-adjusted life expectancy (HALE) template containing WHO estimates of life expectancy and HALE for a given Member State and its region, with the option of incorporating locally derived estimates and com-
paring these with WHO figures;

4. A CRA template containing WHO estimates of attributable mortality and burden from twenty-four selected risk factors for a given Member State and its region, with the option of incorporating locally derived estimates and comparing these with WHO figures; and

5. A presentation template for generating graphs and tables on key aspects of the above.

www.who.int/healthinfo/global_burden_disease/tools_nbd_toolkit/en/

The FERG experts agreed that the NBD toolkit could be useful for the national burden of FBD studies, but that some adaptations would be necessary since it follows the GBD approach and it does not include the source attribution issues. For instance, the burden of diarrheal diseases must be split for FBD. The toolkit does not aim at replacing DISMOD II. DISMOD III is under development and would allow starting DALY calculations with raw study data collected in systematic reviews. It would use Bayesian modeling and would be usable through the WHO website.
4. Summary of discussions and outcomes

4.1 Introduction

As in the previous FERG meetings, each of the FERG task forces met individually during FERG 4 to:

- Review, revise and appraise the work commissioned over the past 12 months; and
- Develop work plans, including proposals for new work to be commissioned.

In addition, plenary sessions were organized to bring the experts from the different task forces together, allowing them to share, discuss and appraise their progress and research findings. In this way, all the commissioned work could benefit from the critical viewpoints and comments of the researchers and academics with a wide range of expertise.

The five FERG task forces work together to estimate the global burden of FBD. Within the FERG, the Source Attribution Task Force (SATF) and the CSTF play a special role, as they build their work on the expertise available in the three other task forces. The SATF consists of researchers specialized in source attribution and expert elicitation, while the CSTF brings together experts in the fields of disease burden estimation, knowledge translation and policy-making. Through an established two-way interface, these technical experts join hands with the experts from the other task forces to complete their tasks, i.e., the estimation of the proportion of disease that can be attributed to food sources, and the development of tools and guidelines to estimate, and eventually reduce, the burden of FBD on a national level.

The following sections summarize the task force and plenary discussions, and outline the recommendations and work plans proposed by the different task forces. This chapter is then concluded by giving an overview of the Initiative’s Mid-term evaluation and the proposed future directions of the FERG.

4.2 Source Attribution Task Force (SATF)

4.2.1 Progress to date and issues arising

Since its establishment in 2008, the SATF has made considerable progress on its priority activities:

1. Defining “foodborne disease” and “source attribution”, and agreeing on levels of food categorization and points of attribution; and
2. Assessing currently available SA methods, proposing suitable methods for the various causative agents considered by FERG, and/or developing new methods.

Structured expert elicitation (EE) has been agreed to play an important part in the SA process. The main objectives of EE, as defined by the SATF, are:
1. For each specified hazard/contaminant, estimate the proportion of disease that is transmitted by different major pathways at the point of exposure, for each Global Environment Monitoring System (GEMS) region. The pathways include exposure via: food consumption, animal contact (livestock, pets and wildlife), human-to-human contact, water, and environment (soil and air);
2. Within the pathway food, estimate the proportion of disease that is transmitted by different food categories at the point of consumption; and
3. As one or two qualitative steps after the food attribution, estimate by ranking the importance of each of the non-food pathways’ contribution to the contamination of food. This will only be applied for some hazards, where it is particularly relevant.

In addition, work is in progress on the other priority activities of the SATF:
1. Developing a “Global Atlas of Food consumption”;
2. Evaluating the use of outbreak and surveillance for SA;
3. Linking food consumption data with food concentration data for chemicals to explore exposure through comparative exposure assessment (CEA); and
4. Modeling the global Salmonella source attribution.

During FERG 4, decisions were made on the regions and delineation levels to be used in the EE process. Furthermore, an update was given on the evaluation study of SA methods, and a presentation was given on the theoretical framework of structured expert judgment.

At the moment, the SATF has not yet commissioned any SA studies. During FERG 4, however, the following items were identified as possible commissioned work for SA studies based on the “evaluation of SA methods” reports:

- Systematic reviews of case-control studies of sporadic infections of:
  - *E. coli* STEC
  - *Shigella* spp.
  - *Giardia lamblia*
  - *Cryptosporidium*
  - *Toxoplasma gondii*

- Comparative exposure assessments for the following chemical hazards, including exploring the possibility to use results from relevant total diet studies:
  - *Lead*
  - *Cadmium*
  - *Dioxins*

Finally, the SATF made the following recommendations for commissioned work on identifying data and information that should be requested by the SATF to the Country Studies:

- Review of which data are already available internationally;
- Description of the use of the data and the ownership;
- Exploration of expert availability in the countries for the EE; and
• Exploration of the feasibility of conducting an EE SA study.

The following sub-sections give an overview of the TF discussions on the expert elicitation protocol, the evaluation of SA methods report, and the modalities of structured expert judgment. The SATF section will be concluded by presenting the endorsed work plan for the coming year.

4.2.2 Modalities of the expert elicitation protocol

Since clarification was needed on the regions and definitions for the expert elicitation process before the start of the Pilot Studies, an extra-curricular SATF meeting was organized on November 10. During this meeting, agreements were found on the modalities of the EE protocol, and it was also decided that the feasibility of this protocol should be pre-tested in a simulation study with FERG members. The actual EE shall be performed with experts who have expertise in food safety, water and sanitation, and other relevant fields, and shall be conducted through comprehensive in-person interviews. The optimal size of one expert panel is estimated to be around ten experts.

4.2.2.1 Selection of regions

Previously, it had been decided that the EE adopted by the SATF should be conducted on a regional level. The selection of these regions, however, was still an unresolved issue. Three possible options were presented:

1. **The GDB regions**: 21 regions based on mortality estimates from WHO and the UN, and current knowledge on country-specific epidemiological conditions;

2. **The WHO regions**: These six regions are similar to the GBD regions based on mortality strata, but also have political considerations; and

3. **The GEMS/Food Consumption Cluster Diets**: The 13 GEMS regions include countries that were clustered according to diets and reflect the food consumption patterns of regional and cultural groups around the world.

The experts agreed that the GEMS cluster diet regions are most suitable for the purpose of SA. Due to reasons of representativeness, feasibility, burden and logistics, the SATF decided on recruiting experts in the six WHO regions, but to ask for an estimate for each GEMS region. For each of the three groups of hazards (i.e., enterics, parasites and chemicals), a separate expert panel will be formed. Whether to use a global panel or regional panels is still to be decided, but will be tried out in a pre-test of the EE protocol, using FERG members as experts.
4.2.2.2 Formulation of definitions and delineation levels

The EE process will be conducted in three consecutive steps. For each step, clear definitions and delineation levels had to be formulated and agreed on:

1. **Overall proportion foodborne**
   The first step in the EE process will be the estimation of the overall proportion of the burden of a certain FBD that is attributable to the ingestion of contaminated food, as well as to other major pathways: animal contact, human-to-human contact, water, and environment (soil and air). The SATF agreed to apply the point of consumption to estimate these overall proportions.

2. **Contribution of specific food items**
   As a second step in the EE process, the contribution of different food items to the FBD burden will be assessed for each considered hazard. The point of consumption will be used as the basis for these specific food attribution estimates. Previously, a food categorization scheme had been agreed on *(Figure 5)*, and during FERG 4, it was decided to add seaweed to the seafood category.

3. **Attribution within the food production chain**
   In order to inform risk managers, the TF members decided to include a final step in the EE process, where the contribution from each of the non-food pathways to the contamination of food should be qualified or quantified,
for instance by ranking (Figure 6). The estimates for this step will be based on the point where the contaminant enters the food-production chain. During FERG 4, an agreement was reached on the categorization of the major pathways to contamination in the primary production: environment (including soil and air), water, animals (including livestock, pet, and wildlife), and humans.

Figure 5:
Food categorization scheme

Figure 6:
Schematic overview of the expert elicitation process proposed by the SATF

Based on these definitions and delineation levels, the Chair of the SATF will revise the terms of reference for the EE study.
4.2.3 Evaluation of SA methods

An update was given on the evaluation of SA methods. One of the aims of FERG is to estimate the overall proportion of the burden of disease that can be attributed to foods, and as a second step estimate the relative importance of specific foods. The SATF has as a primary objective to assess all currently available methods used for attributing foodborne disease to sources, and propose appropriate source attribution methods for the foodborne hazards prioritized by the three thematic task forces. A variety of methods to attribute foodborne diseases to specific sources are available, each presenting advantages and limitations, and the usefulness of each depends on the public health questions being addressed. Additionally, methods have different data requirements and attribute human illness at different points of the farm-to-consumption chain (i.e., production, processing or exposure), and therefore their utility will vary depending on the hazard and/or the country or region in question. Source attribution methods based on occurrence data and on epidemiological studies are useful to estimate the contribution of specific sources (or sub-pathways) within the general pathway food, but they are not able to estimate the proportion of disease that can be attributed to major pathways: foodborne, waterborne, person-to-person and direct contact transmission. To estimate the overall contribution of food to the burden of disease, expert elicitations or intervention studies are required. All available SA methods were reviewed, and their applicability to attribute the foodborne hazards from each hazard-group (enteric pathogens, parasites and chemicals) to the responsible sources of human illness was assessed. It was concluded that an expert elicitation is necessary in order to estimate the proportion of a disease that is foodborne for hazards that are not 100% foodborne. It was also suggested that the proportion of disease that can be attributed to specific foods items or transmission routes can be estimated for almost all of the FERG prioritized hazards commonly transmitted to foods for which burden of disease estimates are to be derived. Some exceptions, e.g., Ascaris lumbricoides and Echinococcus spp., were identified. The most appropriate methods to attribute human disease caused by each hazard were described.

4.2.4 Structured expert judgment

In structured expert judgment, a clear distinction has to be made between the concepts of uncertainty, ambiguity and indecision. In this case, uncertainty is the lack of knowledge about the impact of a disease on public health, if uncertainty cannot be removed by measurement, it must be quantified via expert elicitation. Ambiguity refers to the meaning of terms (what is diarrhea?) and depends on semantic analysis. Indecision is hesitation in choosing a control option and is addressed by quantifying uncertainties and values. Three possible goals of expert elicitation may be distinguished:

1. making a census of experts’ knowledge;
2. making a political consensus; or
3. making a rational consensus.

Expert judgment for rational consensus implies that parties pre-commit to a method which satisfies necessary conditions for scientific method: traceability/accountability, neutrality
(avoiding untruthfulness), fairness (ad initio equality between experts) and empirical control (performances measurement). The final goal of a rational consensus is to comply with principals and combine experts’ judgments to get a good probability assessor. A good probability assessor has to be statistically accurate and informative. Measuring the performances of expert elicitation consists of putting credibility intervals around their estimates.

Some important issues on expert judgment are the following:

- Expert judgment is not knowledge but a way of quantifying uncertainty;
- Experts can quantify uncertainty as subjective probability;
- Experts confidence does not predict performance;
- Experts are sometimes well-calibrated and sometimes not;
- Experts sometimes agree and sometimes do not;
- Classical models usually work but not always;
- There might be better alternatives to equal weighting;
- Experts like performance assessment; and
- The choice is not whether to use expert judgment or not, but: do it well or do it badly?

Textbox 1:

Summary of SATF discussions, recommendations, and action points

**Recommendations**

- It was reiterated that an expert elicitation is necessary to estimate the proportion of a disease burden that is foodborne for hazards that are not 100% foodborne;
- For this EE process, experts will be recruited in the 6 WHO regions, and asked to provide estimates for each GEMS region;
- Categorization schemes of food and contamination pathways were formulated, as well as definitions of the points of attribution to be used in the EE protocol.

**Action points**

- The decisions on the EE process will be worked out in a draft protocol, and a simulation study will be organized with FERG members to pre-test this protocol;
- Based on the “evaluation of SA methods” report, possible commissioned work for SA studies was presented;
- Finally, recommendations were made for commissioned work on identifying data and information that should be requested by the SATF to the Country Studies.

**Next meeting**

- To be organized on November 9, 2011.
4.2.5 SATF work plan 2010-2011

The 2010–2011 work plan for the SATF is summarized in Table 1.

<table>
<thead>
<tr>
<th>Specific priority activities</th>
<th>Timeframe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revise ToR for EE</td>
<td>To be discussed at the FERG meeting in November 2011</td>
</tr>
<tr>
<td>Finalize draft position paper delineating the major routes of transmission</td>
<td>November 2011</td>
</tr>
<tr>
<td>Discuss EE study issues</td>
<td>Teleconference Dec-Jan 2010</td>
</tr>
<tr>
<td>Finalize review report on Evaluation of SA methods</td>
<td>December 2010</td>
</tr>
<tr>
<td>Provide final list of hazards and pathways/food commodities etc. to the EE contractors</td>
<td>Early March 2011</td>
</tr>
<tr>
<td>Discuss draft protocol of EE study (possible pre-testing)</td>
<td>To be confirmed</td>
</tr>
<tr>
<td>Revised version of the Global Atlas of Food Consumption publicly available</td>
<td>To be confirmed</td>
</tr>
<tr>
<td>Link food consumption data with food concentration data for chemicals to explore exposure (Food Safety Portal)</td>
<td>To be confirmed</td>
</tr>
</tbody>
</table>
| Continue work on the use of outbreak data for SA:  
  1. Publish outbreak model using LA data  
  2. Enhance data collection through GFN courses/workshops | 1. End 2010  
  2. Timeline depends on success of data collection |
| Modeling on the global Salmonella source attribution:  
  1. Discuss and try out different modeling approaches  
  2. Proceed with data collection | Presentation at the FERG meeting in November 2011 |

Table 1: SATF work plan for 2010–2011

4.3 Enteric Diseases Task Force (EDTF)

4.3.1 Progress to date and issues arising

Since the last FERG meeting, the EDTF has concentrated on the intellectual support and follow-up of the systematic reviews for priority enteric diseases. Diarrheal diseases continued to be an important focus for the EDTF, as a number of priority etiological agents contribute to the diarrheal disease burden.

The EDTF continued to work in close collaboration with the WHO Child Health Epidemiology Reference Group (CHERG) to estimate the global burden of diarrheal diseases. The CHERG finalized its assessment of the number (and location) of deaths due to diarrheal disease in children under five, and progress has been made on the review on diarrhea morbidity. In addition, the preliminary estimates on the cause-specific microbial etiology of diarrheal mortality and morbidity in children under five have become available.

In addition to the work on diarrheal diseases, the commissioned systematic reviews for hepatitis A and E, norovirus, *Mycobacterium bovis*, and *Brucella* spp. are underway. The progress of the EDTF priority activities is summarized in Table 2.
The following sub-sections summarize the presentations and discussions on the commissioned systematic reviews on diarrheal diseases, foodborne hepatitis, brucellosis, and bovine tuberculosis. The EDTF section then continues by summarizing the discussion on intervention studies, and is concluded by presenting the endorsed work plan for the coming year.

### 4.3.2 Global burden of diarrheal diseases

The Child Health Epidemiology Reference Group (CHERG) summarized its progress on estimating the cause-specific microbial etiology of diarrheal mortality and morbidity. An overview of the progress on two commissioned systematic reviews that will contribute to the assessment of the global burden of diarrheal diseases was given, i.e., the pathogen-specific burden of salmonellosis and the burden of norovirus infection. Finally, a presentation was given on the importance of Campylobacter-associated Guillain-Barré syndrome in Bangladesh, to demonstrate the potential burden of chronic sequelae of enteric diseases.

#### 4.3.2.1 Etiology of diarrheal disease in children under five years: an update from CHERG

The CHERG is working to develop the most accurate estimate of the most important causes of children’s morbidity and mortality. In collaboration with FERG, a sub-group of CHERG members is working to estimate the burden of diarrhea’s...
morbidity and mortality in the world, and by WHO region, in general and by cause. It was noticed that in contrast to the sharp reduction of deaths attributable to diarrheal diseases (from 4.6 million deaths in children <5 in the 1980s to 1.3 million in 2008) there has not been any change in the incidence of diarrheal diseases (2.2 episodes per child per year in the 1980s to 3.6 in 2005). This means that in this period effective measurements have been implemented in the management of diarrheal diseases (like oral rehydration solutions, antibiotics, etc.) but no effective interventions to prevent diarrhea are in place, despite the efforts and achievements in water and sanitation. That is why FERG is important, since contaminated food may be playing an important role in diarrheal transmission, where no intervention is available in developing countries.

CHERG has completed the work needed to estimate the number (and location) of deaths due to diarrheal diseases. The progress made in the review of the literature and in models (single cause initially and multiple-cause models at the end) has resulted in precise estimates of diarrheal deaths on each country in the world, recently published in Lancet. India, Nigeria, Congo, Afghanistan, Pakistan, Ethiopia, Uganda, Kenya, Angola, and Indonesia are the top 10 countries having the highest number of deaths due to diarrheal diseases in children <5 in the world. The review on diarrhea morbidity is in progress and preliminary results estimating a median incidence of 3.6 episodes of diarrhea per child per year were presented. In FERG 4, the efforts to estimate the most important causes of diarrhea morbidity and mortality by CHERG were presented. A systematic and comprehensive literature review covering the period 1990–2008 was presented. In reviewing the literature it became evident that most publications presenting proportion of diarrheal diseases by cause are inflating the numbers, since when more than one organism is identified in a stool sample (mixed infections are present between 20 to 40% of diarrheal stool samples) those organisms are presented independently, explaining why the sum of all median proportions is more than 100% in studies done in children hospitalized with severe diarrhea. There is a need to establish a mechanism to assign only one cause to each diarrheal episode in the presence of mixed infections. To partially control for this problem, CHERG obtained the median rate of diarrheal episodes where no cause of diarrhea was found in studies that searched for five or more organisms (47% unknowns in community-based studies and 35% in in-patient studies) to subtract from the “envelope” of total diarrheal episodes and deaths in children <5 in 2008. It was also noted that for some agents, particularly rotavirus, the median proportion in studies that only looked for it was significantly higher than in studies that searched for two or more agents, suggesting that single-cause studies were biased by selecting a high-risk population. Therefore, to produce a more credible estimate, CHERG applied median proportions obtained from studies that searched for two or more pathogens to the corrected “envelope” of diarrhea cases and deaths. Norovirus, Giardia lamblia, enterotoxigenic E. coli and Campylobacter where the most frequent causes of diarrheal episodes, ex-
plaining more than 100 million cases each. Rotavirus, Norovirus, enteropathogenic *E. coli* and enterotoxigenic *E. coli* explained more than 50% of the diarrheal deaths.

For FERG, these investigators have also produced estimates for children 5 years of age and older, and for adults, which have already been published. Following a systematic literature review of articles published between 1980 and 2008, it has been estimated that 2.8 billion diarrheal episodes occurred in older children and adults in the world, being steady across the study period, as seen with younger children, again suggesting that none of the actions taken to prevent diarrhea have been effective in this age group. From 0.4 million deaths due to diarrheal diseases in older children and adults estimated by the GBD study in the past, the current estimate has significantly being increased to 48.1 million thanks to the review done for FERG.

One of the limitations that affect the current estimates is the problem created by agents being isolated in stool samples taken during diarrheal episodes that represent asymptomatic infections, which are currently being considered as etiological agents. Future work to be done by CHERG will correct the estimates adjusting for this and other problems.

*The plenary lauded the work performed by CHERG, and recommended the FERG and CHERG methodologies to be made compatible, as this will allow the integration of both estimates in an overall diarrheal disease burden assessment.*

**4.3.2.2 Pathogen-specific burden of salmonellosis**

The estimates of salmonellosis burden determined by two different approaches were compared. The first was “The global burden of non-typhoidal *Salmonella* gastroenteritis”, by Majowicz et al. (2010). This is a systematic review of a variety of data sources, evaluated in a “best evidence” hierarchy, with the best available data used to make estimates for each of the 21 Global Burden of Disease (GBD) regions. Population-based data were used for one region, followed by laboratory-based multiplier studies (5 regions), disease notification data (2), returning traveler data (11) and extrapolation from nearby regions (2). Sophisticated uncertainty analyses were performed. Limitations include sparse data from prospective studies, limited data on *Salmonella*-specific multipliers for incidence estimates, use of returned traveler data which has been controversial, and use of a single multiplier (86%) for attribution of disease to a foodborne source, which was based on limited data.

The second set of estimates were derived from several sources. Cause-specific morbidity and mortality data for children under age 5 were from unpublished studies performed by Lanata, Black, Walker *et al.* for CHERG (“CHERG
study"), and data for children ≥5yo from reports by CF Walker commissioned by FERG ("Walker study"). These studies used similar CHERG methodology, with rigorous literature reviews involving multiple pathogens. Strict inclusion and exclusion criteria led to a small number of studies ultimately used for the analyses. These criteria led to exclusion of studies lasting less than 12 months, not adhering to a strict definition of diarrhea, not differentiating clearly among inpatient and outpatient populations, or based on outbreak data. Mortality estimates have not been published by Walker and were not provided for all regions in the report. "Multipliers" were applied to CHERG estimates to correct for the proportion of diarrheal disease cases (47%) and deaths (35%) with unknown etiology. Because the CHERG and Walker studies used similar methodologies and non-overlapping populations, combining these data is reasonable. Basic calculations were performed to combine these data, using a very conservative estimate for mortality in regions missing from the Walker report, applying the CHERG multipliers to appropriate Walker data, and applying the Majowicz “foodborne proportion” multiplier to totals. With these adjustments, the rough overall estimates of Salmonella burden are:

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Majowicz:</td>
<td>93.8M (62-132M)</td>
<td>155,000 (39,000-303,000)</td>
</tr>
<tr>
<td>CHERG+Walker</td>
<td>225M</td>
<td>64,000</td>
</tr>
</tbody>
</table>

In order to optimize the comparison of the Majowicz and CHERG+Walker estimates, final CHERG and Walker estimates of cases and deaths are needed, which can then be combined. In addition, uncertainty calculations should be performed for the CHERG+Walker estimates.

Final FERG multipliers for the proportion of cause-specific disease that is foodborne should be applied to both the CHERG+Walker estimates, and those of Majowicz for comparison.

Because the CHERG+Walker studies used a well-accepted methodology, will be published and used for GBD work, include data for other pathogens, and are fairly similar to the Majowicz estimates resulting from very different methodologies and data sources, it is reasonable for FERG to use the final CHERG+Walker estimates for its work. Therefore, FERG should consider to apply the same approach to CHERG+Walker data to make final estimates for the burden of multiple other pathogens (including bacteria, viruses and parasites) that are included in those studies, or to use this approach to validate other commissioned work.

4.3.2.3 Update on the burden of norovirus

The proposed norovirus work is expected to provide knowledge-driven information on:
1. The incidence rates of gastroenteritis due to norovirus, by age and WHO region;
2. The health effects resulting from norovirus infection; and
3. The proportion of norovirus infection that is foodborne.

Three approaches to meeting the objectives were presented:

1. Classical epidemiology: estimating the proportion of community gastroenteritis caused by norovirus (by age and region), and estimating the proportion foodborne using outbreak data and case-control studies;
2. Molecular epidemiology: estimating the proportion foodborne based on molecular typing studies and the emerging evidence that norovirus genogroup 1 is more likely to be foodborne, and the consideration that infections with multiple types are more likely to be acquired via fecally contaminated food or water.
3. Extrapolation from telephone surveys of acute gastro-enteritis.

In order to enhance comparability with the CHERG estimates, it was suggested that the same strict criteria should be followed. The exception would be the exclusion of vomiting and outbreaks, as these two phenomena are specifically associated with norovirus infection. Then, a subgroup of the data can be presented that is similar to that of CHERG, allowing the results to be compared.

4.3.2.4 Sequelae and outcome trees: Campylobacter infection and Guillain-Barré syndrome in Bangladesh

Guillain-Barré syndrome (GBS) is the most frequent cause of acute flaccid paralysis (AFP) in Bangladesh. GBS is characterized by demyelination and axonal degeneration of peripheral nerves, leading to a typical acute, progressive, symmetric paralysis with areflexia of arms and legs. Some patients show involvement of cranial nerves or paresis of respiratory muscles for which they require ventilation. GBS is a post-infectious immune mediated diseases and Campylobacter jejuni is considered to be the predominant cause of these antecedent infections. Molecular mimicry between Campylobacter lipo-oligosaccharides (LOS) and gangliosides in nervous tissue most likely induces a cross-reactive antibody response leading to nerve damage and the clinical symptoms of GBS.

A prospective matched case-control study was conducted in the Dhaka area of Bangladesh with a follow-up of six months including 100 hospital-admitted patients fulfilling the NINDS diagnostic criteria of GBS. Pure motor variants of GBS are common in Bangladesh. Cranial nerve involvement is infrequent. C. jejuni and anti-ganglioside antibodies are significantly associated with GBS in Bangladesh. The axonal variant of GBS is associated with C. jejuni infection, severe residual disability, and high mortality. There is no significant association between cytomegalovirus, Epstein-Barr virus, Mycoplasma pneumoniae, and Haemophi-
lue influenza and GBS in Bangladesh. A new *C. jejuni* HS:23 serotype and ST-3219 is highly prevalent among GBS-related *C. jejuni* strains from Bangladesh. Comparative genotyping analysis by MLST, AFLP and PFGE demonstrate that HS:23 strains from GBS or enteritis patients are clonal. Specific genetic determinants that differentiate GBS-associated *C. jejuni* strains from enteritis strains were not identified. The population structure of *C. jejuni* isolated from poultry, and humans are highly heterogeneous. The most common ST-353 clonal complex in poultry is infrequent among human isolates. The most frequent sequence type that is associated with GBS is not found in poultry and another reservoir is likely to be involved.

The crude incidence rate of GBS in children in Bangladesh (<15 years) was determined using the data from a WHO surveillance on AFP. The crude incidence rates of GBS in children from Bangladesh varied from 1.5 to 2.5 per 100,000 per year. Most incidence studies reported in the literature originate from Europe and North America. A recent review reported that the best estimate of the global incidence of GBS in children <15 years is 0.6 per 100,000 per year. Reports on incidence rates in developing countries are scarce. The crude incidence rate of GBS in Bangladesh in children <15 years of age reported here appear 2.5 to 4 times higher as compared to available data from the literature.

After eradication of poliomyelitis in Bangladesh in 2000, GBS is now the dominant cause of AFP in Bangladesh and associated with high mortality and permanent disability. This project is the first thorough initiative on GBS in Bangladesh where the population, in particular children and young adults, are likely to be infected by *C. jejuni* through frequent exposure from various sources. The program will help to identify the source of the infection and the routes of transmission of Campylobacter in the environment and the in the community. Increased insight into the mechanisms of disease at a molecular level may ultimately lead to the
development of new prevention and treatment strategies and interventions. The possibility of GBS being related to the H1N1 influenza pandemic and the affiliated H1N1 vaccination campaign has resurfaced again recently. For the surveillance of excess cases of GBS after H1N1 influenza and also for post-marketing surveillance of the safety new vaccines in general, background GBS incidence data are critical. Available data indicate that the burden of GBS in Bangladesh is substantial, and suggests that data obtained through the on-going global AFP surveillance program can be used to obtain crude incidence data of GBS worldwide.

The plenary group recognized the importance of getting estimates from developing countries because, as shown in this presentation, the epidemiology of foodborne diseases can be significantly different in these settings.

4.3.3 Global burden of foodborne hepatitis

Results were presented on the models used to estimate the global age-wise seroprevalence of hepatitis A, and on the work done to assess the global burden of foodborne hepatitis A infection.

4.3.3.1 Global prevalence of hepatitis A

Hepatitis A virus (HAV) is transmitted via the fecal-oral route, either through direct contact with an infectious person or through the ingestion of contaminated food or water. Outbreaks of hepatitis A have been linked to vegetables (such as green onions and lettuce), fruits (such as berries), seafood (such as mussels, oysters, and clams), and water. Young children are usually asymptomatic. After a 15 to 50 day incubation period, most older children and adults present with one week of gastrointestinal and flu-like symptoms, several weeks of jaundice, and several weeks of convalescence. The risk of severe disease (such as acute liver failure) and death increases with age.

The incidence rate for hepatitis A has decreased significantly in most parts of the world in recent decades as socioeconomic status has increased and as a greater proportion of the global population has access to water and sanitation. In many regions, the decrease in incidence has caused a shift in the average age at infection from childhood to adulthood. As the average age of cases increases, the proportion of cases that result in severe disease and death also increases. The costs per case also increase.

Vaccination is cost-effective when the incidence rate is high enough to yield a significant risk of infection yet low enough that children would not usually develop immunity at an early age without the vaccine. In low-income/high-endemicity regions, nearly all children get infected at an early age when asymptomatic infection is likely; in this situation, vaccination is not recommended. In middle-in-
come/intermediate-endemicity regions, however, the average age at infection is gradually increasing; universal childhood vaccination may then be appropriate. In high-income/low-endemicity regions, few individuals become infected in childhood and many adults remain susceptible to infection; targeted vaccination of high-risk populations may be the best approach.

A systematic review of studies of IgG anti-HAV seroprevalence identified 637 eligible articles in 17 languages from more than 125 countries and territories that were published in or after 1980. (Articles were excluded if, for example, they focused on a high-risk population or on patients with acute or chronic liver disease.) Meta-analysis was used to fit age-seroprevalence curves for each of the 21 Global Burden of Disease (GBD) world regions for 1990 (1985-1994 data) and 2005 (1995-2009 data).

Sub-Saharan Africa and South Asia remain high endemicity regions where ≥90% of children develop immunity via infection by age 10. Latin America, Central Asia, North Africa and the Middle East, and Oceania are intermediate endemicity regions where about half of children develop immunity by age 15. Eastern and Central Europe, East Asia, and Southeast Asia are estimated to be low endemicity regions where about half of residents develop immunity by age 30. High-income Asia Pacific, North America, Australasia, and Western Europe are very low endemicity regions where more than half of 30-year-olds remain susceptible to infection.

However, the estimates for many regions were based on limited evidentiary support. More current country and sub-country level information is required for policy and planning.

The SATF will elucidate the role of foodborne transmission in hepatitis A infection, as compared to environmental transmission. This information can then be included in the existing models. It was also suggested that the models could be expanded by incorporating human migration. Finally, the plenary recommended the results to be presented by WHO region, through extracting the current data to the country level and reassembling them to each of the six WHO regions.

4.3.3.2 Global burden of hepatitis A

Annual incidence of hepatitis A is strongly inversely related to levels of economic development and modern water sanitation. The annual incidence of hepatitis A has decreased between 1990 and 2005 as global economic development has increased. Paradoxically, because the probability of symptomatic disease resulting from incident infections increases as the age of infection increases, global disease burden from hepatitis A may have increased over the time period as incidence declined. The annual disease burden of hepatitis A virus was mod-
eled for the 21 GBD regions for the years 1990 and 2005. To estimate annual infections, the WHO estimates of disease seroprevalence at different ages were converted into annual age-specific force of infection estimates and multiplied force of infection rates times the susceptible population. Incident infections were converted into 5 mutually exclusive results of infection: 1) asymptomatic episode; 2) mild symptomatic disease; 3) moderate symptomatic disease; 4) fulminant liver failure; and 5) death from hepatitis A. The probabilities of each infection outcome were drawn from published studies and stratified by age and pregnancy status. It was estimated that the annual incidence of hepatitis A declined from 2.1% per year in 1990 to 1.9% per year in 2005. Hepatitis A infected an estimated 115 million people in 1990 and 119 million in 2005. These infections resulted in 24.7 million cases of symptomatic illness and 29,000 deaths in 1990 and 31 million cases of symptomatic illness and 34,000 deaths in 2005. Epidemiological changes in East Asia strongly influenced global results. When East Asia was excluded from the calculation, the percentages of infections that resulted in symptomatic disease increased from 15.4% in 1990 to 23.4% in 2005. The model was most sensitive to estimates of age-specific prevalence of HAV disease and the age-specific probability of symptomatic infection. This research suggests that the hepatitis A virus remains a global health challenge even as its incidence is declining.

An important issue arising from the presented model is the possible perverse effect of vaccination, as symptomatic illness might increase due to a loss of protection in older ages. The plenary suggested that this effect should be further clarified.

4.3.4 Global burden of brucellosis

Brucellosis is one of the most common zoonotic infections globally, with serious medical and economic ramifications. A systematic review of scientific literature published between 1990-2010 relating to the frequency and morbidity of human brucellosis was commissioned by the FERG. The primary objective of this review was to contribute to an informed global burden of disease estimate.

Thirty-three databases were searched and, following the application of strict screening criteria, 30 original studies relating to disease frequency and 58 relating to morbidity were selected for data extraction. Data relating to study population and design, diagnostic methods, estimated prevalence/incidence by sex and age, and proportions of cases with specific symptoms/syndromes by age category were extracted.

Prevalence data were mainly available from northern Africa and the Middle East. Disease incidence data were also available from these regions as well as from western Europe and North America. Comprehensive age-related and sex-related data were lacking. In
general, a wide variation in disease frequency estimates was evident both within and between countries. Comparison with data from national health ministries suggested significant under-reporting.

Severe complications of infection were not rare, with 1-2 and 2-5 cases of endocarditis and neurological outcomes per 100 patients, respectively, depending on age category. One in 10 men were affected by epididymo-orchitis. Debilitating conditions such as arthralgia, myalgia, and back pain were common and the diagnostic delay for patients with osteoarticular disease was reported to be longer than for other cases.

This systematic review highlights the severe and debilitating impact of brucellosis. Due to data heterogeneity and the absence of data from several regions, an overall global disease burden estimate could not be calculated. The research agenda should focus on formal epidemiological and statistical training to maximize study quality, particularly in Asia, Central/South America, and Sub-Saharan Africa. In malaria-endemic countries, a brucellosis surveillance system amongst acute febrile illness patients could identify cases otherwise overlooked by health practitioners.

The overall assessment of the global burden of brucellosis has been split into two sections:
1. The global disease frequency of brucellosis; and
2. The global evidence for brucellosis disease sequelae.

For both parts a draft manuscript has been prepared. The paper on disease frequency is currently revised aiming a publication in the Bulletin of the WHO.

4.3.5 Global burden of Mycobacterium bovis

A similar effort as for brucellosis has been made for Mycobacterium bovis, the causative agent of bovine tuberculosis. The databases are completed and the analyses are ongoing. As for brucellosis, the quality of the available data for M. bovis is not sufficient for a full assessment of the worldwide disease frequency. However, the available data should allow estimating key DALY parameters like the disability weight, the duration of untreated disease and the age at onset of disease.

The expert group commented that the key part of the study will be to estimate the proportion of human tuberculosis cases caused by M. bovis. Since the burden of human tuberculosis is very high, even a small proportion caused by M. bovis can yield a high burden. Molecular studies were deemed to be most appropriate for providing such information.

With regards to source attribution, it was considered that the vast majority of human M. bovis infections is foodborne. Airborne infection is also possible, and is shown by the occurrence, albeit rare, of pulmonary tuberculosis caused by M. bovis. Given the importance of food as main transmission route, the worldwide consumption of unpasteurized milk should be studied in more detail.
Textbox 2:
Summary of EDTF discussions, recommendations, and action points

Discussions

- The EDTF efforts have continued to concentrate on supporting the systematic reviews for priority enteric diseases. Diarrheal diseases have played an important part of the EDTF’s focus, as a number of priority etiological agents contribute to the diarrheal disease burden. In addition, progress has been made on assessing the global burden of foodborne hepatitis, and the first steps have been set towards assessing the global burden of *Brucella* spp. and *Mycobacterium bovis*;

- The systematic literature review on diarrhea morbidity and mortality pointed out that the management of diarrheal diseases has improved, but that its prevention has not. This might be due to the underestimation of the role of food in diarrheal transmission, stressing the importance of the *Initiative* and FERG;

- Paradoxically, because the probability of symptomatic disease resulting from incident infections increases as the age of infection increases, global burden disease from hepatitis A may have increased over the time period as incidence declined. Hepatitis A infected an estimated 115 million people in 1990 and 119 million in 2005. These infections resulted in 24.7 million cases of symptomatic illness and 29,000 deaths in 1990 and 31 million cases of symptomatic illness and 34,000 deaths in 2005. Epidemiological changes in East Asia strongly influenced global results.

Recommendations

- The leadership of CHERG was lauded by the experts, and it was suggested that the CHERG methodology should be used as reference in further studies;

- The issues of mixed infection and asymptomatic carriers should be addressed in order to optimize the etiological disaggregation of enteric diseases.

Action points

- The EDTF has recommended a systematic review on the outcome trees of all priority pathogens, and will consider commissioning a systematic review of the possible interventions and policy issues to reduce the burden of foodborne disease in developing countries.

Next meeting

- To be organized in June 2011, possibly in collaboration with the PDTF.
4.3.6 Intervention studies

FERG is making important progress in estimating the burden of illnesses due to food-borne pathogens in the world. This will generate important attention to this neglected public health problem, particularly in developing countries, which should lead to the search for effective interventions that could be implemented in resource-limited populations, to reduce this burden. The high food safety standards available and implemented in developed countries, as well as in food products exported from developing countries to developed countries, cannot be applied in an effective way to all food production, commercialization and consumption in developing countries. In many of those countries existing legislation promoting food safety is not enforced. The underlying factor is that by applying those standards, the price of food increases to a level not affordable by most of the population. There is a need to identify cost-effective interventions that could be applied in resource-limited situations which could be effectively enforced, with the ultimate aim of reducing foodborne illnesses in these populations. Some of the interventions traditionally conceived to reduce this burden, like water and sanitation programs, are failing. This is due in part to the fact that most sewage collected in sanitation systems is dumped untreated into rivers, lakes or oceans, which then contaminate food consumed by the local population. Sewage-contaminated water is commonly used for irrigation of food produce, which is appreciated by farmers due to its fertilizing effect and by the fact that contamination by enteric pathogens do not change the organoleptic characteristics of vegetables or fruits. Most markets in developing countries lack adequate water and sanitation systems where very poor hygiene practices exist, further contaminating food sold in those markets. Finally, the hygiene level at home kitchens is also poor, with heavy cross-contamination of raw and cooked food prepared for young infants and children.

There is a need for FERG to commission systematic reviews on interventions that could be implemented in these settings, learning from experiences in countries that have migrated from middle to high levels of developments, to control parasitic, enteric and chemical contamination of food products. Cost-effective methods to treat sewage and protect irrigation water is needed. How markets could avoid contamination of food sold to poor customers is also another important area to evaluate cost-effective interventions. And interventions that could be implemented and be sustained at the home level of poor families are also urgently needed. Some interventions like solar disinfection of drinking water, avoiding baby bottles, increasing water availability at the kitchen, use of fermented foods for weaning children, and hand washing are some of those interventions that need further evaluation.

4.3.7 Enteric Diseases Task Force work plan for 2010–2011

The 2010–2011 work plan for the EDTF is summarized in Table 3:
Table 3:
EDTF work plan for 2010–2011

4.4 Parasitic Diseases Task Force (PDTF)

4.4.1 Progress to date and issues arising

The progress of the PDTF was marked by the publication of two peer-reviewed articles in 2010, as mentioned on page 8.

Furthermore, the reviews on foodborne trematodiasis, cystic echinococcosis, neurocysticercosis, trichinellosis and anisakiasis have been nearly completed, and draft estimates were presented. The reviews on ascariasis, toxoplasmosis and intestinal protozoal infections are in progress.

In addition to the already commissioned work, the PDTF requested to commission four new systematic reviews. These reviews will focus on the incidence, prevalence and associated health outcomes of four parasites that appear on the original list of 40+ priority
agents, but are likely to have a low burden:

1. *Angiostrongylus cantonensis* and *Angiostrongylus costaricensis*
2. *Capillaria philippinensis*

The progress of the PDTF priority activities is summarized in Table 4.

<table>
<thead>
<tr>
<th>Activity</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global burden of foodborne trematodiasis</td>
<td>Estimation completed, manuscript in progress</td>
</tr>
<tr>
<td>Global burden of cystic echinococcosis</td>
<td>Estimation completed, manuscript in progress</td>
</tr>
<tr>
<td>Systematic review on neurocysticercosis</td>
<td>Review completed, burden estimation in progress</td>
</tr>
<tr>
<td>Systematic review on trichinellosis</td>
<td>Review completed, burden estimation to be commissioned</td>
</tr>
<tr>
<td>Systematic review on anisakiasis</td>
<td>Review completed, burden estimation to be commissioned</td>
</tr>
<tr>
<td>Systematic review on toxoplasmosis</td>
<td>Review in progress</td>
</tr>
<tr>
<td>Systematic review on intestinal protozoa</td>
<td>Review in progress</td>
</tr>
<tr>
<td>Systematic review on ascariasis</td>
<td>Review in progress</td>
</tr>
<tr>
<td>Systematic review on angiostrongyliasis</td>
<td>Future commissioning</td>
</tr>
<tr>
<td>Systematic review on capillariasis</td>
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</tr>
<tr>
<td>Systematic review on toxocariasis</td>
<td>Future commissioning</td>
</tr>
<tr>
<td>Systematic review on trichuriasis</td>
<td>Future commissioning</td>
</tr>
</tbody>
</table>

**Table 4:**
Summary of PDTF activities and progress

The following sub-sections summarize the PDTF sessions on the commissioned systematic reviews on foodborne trematodiasis, cystic echinococcosis, neurocysticercosis, trichinellosis, anisakiasis, intestinal protozoa, and toxoplasmosis. The PDTF section is concluded by presenting the endorsed work plan for the coming year.

### 4.4.2 Global burden of foodborne trematodiasis

**Background**

Foodborne trematodiasis (FBT) is defined as a human infection caused by parasitic trematodes, which are predominantly transmitted via food. Thus far, over 80 different trematode species have been identified as causative agents for FBT in humans. From a public health point of view, *Clonorchis sinensis*, *Opisthorchis* spp., *Fasciola* spp., *Paragonimus* spp. and *Echinostoma* spp. are the most significant species (Keiser et al., 2009; Sripa et al., 2010). It is noteworthy that new species are still being discovered and considerable uncertainty remains about taxonomy.

Foodborne trematodes have a distinct and complex life cycle, which begins with the excretion of eggs via the feces by the definitive human and animal hosts. Outside the
definitive host, the parasites undergo different development stages with snails as first intermediate hosts and mainly aquatic animals (freshwater fish, crabs, mussels) or aquatic plants (e.g., water cress) as second intermediate hosts. When humans eat raw or undercooked aquatic products (fish, crabs, mussels and water plants) they become infected (Keiser et al., 2009; Sripa et al., 2010).

FBT is among the most neglected of the neglected tropical diseases and its occurrence tends to be focal. The natural history depends on the infective species, infection intensity, duration and host susceptibility. In the human body, the parasites either stay in the intestines or migrate to the liver or lung, where they mate and reproduce. Based on their location in the human body, the foodborne trematodes are also known as intestinal, liver and lung flukes. Pathological changes due to FBT range from light tissue irritation and inflammation to abscess formation, ectopic infections and cholangiocarcinoma (Keiser et al., 2009; Sripa et al., 2010). Consequentially, the signs and symptoms are also diffuse and range from completely asymptomatic cases to severe abdominal or chest pain, convulsions and even death.

Global burden of FBT
A computer-aided literature review on 11 different databases was performed in order to obtain useful information for the estimation of the global burden of FBT. However, only 0.5% of almost 34,000 initial references contained relevant quantitative data. Three different simplified disease models for intestinal, liver and lung flukes were established based on qualitative information about the natural history of the disease, but also largely driven by the availability of quantitative data. Preliminary global results for the year 2005 indicate that more than 50 million people were infected with foodborne trematodes, about 9 million of them experienced severe signs and symptoms and 10,000 died. Previous estimates put forth by the WHO for the year 1995 reported 42 million infected and 10,000 cases of death (WHO, 1995).

By now, the expert group has almost finished data analysis and in a next step results will undergo internal review. A manuscript for the peer-reviewed literature is in preparation. Problems encountered thus far are mainly related to very scattered and limited data. Better quantitative data on the natural history of FBT would help to further improve the simplified disease models and to include additional morbid sequelae for more accurate burden calculations. Furthermore, only country-wide prevalence estimates could be used to estimate total national numbers of infections due to the focal nature of FBT. However, such country-wide prevalence estimates exist only for a limited list of countries and many countries with known human cases are therefore illegitimately ignored. One solution to overcome this deficit would be to define a set of environmental, socioeconomic and dietary covariates in countries with national prevalence estimates and use these covariates as predictors for countries with missing national prevalence data. However, the study sample of countries with complete data is most likely too small to elicit any meaningful predictors. New methodological approaches to deal with focality such as spatial modeling using geographical information systems, remote sensing and Bayesian
statistics would be another, more sophisticated solution. Unfortunately, these methods may also not be applicable in most countries as even sufficient localized cross-sectional studies to feed into such models are not available.

*In the plenary discussions, it was added that purging studies could clarify the attribution of the various species to the burden of FBT, as the morphology of the eggs does not always allow a clear species distinction. Furthermore, it was recommended that the question of source attribution for FBT should be dealt with in collaboration with the SATF.*

### 4.4.3 Global burden of cystic echinococcosis (CE)

**Background**

The objective of this work was to conduct systematic reviews of studies reporting the frequency of cystic echinococcosis (CE) worldwide as well as the distribution of clinical manifestations associated with CE.

**Procedures**

A systematic search was conducted in PubMed, Commonwealth Agricultural Bureau (CAB) Abstracts, and 22 international databases for literature related to CE frequency and clinical manifestations. Articles published from January 1, 1990 to June 1, 2008 were considered. Official surveillance data were also reviewed where available. Results from individual studies providing an overall prevalence or incidence rate of CE were reported. In addition, the distribution of clinical manifestations was reported for eligible studies. Meta-analyses were run where appropriate.

**Results**

Prevalence of CE was available from community-based abdominal ultrasound studies conducted in 14 countries, with estimates ranging from less than 1% to 7.5% in highly endemic communities. Surgical incidence was available from studies conducted in 14 countries, with official government data reported for a number of additional countries. Hepatic lesions were found in 66% (95% CI: 56%-75%) of CE patients treated in hospitals, with 30% (95% CI: 16%-45%) of patients having pulmonary lesions. An estimated 58% (95% CI: 53%-61%) of hepatic CE cases detected in community studies were female, with hospital-based findings in agreement with this estimate. Age breakdowns, from community studies, are available for use along with country-specific age distributions to determine the number of CE cases per age category for individual countries. Reported post-surgical morbidity ranged from 10%-25%, with post-surgical mortality ranging from 1%-5%. Abdominal pain, fever, jaundice, nausea/vomiting and weight loss were the most commonly reported manifestations of hepatic CE and cough, chest pain, fever, hemoptysis, and dyspnea the most commonly reported clinical manifestations associated with pulmonary CE.

**Discussion**

The quality of data available to estimate the frequency of CE worldwide is variable, with
data gaps clearly evident in parts of Africa and Asia. Estimates from hospital-based data are likely to be biased due to a lack of valid denominators. Officially reported data are likely to be gross underestimates of the truth. While some data does exist for manifestations associated with clinical CE, information on the duration of manifestations is limited.

During the plenary discussion, the question was raised whether DALYs should be calculated only for the severe (hospitalized) cases, or for the non-surgical pathway as well, using the data from community-based studies. However, as not all CE cases progress to the severe state, DALYs from non-severe community cases might not add greatly to the overall burden of CE.

In addition, the plenary group suggested to make a pre-assessment of the potential burden of CE associated with manifestations in organs other than the liver and the lungs. This contribution will depend on the proportions of these manifestations (which are considered to be low) and the associated symptoms.

4.4.4 Global burden of neurocysticercosis (NCC)

Background
The objective of this work was to conduct systematic reviews of studies reporting the frequency of neurocysticercosis (NCC) worldwide as well as the distribution of neurological manifestation among cases of NCC who seek medical care.

**Procedures**
PubMed, Commonwealth Agricultural Bureau (CAB) Abstracts and 23 international databases were systematically searched for articles published from January 1, 1990 to June 1, 2008. Articles were evaluated for inclusion by at least two researchers focusing on study design and methods. Data were extracted independently using standardized forms. A random-effects binomial model was used to estimate the proportion of NCC among people with epilepsy (PWE) as well as to evaluate the distributions of manifestations among NCC cases seeking care where more than two articles were eligible for a specific manifestation.

**Results**
The prevalence of NCC in a random sample of village residents was reported from one study where 9.1% of the population harbored brain lesions of NCC. The proportion of NCC among different study populations varied widely. However, the proportion of NCC among PWE in endemic areas was more consistent. The pooled estimate for this population was 29.0% (95% CI: 22.9%-35.5%). These results were not sensitive to the inclusion or exclusion of any particular study. People diagnosed with NCC presented in neurological clinics with a wide range of clinical manifestations. In all age groups, seizures and epilepsy were the predominant manifestations (78.8%, 95% CI: 65.1%-89.7%) followed by severe headaches (37.9%, 95% CI: 23.3%-53.7%), with focal deficits (16.0%, 95% CI: 9.7%-23.6%) and signs of increased intracranial pressure (11.7%,
95% CI 6.0%-18.9%) also being common.

**Discussion**

Only one study has estimated the prevalence of NCC in a random sample of residents. Hence, the prevalence of NCC worldwide remains unknown. However, the pooled estimate for the proportion of NCC among PWE was very robust and could be used, in conjunction with estimates of the prevalence and incidence of epilepsy, to estimate this component of the burden of NCC in endemic areas. The previously recommended guidelines for the diagnostic process and for declaring NCC an international reportable disease would improve knowledge on the global frequency of NCC. More than three-quarters of symptomatic NCC patients seeking medical care had seizures or epilepsy, with other manifestations less frequent. There is a need for standardization in definition and reporting of NCC-associated manifestations.

*In order to come to an assessment of the global burden of NCC, the FERG will collaborate with the WHO Mental Health Unit, who will provide data on the global burden of epilepsy in *Taenia solium*-endemic countries. By combining these data with the here presented proportion of NCC-associated epilepsy, the global burden of NCC can be assessed.*

As severe headaches appear to be present in over one third of the people diagnosed with NCC, this outcome might have a significant contribution to the overall burden of NCC. Therefore, the plenary group recommended to make a pre-assessment of the contribution of this and other sequelae to the burden of NCC. The PDTF will then decide whether or not other sequelae have to be included in the final estimates.

**4.4.5 Global burden of trichinellosis**

**Background**

Trichinellosis is a zoonotic disease caused by nematodes belonging to the genus *Trichinella*. The genus is composed of eight species (all of which are meatborne), and are distributed world-wide. The parasites have been documented in 55 countries. Gastroenteritis, myalgia, malaise, facial edema, headache, subungual or conjunctival hemorrhages, and an increase in eosinophils are the clinical hallmarks of trichinellosis.

**Procedures**

A systematic review of the literature on trichinellosis was conducted to estimate the morbidity (including sequelae) and mortality resulting from human infection with *Trichinella* spp. by age and sex for all regions of the world, and to identify the animal hosts (source of infected meat) implicated in each region of the world. The literature retrieved from searches was screened by the FERG draft systematic review protocol, and this resulted in selecting 289 reports from which the database was constructed.

**Incidence and prevalence**

Globally, from 1986-2009, there have been about 62,000 cases reported world-wide.
However, reliable estimates of prevalence in countries were either not conducted or available if performed. The EURO Region reported 83% of all cases, followed by the AMRO with 13% and the SEARO and WPRO accounted for 3%; few cases occurred in the AFRO and EMRO regions. Overall, the incidence is low in developing countries, and usually outbreak-associated. In developed countries, trichinellosis is increasingly associated with the consumption of game and exotic meat. From a third to half of all cases world-wide have occurred in the former Soviet Union states during the 1990s, probably the result of a temporary breakdown in food safety infrastructure during a period of profound political and social change. For example, Romania accounts for nearly one-half of the total cases (28,293).

**Gender and age**
For gender, 51% occurred in males. Overall, the highest proportion of cases, for both genders, was in the 20-50 year class, with a median of 33.1 years of age. Age-specific incidence data, however, were very limited.

**Disease duration and sequelae**
The chief clinical symptoms of trichinellosis, based on 5069 cases with adequate data was myalgia (68%), diarrhea (24%), fever (52%), facial/ocular edema (54%), headaches (17%) and eosinophilia (54%); these are usually resolved within 2-4 weeks after treatment. A total of 43 deaths occurred world-wide during the period. Sequelae assessment is somewhat compromised by an overwhelming lack of follow-up data on former patients; in the few studies that do report on follow-up examinations or the monitoring of patients post-treatment, prolonged symptoms such as myalgia and malaise occur frequently.

**Sources of infection**
Of 40 countries with outbreak source data, 23 (58%) reported pork as the only or chief source of infection. However, 17 countries (42%) reported wild game or non-pork domestic animal meat (e.g., wild boar, horse, dog) as major sources.

**Discussion**
Human behavior is the biggest determinant in the persistence of trichinellosis in the face of increasing regulations directed at ensuring the safety of meat and at the enhancement of Good Management Practices in farming, especially in highly endemic areas. As with other foodborne zoonoses, cultural traditions in food behaviors, and in the use of domestic and wild animals, are not easily altered and it can be expected that trichinellosis will remain a public health concern in many areas of the world for the foreseeable future.

In the plenary discussion, a question was raised whether or not serological data could be used in the burden assessment of trichinellosis. Although serology can be very useful for other pathogens, such as hepatitis viruses, seroprevalence studies should be reviewed with caution. Trichinella spp. share various antigens with other nematodes, giving rise to many cross-reactions, especially in developing countries. It is therefore recommended...
to separate the seroprevalence data from the outbreak reports. However, seroprevalence studies can be useful to estimate the level of underestimation, since outbreak data alone probably underestimate the true burden. This comparison can then be used to express the level of uncertainty of the disease burden data.

The FERG was pleased with the outputs of this systematic review, and considered that it had identified sufficient data for a DALY estimation.

4.4.6 Global burden of anisakiasis

Background
This systematic review aimed at summarizing the English literature on the burden of anisakiasis in terms of:

1. The incidence and prevalence of Anisakis infections;
2. The health effects resulting from these infections; and
3. The species of sea fish involved.

 Procedures
Relevant literature was systematically searched for in leading databases, including PubMed and Scopus. Based on several inclusion and exclusion criteria, articles were assessed, resulting in the final inclusion of 25 articles. Of these articles, 18 presented data from the EURO region, four from the WPRO region, two from the PAHO region and one from the AFRO region.

Results
Although little information on incidence and prevalence rates was available, health effects of Anisakis infections were reported frequently. Commonly found symptoms were nausea and vomiting for gastric or enteric anisakiasis, urticaria and epigastralgia for gastroallergic anisakiasis and cough and pharyngeal tickling or pain for cases of pseudoterranovosis. In patients with allergic anisakiasis, only urticaria, angioedema and anaphylaxis were described. The species of sea fish that most often constituted the source of infection were anchovies in the EURO, mackerel in the WPRO and hake in the PAHO region. Furthermore, rates of sensitization to Anisakis were described in the literature, with prevalence rates ranging between 0.43% to 27.0% in different regions. Last, several associations between anisakiasis or Anisakis sensitization and other diseases/sensitizations have been reported.

Discussion
Although this systematic review does not allow the estimation of incidence or prevalence rates of Anisakis infections, the information on symptoms, species of sea fishes involved and prevalence of sensitization to Anisakis can contribute to estimations of the burden of disease.

In order to complement the currently collected data, it was agreed to include non-English
literature in the systematic review. Based on this updated systematic review, the PDTF will then assess whether the global burden of disease due to anisakiasis can be estimated, and will proceed to commission another scientist with the DALY calculation if this appears to be possible.

4.4.7 Update on intestinal protozoa

Introduction
A systematic literature review was conducted to estimate the global burden of illness due to *Entamoeba histolytica*, *Giardia lamblia* and *Cryptosporidium* spp. by age and sex for all countries and WHO regions, and to assess the proportion of those infections transmitted by food.

Procedures
PubMed, CAB Abstracts, SIGLE, OVID EMBASE, and other electronic databases and sources were searched. Search terms included: Morbidity, Mortality, Incidence, Prevalence, Epidemiology, Sequela, Food, Mode of Transmission, Transmission, Outbreak, *Entamoeba histolytica*, Amoebiasis, Giardia, Giardiasis, Cryptosporidium, and Cryptosporidiosis. References from studies reviewed in full were searched to identify any other potentially relevant studies. Descriptive statistics were calculated.

Results
10,327 studies were retrieved using the search terms listed above. Of those, 3,547 (34.3%) were reviewed in full and 487 (4.7%) were included in the analysis. The vast majority of published information retrieved came from cross-sectional (prevalence) studies (N=366; 75.6%); few long-term follow-up or country-level studies were found. Twenty-five (5.1%) of the included studies linked food with protozoal infection. The highest burden of these parasitic diseases appears to be in the Americas and *Giardia* is the most important of the three parasites studied in terms of prevalence (median=10%, mean=12.7%; *Cryptosporidium*: median=4.3%, mean=10.5%; *Entamoeba*: median=4.1%, mean=9.1%). Children between 5-14 years of age had the highest median burden of *Entamoeba* (8.3%), while children between 1-4 years had the highest median burden of Giardia (18.1%). The highest median prevalence of *Cryptosporidium*, 3.8%, was found in adults over 18 years of age.

Discussion
The results of this study should provide insight into the scope and quality of the available published literature describing the burden of disease due to *Giardia*, *Entamoeba*, and *Cryptosporidium*; however, the studies found were highly heterogeneous with regard to the populations studied as well as the sampling and diagnostic methods employed. The estimates presented here should therefore be interpreted with caution, and it may not be appropriate to generalize results from individual studies to broader populations.

The FERG recommended to compare the presented estimates for giardiasis and cryp-
tosporidiosis with the CHERG and Walker estimates. Applying the same strict inclusion criteria as the CHERG and Walker studies might reduce the heterogeneity in the current estimates.

In order to come to the global burden of intestinal protozoa, additional data is required. The plenary group formulated the following recommendations:

- Provide data on other health outcomes than diarrhea, such as liver abscesses due to E. histolytica and malnutrition associated with cryptosporidiosis;
- Generate incidence estimates based on the available data, e.g., through random effects meta-analysis or meta-regression;
- In order to interpret the data in terms of FERG, source attribution data for intestinal protozoa would be requisite, which can be provided by the SATF.

Finally, to reduce potential bias in the results, the FERG members recommended to incorporate the following three points in the further work:

- As microscopic diagnosis cannot distinguish the pathogenic E. histolytica from the non-pathogenic Entamoeba dispar, the ratio histolytica:dispar should be assessed and taken in account;
- A distinction should be made between symptomatic infection and asymptomatic secretion. Especially in the case of Giardia, a high exposure does not necessarily mean a high burden;
- As a final point, the possible overestimation of incidence and prevalence due to mixed infections should be considered.

4.4.8 Update on toxoplasmosis

Introduction

A systematic review has been completed to find the best country estimate of toxoplasmosis IgG seropositivity in women of childbearing age or in pregnancy. Data was searched across all WHO regions and all countries. This data will be used to estimate the incidence of congenital toxoplasmosis. Reviews with regard to other sequelae of toxoplasmosis are planned, as well as reviews examining the proportion of these sequelae that are the result of ingestion of unsafe food.

Procedures

Literature was searched in PubMed, Embase, Google Scholar, Scopus, SciELO MyAIS, Science Links Japan, Index Medicus for South-East Asian Region, Free Medical Journals, Asia Journals on Line, African Journals on Line, African Medical Journals (WHO Regional Office for Africa), Eastern Mediterranean Region Journal Information Directory (WHO Regional Office for the Eastern Mediterranean), and in the references of each paper identified. The most relevant studies were identified for each country (WHO list = 193) or large area within a country.
Results
A total of 430 full texts were evaluated. Of these the data was extracted from 188 and entered into an Excel spread sheet. From this data 53 unique selected papers from 53 countries were entered. Also, a further 90 multiple selected papers in 21 countries were used. There were an additional 45 papers which were not used to make the best estimates. In total best estimates of prevalence of women of child bearing age are available in 74 countries.

Toxoplasmosis is a well-known problem in HIV patients. However, other sequelae are being increasingly reported. A preliminary search for other sequelae associated with non-congenitally acquired toxoplasmosis suggests an etiological link with retinal lesions, epilepsy, schizophrenia, Parkinson's disease, and migraine.

The limited literature so far examined indicates foodborne infection is responsible for 40-60% of toxoplasmosis.

Discussion
These data will be used to make estimates of the incidence of congenital toxoplasmosis. The changes in prevalence with age can indicate the risk of seroconverting during pregnancy. Other modeling techniques will also be used to estimate the incidence of congenital toxoplasmosis. This data can also assist in estimating the incidence of seroconversion in the rest of the population which may give an indication of the incidence of other toxoplasmosis-associated sequelae.

During the subsequent plenary discussion, it was remarked that seroprevalence time trends were not taken in account. Indeed the best available data for recent times were used, but sometimes only one study was available.

With regards to comorbidity, cerebral toxoplasmosis in HIV patients is viewed as a HIV comorbidity, and should therefore be taken in account in HIV burden assessment. Comorbidity could be calculated by comparing the severity of disease with and without HIV.

Finally, it was suggested that a meta-analysis of case-control studies, assessing various risk factors, could be performed to obtain estimates on the foodborne exposure. It would be possible to estimate the proportion foodborne, but difficult to attribute to various food sources. Toxoplasmosis is a chronic disease with many source pathways, and risk factors may differ between countries.
4.4.9 Parasitic Diseases Task Force work plan for 2010–2011

The 2010–2011 work plan for the PDTF is summarized in Table 5.
<table>
<thead>
<tr>
<th>Causative agents and priority activities</th>
<th>Specific associated activities</th>
<th>Timeframe</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trichinella spp.</strong></td>
<td>Define parameters required for calculation of DALYs and calculate global DALYs lost due to trichinellosis based on data from systematic review</td>
<td>End May 2011</td>
</tr>
<tr>
<td><strong>Anisakis simplex</strong></td>
<td>1. Assess data presented in the systematic review for suitability to estimate the global burden of disease due to anisakiasis 2. If sufficient data is available, define parameters for DALY estimation and calculate global DALYs lost due to anisakiasis</td>
<td>End May 2011</td>
</tr>
<tr>
<td><strong>Toxoplasma gondii</strong></td>
<td>1. Provide a comprehensive, multilingual, review (and appraisal) of the literature on the prevalence and incidence of toxoplasmosis 2. Provide a comprehensive, multilingual, review (and appraisal) of the literature on the health effects of toxoplasmosis 3. Provide a comprehensive, multilingual, review (and appraisal) of the literature on comorbidity associated with toxoplasmosis 4. Provide a comprehensive, multilingual, review (and appraisal) of the literature on the transmission of toxoplasmosis through food</td>
<td>November 2011</td>
</tr>
<tr>
<td><strong>Ascaris spp.</strong></td>
<td>1. Provide a comprehensive, multilingual, systematic review (and appraisal) of the literature on the proportion of ascariasis acquired through food 2. Provide a comprehensive, multilingual, review (and appraisal) of the literature on comorbidity associated with ascariasis</td>
<td>End of May 2011</td>
</tr>
<tr>
<td><strong>Intestinal protozoa</strong></td>
<td>1. Provide a comprehensive, multilingual, systematic review (and appraisal) of the literature on the prevalence and incidence of intestinal protozoa 2. Provide a comprehensive, multilingual, systematic review (and appraisal) of the literature on the health effects of intestinal protozoa</td>
<td>End of May 2011</td>
</tr>
<tr>
<td><strong>Taenia solium</strong></td>
<td>Estimate global burden of neurocysticercosis-induced epilepsy (in collaboration with WHO Mental Health Unit)</td>
<td>End of May 2011</td>
</tr>
<tr>
<td><strong>Angiostrongylus spp.</strong></td>
<td>Commission systematic review of incidence, prevalence, and health effects of infection</td>
<td>To be decided</td>
</tr>
<tr>
<td><strong>Capillaria philippinensis</strong></td>
<td>Commission systematic review of incidence, prevalence, and health effects of infection</td>
<td>To be decided</td>
</tr>
<tr>
<td><strong>Toxocara spp.</strong></td>
<td>Commission systematic review of incidence, prevalence, and health effects of infection</td>
<td>To be decided</td>
</tr>
<tr>
<td><strong>Trichuris spp.</strong></td>
<td>Commission systematic review of incidence, prevalence, and health effects of infection</td>
<td>To be decided</td>
</tr>
<tr>
<td><strong>CSTF interface</strong></td>
<td>Report to the CSTF on outcome of discussions and proposed amendments to the “Appendix 3”-spreadsheet</td>
<td>December 2010</td>
</tr>
<tr>
<td><strong>SATF interface</strong></td>
<td>Report to the SATF on outcome of discussions and proposed amendments to the SA matrix and the terms of reference and priorities for expert elicitation</td>
<td>December 2010</td>
</tr>
</tbody>
</table>

**Table 5:**

PDTF work plan for 2010–2011
4.5 Chemicals and Toxins Task Force (CTTF)

4.5.1 Progress to date and issues arising

In addition to the ongoing commissioned work, the CTTF discussed during FERG 4 the commissioning of new systematic reviews:

1. The TF reached consensus on including inorganic arsenic in its burden of disease estimates. Inorganic arsenic is found in rice, which is consumed by a large percentage of the world’s population. An increased risk of cancer and diabetes has been associated with arsenic in drinking water in Bangladesh and India. The Joint FAO/WHO Expert Committee on Food Additives (JECFA) did an assessment of arsenic in February 2010, and there are credible and specific data for inorganic arsenic in food, especially rice. Dose-response relationships that have been developed for arsenic in drinking water could lead to a burden of disease estimate for food. However, as most dose-response data still come from such studies, more work needs to be done to assess how much exposure occurs through food consumption and particularly rice consumption.

2. Methylmercury is a second chemical agent that will be considered for burden of disease estimation. Good dose-response and exposure data exist, particularly in the JECFA assessments.

3. Organophosphates will be reviewed for consideration as a priority chemical. A systematic review needs to be performed to identify the use of organophosphates in different countries, to identify acute poisoning from misuse on food, and to identify the acute and chronic health effects from organophosphate exposure.

4. The CTTF opined that measuring the burden of disease from adulterants in food could be difficult. Antibiotics are routinely being used in China, but no evidence exists that antibiotics in food are linked to a disease outcome. Furthermore, the amount of antibiotics in food ingested by humans is unknown. The recent problem with melamine in infant formula should be considered as episodic. Adulterants may be too unpredictable to work with, particularly if there is little existing health information on the adulterant. An argument to include antibiotics is that there is evidence that they are often used quite heavily, especially in the developing world. Pharmaceutical pollutants (e.g., oral contraceptives) sometimes end up in waterways used for drinking water. Although some thought this was primarily a drinking water issue, such water might be used for food processing and irrigation, and the adulterants may end up in the food supply. While it may be difficult to estimate the burden of disease from adulterants, it may be worth providing a discussion piece on the issue.

In addition to discussing the systematic reviews, the group discussed membership recruiting for the TF. It is preferable to recruit an expert from South East Asia or China who is proficient in speaking and writing English. With regards to the pilot country studies,
the Centers for Disease Control and Prevention offered to analyze samples of blood and urine. The group engaged in a brainstorming session to match appropriate contaminants to be studied in the chosen countries. The need to contribute to the country studies guidance document was also stressed.

The progress of the CTTF priority activities is summarized in Table 6.

<table>
<thead>
<tr>
<th>Activity</th>
<th>Status</th>
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</thead>
<tbody>
<tr>
<td>Global burden of disease from aflatoxin ingestion</td>
<td>Incidence estimation completed, manuscript in progress</td>
</tr>
<tr>
<td>Global burden of disease from cassava (cyanide) ingestion</td>
<td>Incidence estimation completed, manuscript in progress</td>
</tr>
<tr>
<td>Global burden of disease from peanut allergens</td>
<td>Incidence estimation completed, manuscript in progress</td>
</tr>
<tr>
<td>Global burden of disease from dioxin and dioxin-like PCB ingestion</td>
<td>Review completed, incidence estimation in progress</td>
</tr>
<tr>
<td>Global burden of disease from lead ingestion</td>
<td>Review in progress</td>
</tr>
<tr>
<td>Global burden of disease from cadmium ingestion</td>
<td>Review in progress</td>
</tr>
<tr>
<td>Global burden of disease from arsenic ingestion</td>
<td>Future commissioning</td>
</tr>
<tr>
<td>Review of the potential for estimating a global burden of disease from organophosphate ingestion</td>
<td>Future commissioning</td>
</tr>
<tr>
<td>Global burden of disease from methylmercury ingestion</td>
<td>Future commissioning</td>
</tr>
</tbody>
</table>

**Table 6:** Summary of CTTF activities and progress

The following sub-sections summarize the results arising from the commissioned systematic reviews on aflatoxins, cassava cyanide, cadmium, lead, and dioxins and dioxin-like compounds. The CTTF section is concluded by presenting the endorsed work plan for the coming year.

**4.5.2 Global burden of disease from aflatoxins**

Aflatoxins are mycotoxins produced mainly by *Aspergillus flavus* and *Aspergillus parasiticus*. Aflatoxins can occur on a variety of food and feed crops, but levels are highest on maize and peanuts. Other sources include cereals (sorghum and millet, less commonly rice, and rarely wheat), tree nuts (almonds, pistachios, and hazelnuts), figs and spices. Exposures are highest where maize is a dietary staple, especially in developing countries where monitoring and control are often poor.

Aflatoxin is a potent human liver carcinogen and is synergistic with chronic hepatitis B virus (HBV) infection, a combination that increases the risk of hepatocellular carcinoma (HCC) by a factor of about 30x. Aflatoxin has also been associated with acute toxicity, stunted growth in children, liver cirrhosis, and immune system disorders.

An influence diagram was presented linking aflatoxin exposure in foods with various
health effects by strength of association, determined by application of the Bradford Hill criteria. As a result, the report focuses on evaluating the global burden of aflatoxin-induced HCC, the age distribution of aflatoxin-induced HCC, and a preliminary estimate of stunting in children in selected African countries associated with aflatoxin.

It is estimated that, globally, between 25,200 and 155,000 liver cancer cases per year are induced by aflatoxin. This represents about 5 to 30% of all liver cancer cases of all etiologies. Most of these cases occur in three WHO regions: Africa, Southeast Asia, and the Western Pacific Region (primarily in China). The age distribution of aflatoxin-induced liver cancer cases was determined by using a study by Kensler et al. (2003), which estimated HCC age distribution in two Chinese populations where risk factors for liver cancer except aflatoxin exposure were similar: Qidong, where the population has very high aflatoxin exposure and Beijing, where aflatoxin exposure is low. The difference in age distribution of HCC in these two populations was taken to be the amount that could be attributed to aflatoxin. It was found that aflatoxin-induced HCC appears to peak between the ages of 40 and 54, whereas in HCC cases in general, the peak is at older ages. This implies that aflatoxin causes liver cancer earlier in life than other risk factors. Potential problems in extrapolating this result from China to the rest of the world include the possibilities of genetic and dietary differences, and the age distribution of HBV.

Based on a dose-response curve linking aflatoxin exposure with stunted growth in children in Togo and Benin, aflatoxin-associated stunting was estimated in ten selected African nations with socioeconomic factors similar to those in Togo and Benin. It was estimated that in Benin from 470,000 to 544,000 stunting cases in children age 5 and under could be associated with aflatoxin intake, and in Togo the figures were from 298,000 to 322,000 cases. This indicated that it was worth noting that even within a relatively small population the number of aflatoxin associated stunting cases appears to be greater than the total global burden of aflatoxin-induced HCC.

The issue about the mechanism of the association of aflatoxin and stunting was discussed. As aflatoxin is just one of many causes of stunting, the group was interested in evidence that evaluated the association of aflatoxin exposure with stunting while addressing potential confounders (e.g., poor nutritional status).

The presenter mentioned four outbreaks of acute aflatoxicosis since 1974. In one outbreak in Kenya, concentration levels of aflatoxin in maize flour were found to be highly variable. Animal studies indicate that aflatoxin causes reduced weight gain, and it is likely that the effects in humans could be similar; however animal feed may have much higher levels of aflatoxin.

It is difficult for farmers to remove aflatoxin. Temporal variability in the concentration of aflatoxin in food is another caveat to determining BoD. There is still insufficient data on aflatoxin levels ingested from subsistence farming, as the data from developing economies are often from commodity lots sampled for export to developed countries.
It was suggested that the country studies use expert opinion on what models are appropriate, trying out different models to retrieve data and compare for best fit. The WHO Secretariat encouraged papers to be submitted and published under the WHO umbrella. DALYs are not required; it is a quite complex process if all the inputs are not available.

4.5.3 Global burden of disease from cassava cyanide

Cassava is the staple food for over 750 million people and its cultivation is increasing worldwide. Cyanide is produced in the roots of bitter cassava, which contain high concentrations of cyanogenic glycosides that also protect the plant from predation. This presentation reported progress on the development of incidence and/or prevalence estimates for (1) acute cyanide intoxication, and (2) konzo, the disabling neurological disorder characterized by spastic paraparesis. Both are associated with ingestion of cassava with a high cyanogenic glycoside content.

The epidemiology of acute cyanide poisoning from cassava is variable. First, sporadic accidental poisoning has been reported from South East Asia, Oceania, Central Latin America and Sub-Saharan Africa. Second, epidemics during drought and/or in association with konzo epidemics have been reported from Mozambique and Tanzania. Third, acute intoxication is reported to be frequent in some of the poorest cassava-consuming areas in Africa, in the Democratic Republic of Congo (DRC) (South Kivu), Ethiopia, Malawi, Mozambique, and Tanzania. The case fatality rate is low, except in sporadic accidents. There are no sequelae. It is unlikely that sufficient data exist to include acute cyanide poisoning in burden of disease estimates.

Konzo has only been reported from Sub-Saharan Africa. It was first reported from the DRC in 1938. Since 1975, konzo has been reported from the DRC (2222 cases), Mozambique (2404), Tanzania (359), Cameroon (469) and the Central African Republic (CAR; 97). The estimated annual incidence rate in konzo-affected areas is 0.6/1000, in a population at risk estimated at 2,500,000. Incidence is highest in children over two years old of both sexes, and women of reproductive age. The spastic paraparesis of konzo is a permanent sequela. The other disabling sequela is loss of vision, but recovery occurs in most cases. Case fatality rates are high in severe cases and elevated compared to case fatality rates for mild and moderate cases.

Changes in prevalence and/or incidence estimates may happen with time as cassava consumption increases, and climate change results in more droughts. Underlying causes which may change with time include: poverty, nutritional status, wars and displacement. Knowledge gaps include the incidence of acute poisoning and the prevalence of konzo.

The report used previous work from Dr Oluwole, searched the PubMed database for peer reviewed literature, consulted the reports of two international workshops on cassava, and an expert network, the Cassava Cyanide Disease Network. A total of 586 references were used and covered all of the literature.
Acute cyanide poisoning can start a few hours after ingestion. Symptoms include nausea, vomiting, dizziness, weakness, headache, abdominal pain, diarrhea and occasional death. Although cases of acute cyanide poisoning from cassava are sometimes reported in both the medical and grey literature, it is difficult to obtain incidence data because consuming bitter cassava is usually the result of sporadic accidents, mostly in children, and especially during droughts. Incidence often goes unreported because cases mostly occur in the poorest areas of Africa.

Community studies in Mozambique and Tanzania have shown that mean urinary thiocyanate concentrations are high in these populations often with seasonal variation, confirming that cyanide intoxication is occurring. Cyanide exposure can aggravate Iodine Deficiency Disorder (IDD). In one IDD study in Ethiopia, a high rate of goitre and acute cyanide intoxication was attributed to the frequency of cassava consumption. Knowledge gaps include the extent of cassava-induced acute poisoning, and the impact of chronic cyanide intoxication.

It is estimated that 2 to 4 million of the African population are affected by konzo. A lot of assumptions were made to produce this figure. Tylleskar (1994) estimated that it affected <1% of the total cassava eating population, currently estimated at >250 million in Africa. Reported cases are likely to be largely underestimated, as konzo occurs in remote rural areas, and epidemics occur at times of crisis.

Data on both prevalence and incidence rates are lacking. The data available often come from reports of epidemics, with inconsistent reporting. It is possible that this problem of underreporting might be helped by the application of multipliers. Diseases like trypanosomiasis are also underreported, perhaps by 10-fold, and also occur in remote rural areas in Africa, and this may serve as a way to estimate incidence. However the CTTF considered this argument weak: stronger lines of evidence were that Tylleskar (1994) indicated that the numbers of cases were underreported by at least half, and the presenter’s own investigation of case clusters found considerably more cases than first believed.

Quantifying deaths from konzo may be difficult. Few studies give case fatality rates, and they are difficult to carry out, owing to the location of konzo cases in remote poor rural areas. Two studies in the DRC gave case fatality rates of 17.9% (Tylleskar et al., 1991) and 27.1% (Banea et al., 1992). The small amount of data available suggests a higher case fatality rate in women than children. However, the experts group agreed that whatever information is available, should be stated, particularly to the stakeholders. Such information will also help to better describe the uncertainty around the estimates.

A final issue for the CTTF is that WHO has not provided disability weights for the diseases induced by cyanide in cassava. Assumptions used for other disabling neurological disorders in Africa such as poliomyelitis could be used to calculate disability weights and perhaps estimate case fatality. However, in this case, it will be important to describe the disease well.
4.5.4 Global burden of disease from cadmium

To estimate the global burden of disease from foodborne illness due to cadmium (Cd), it is desirable to have age-specific rates of disease(s) associated with dietary Cd exposure for all countries throughout the world. In lieu of the ideal situation, estimates of the dose-response and exposure associated with dietary Cd will be used to make estimates of disease incidence. Cadmium is known to produce a wide range of adverse effects, including, cancer, cardiovascular diseases, disorders of bone metabolism and renal dysfunction – which is deemed to be the most sensitive response.

Cadmium contamination of food is ubiquitous and occurs as a result of emissions from natural and anthropogenic sources. It is present in a wide variety of foods, with cereal and grains (particularly rice), nuts, pulses, and vegetables being important sources of exposure. The incidence assessment work will make use of the assessment conducted by JECFA at its 73rd meeting. Key issues will be identified and include (1) the critical health endpoints that would be suitable for a global burden of disease analysis, and (2) the dose-response relationships for these endpoints. Combining these data with dietary exposure estimates by WHO region, estimates of cadmium-associated disease incidence by region will be derived. Age-specific estimates of disease sequelae as well as case fatality rates for diseases should be attempted where possible.

JECFA reevaluated cadmium at its 73rd meeting. The Committee had been asked by the Codex Committee on Contaminants in Food to provide an opinion on whether recent data support the Provisional Tolerable Weekly Intake (PTWI) of 7 µg/kg body weight of Cd, established in 2000.

National exposure estimates are based on 1 to 7 day food consumption surveys. These were supplied to JECFA by the European Food Safety Authority (EFSA), Australia, Japan, China and the USA. For adults, mean dietary exposure ranged from 2.2 to 12.0 µg/kg Body Weight (BW) per month. For children, mean dietary exposures ranged from 3.9 to 20.6 µg/kg BW per month. For vegetarians, EFSA reported a dietary exposure estimated to average 23.2 µg/kg BW per month.

The kidney is the critical target organ and the earliest manifestation of cadmium toxicity is renal tubular dysfunction. Increased exposure has been associated with other endpoints such as cardiovascular disease, bone damage, diabetes, and neurological and reproductive toxicity.

JECFA concluded that renal tubular dysfunction progresses to overt nephropathy at β2-microglobulin concentrations >1000 µg/g creatinine. Tubular dysfunction is likely to be irreversible, although glomerular filtration rates may be normal. β2-microglobulin concentrations of 300-1000 µg/g creatinine are an early response to Cd exposure but

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unlikely indicate compromised renal function; this is usually reversible, and its health significance is uncertain. JECFA suggested that there is some evidence of cadmium-associated effects on bone density, fracture risk and calcium metabolism (calcuria, reduced parathyroid hormone levels), perhaps at urinary Cd concentrations lower than those associated with renal dysfunction; but uncertainty exists whether this is a direct effect or secondary to renal tubular dysfunction. The evidence is not clear enough at this time to warrant selecting the bone effects as critical endpoints for dose-response analysis.

JECFA agreed that the most suitable biomarker for dose-response analysis for the general population is urinary β2-microglobulin. For the dose-response analysis, JECFA conducted a meta-analysis of the relationship between urinary Cd and urinary β2-microglobulin using a database compiled by EFSA. The database included 30,000 adults from 35 countries, who were not occupationally exposed to Cd, and of whom 95% were of Asian descent and 75% were female. Because the half-life of Cd in the body is approximately 15 years, the assumption was made that steady state would be reached only after 45-60 years of exposure. Therefore only individuals over 50 years old were included in the analysis. A bioexponential model provided the best fit to the dose-response relationship, with the slope being essentially flat up to 5.2 µg/g Cd creatinine (95% CI: 4.94-5.57). After this point, the concentration of β2-microglobulin increased rapidly. A one compartment model and Monte Carlo simulation were then used to identify population percentiles for the relationship between dietary Cd exposure and urinary Cd concentration. JECFA estimated that at the 5th population percentile a dietary exposure of 1.2 µg/kg BW per day Cd (95% CI: 0.8-1.8) would result in a urinary Cd concentration of 5.2 µg/g creatinine. JECFA used the lower bound of the CI (0.8) to insure susceptible individuals would remain below the dietary exposure associate with renal pathology. A dietary exposure of 0.8 µg/kg BW per day is equivalent to approximately 25 µg/kg BW per month. Therefore, the existing PTWI (7 µg/kg BW per week) was withdrawn and replaced by a PTWI of 25 µg/kg BW per month.

The presenter stated that the model works well with low exposure levels but it is not appropriate for FERG. JECFA is concerned with the lower end of the dose-response curve, whereas FERG is focused on what is above the break point level on the dose response curve.

For clinical presentations of Cd nephropathy an epidemiological literature review was performed. The FDA was evaluating the relationship between reduced glomerular filtration rate, which is an indication of kidney failure to estimate the global burden of disease, and cadmium exposure. The CTTF is currently looking at studies reporting values of >1000 µg Cd/g creatinine which indicates irreversible renal damage. It is expected that populations with >1000 µg Cd/g creatinine are likely the result of Cd-contaminated rice consumption. Many countries may not have levels above that so other populations may not be included in the literature review.

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Molluscs are a food item for which there have been high concentrations of Cd reported compared to rice, but because rice is eaten more often, it is expected to present more of a problem to the general population where rice is a major staple. Kinetic modeling may not be useful because the relationship between dietary Cd intake and urinary Cd concentration at high concentrations does not hold.

4.5.5 Global burden of disease from lead

At a previous meeting of the CTTF, a decision was made to delay the initiation of work on lead until results were available from GBD 2010 regarding the distribution of lead biomarker levels in the GBD regions and from the 73rd JECFA meeting regarding estimates of dietary lead exposure by region. The survey of human health effects conducted by JECFA provides a starting point for identifying the sequelae associated with lead on which to base a burden of disease. The candidate effects include mortality from all causes (primarily due to cardiovascular diseases), hypertension, renal dysfunction (i.e., chronic kidney disease, end stage renal disease), neurological dysfunction (i.e., cognitive impairment in children and adults, Attention Deficit Hyperactivity Disorder (ADHD), conduct disorder, essential tremor, reduced nerve conduction velocity, amyotrophic lateral sclerosis, postural imbalance, schizophrenia, depression), reproductive dysfunction (i.e., impaired fertility, pregnancy complications such as eclampsia, adverse outcomes such as spontaneous abortion and fetal growth restriction), delayed sexual maturation, and impaired dental health (i.e., caries, periodontal disease). The endpoints that are likely to be included in a BoD analysis are cognitive impairment (children), hypertension, and kidney disease.

JECFA derived estimates of dietary lead exposure primarily on the basis of total diet studies, although limited data were available from developing countries, and no data were available from Africa. The group suggested GEMS/Food Consumption Cluster Diets food data to be used for countries in Africa, or other countries with limited data. Two primary challenges must be faced in conducting a BoD analysis of dietary lead intake. First, how can the unique contribution of lead in food to total body lead burden be estimated? Second, how can adverse health effects due to lead be apportioned to food, as distinct from other sources/pathways of exposure to this widespread contaminant? To address the first challenge, three options can be considered. Based on a toxicokinetic analysis of Scottish infants exposed to lead in drinking water, JECFA estimated that blood lead level increases from 0.052 to 0.16 µg/dL per µg/day of dietary lead exposure. Second, a toxicokinetic model, such as the United States Environmental Protection Agency (US EPA) Integrated Exposure Uptake Biokinetic Model, could be used to estimate the contribution of dietary lead intake to the body burden of lead. A third option is to use expert elicitation. The first option appears to be the best. Use of the second option would require data, which are generally not available for most regions, on lead in air, soil, water, dust, as well as data on other potential sources/pathways of exposure. Similarly, it is unclear how expert elicitation would be useful in the absence of data on which the judgments could be based.
52 Chapter 4: Summary of discussions and outcomes

The TF chair suggested that the CTTF could contribute JECFA’s numbers to the national burden of FBD protocol, but cautioned not to make it too complicated and focus on attribution from food. The FDA volunteered to pick up lead on dietary assessment and hopes to complete the first draft by January. The group discussed endpoints that are causal, ADHD being one of them, where a disability weight can be attributed.

4.5.6 Global burden of disease from dioxins and dioxin-like compounds

The daily exposure from food is the major route of entry of dioxins in the human body. This intake is not restricted to one single compound, but consists of a mixture of dioxins, furans and dioxin-like polychlorinated biphenyls (PCBs) (further referred to as dioxins). As these components share a common toxic mechanism of action the mixture composition is expressed in the aggregate measure Toxicity Equivalents (TEQ). The TEQ expresses the mixture composition in terms of equivalents of the dioxin 2,3,7,8-tetrachlorodibenzodioxin.

In the body dioxins distribute in the lipid fraction and removal from the body is slow, with a half-life of more than 7 years. Therefore dioxins accumulate over time, resulting in increasing levels of dioxins with increasing exposure duration. For this reason, the body burden, rather than the daily exposure, is taken as the key index of exposure and useful for BoD estimates.

Fat levels (blood, milk, adipose tissue) directly reflect the long term accumulation of dioxins in the body and provide a measured dose metric for the body burden associated with long term dioxin exposure. Body fat levels may also be estimated by combining intake calculations with kinetic modeling, leading to an estimated body burden and its corresponding body fat level.

Body burdens which are associated with a certain toxic effects in animal bioassays may be compared with body burdens present in the human population. Body burdens associated with toxicity may be obtained from epidemiological observations in exposed human populations.

In the presented work human milk data were used as a dose metric for the current body burden and its associated toxicity in the human population.

Selected rat toxicity included:

- **Reproductive toxicity**: reduced sperm production in male offspring after prenatal, intrauterine exposure in dams who had received a single dioxin dose at gestational day 15 of pregnancy. This effect, being the most sensitive toxic effect in animals, was previously selected by SCF, WHO and JECFA as the point of departure in deriving the tolerable daily intake for dioxins;

- **Hepatic toxicity**: diffuse fatty change as a measure for cumulative low dose toxicity as induced after chronic exposure; and
- **Thyroid toxicity**: as measured by a lowering of the Total Thyroxine (TT4) hormone in the blood after subchronic exposure.

The animal toxicity data were analyzed by means of benchmark dose (BMD) modeling. This procedure, in which dose-response data from the animal bioassay is modeled, allows for the calculation of the animal BMD (pg TEQ/g body fat) and its lower 5% confidence limit (BMDL) which is associated with a certain effect size (e.g., percentage reduction of sperm count or TT4 hormone level) or occurrence of a dichotomous non-cancer effect in the typical animal (i.e., the ED$_{50}$ for hepatic toxicity). In this paper a 10% effect size was chosen for reduced sperm count and TT4 because this effect size can readily be estimated from the available toxicity data. In this way BMDLs of 164, 186 and 1520 pg TEQ/g body fat were obtained for reproductive toxicity, thyroid toxicity and hepatic toxicity, respectively. The animal BMDLs were extrapolated from the rat to man, resulting in estimated human BMDLs.

Human BMDLs can be compared directly with data on dioxins in human milk fat. For example, given a geometric mean of 18.5 pg TEQ/g milk fat in Dutch milk and a BMDL of 164 pg TEQ/g body fat for reproductive toxicity, it can be concluded that this milk level is well below the body fat level which may cause a 10% decreased sperm production in humans. When this comparison is made for the total milk fat distribution only 0.23% of the values appeared as exceeding the human BMDL. When applied to thyroid toxicity and hepatic toxicity this percentage was 0.17 and <0.01 respectively. From these results it was concluded that the 2004 Dutch body burden data are not associated with discernible reproductive, thyroid or hepatic toxicity.

Europe shows the highest dioxin levels in human milk (2000-2003: up to 20–30 pg TEQ/g milk fat), while dioxin levels outside Europe are lower (2–15 pg TEQ/g milk fat). However, it should be noted that dioxin levels in human milk have been rapidly declining in Europe over the last several decades. For example, in the Netherlands, dioxin levels in human milk have halved every 7 years.

Assuming distribution characteristics for dioxins to be the same in other European milks as in Dutch milk, current levels barely reach levels that may be associated with observable reproductive, thyroid or hepatic toxicity (defined here as 10% lowering of sperm production or thyroid hormone blood level). Outside Europe, estimated effect sizes for these effects are even lower due to the lower body burdens.

Some discussion ensued concerning the use of reduction of sperm count as an indicator of infertility. A 5–20% reduction in sperm count does not equate to infertility, but is more indicative of physiological change, and may therefore not be suitable as a measure of reproductive toxicity. It may be necessary to look at a clinical definition of what percentage of normal sperm count can be associated with infertility in humans. In addition, as infertility currently has no disability weight associated with it, it will be necessary to assess a disability weight for infertility in order to calculate DALYs.
It was agreed that dioxins in food are generally not a health concern for the world’s population. Thirty years ago the effects of dioxins may have been quantifiable, but not today. The question now is if current exposures are a public health concern. However, as it is important not to minimize the potential adverse health effects of dioxin, the publication of a paper was requested.

**Textbox 4:**
Summary of CTTF discussions and action points

**Discussions**
- In addition to the review on peanut allergies, the reviews on aflatoxicosis and disease from cassava cyanide ingestion have been completed. The reviews on disease from cadmium, lead and dioxin ingestion are nearing completion;
- It is estimated that, globally, between 25,200 and 155,000 liver cancer cases per year are induced by aflatoxin. This represents about 5 to 30% of all liver cancer cases of all etiologies;
- The estimated annual konzo incidence rate in affected areas is 0.6/1000, in a population at risk estimated at 2,500,000. Incidence is highest in children over two years old of both sexes, and women of reproductive age.

**Action points**
- The CTTF recommended the commissioning of three new systematic reviews, aimed at assessing the global burden of disease from ingestion of arsenic and methylmercury, and a review of the data on organophosphates to determine if enough data exists to obtain a global BoD estimate.

**Next CTTF meeting**
- Will be organized in 2012.

4.5.7 Chemicals and Toxins Task Force work plan for 2010–2011

The 2010–2011 work plan for the CTTF is summarized in Table 7.
### Table 7:
CTTF work plan for 2010–2011

<table>
<thead>
<tr>
<th>Causative agents</th>
<th>Specific associated activities</th>
<th>Timeframe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aflatoxins</td>
<td>Develop manuscript for journal publication</td>
<td>December 2010</td>
</tr>
<tr>
<td>Cassava cyanide</td>
<td>1. Redraft report based on comments from CTTF</td>
<td>1. March 2011</td>
</tr>
<tr>
<td></td>
<td>2. Develop manuscript for journal publication</td>
<td>2. June 2011</td>
</tr>
<tr>
<td>Peanut allergens</td>
<td>Develop manuscript for journal publication</td>
<td>March 2011</td>
</tr>
<tr>
<td>Dioxins and dioxin-like PCBs</td>
<td>1. Develop manuscript for WHO in journal format</td>
<td>1. February 2011</td>
</tr>
<tr>
<td></td>
<td>2. Develop manuscript for journal publication</td>
<td>2. May 2011</td>
</tr>
<tr>
<td>Lead</td>
<td>1. Estimate dietary lead consumption for all global regions</td>
<td>1. End of January 2011</td>
</tr>
<tr>
<td></td>
<td>2. Estimate blood lead levels resulting from dietary lead for all global regions</td>
<td>2. End of January 2011</td>
</tr>
<tr>
<td></td>
<td>3. Apply dose response for blood lead for neurologic and cardiovascular endpoints (from GBD) to estimate incidence of lead-induced disease</td>
<td>3. End of January 2011</td>
</tr>
<tr>
<td></td>
<td>4. Develop manuscript for TF and WHO</td>
<td>4. End of March 2012</td>
</tr>
<tr>
<td>Cadmium</td>
<td>1. Gather all available information on dietary exposure in different regions</td>
<td>1. January 2011</td>
</tr>
<tr>
<td></td>
<td>2. Link dietary exposure to health endpoints and estimate incidence of renal disease</td>
<td>2. January 2011</td>
</tr>
<tr>
<td></td>
<td>3. Develop manuscript for TF and WHO</td>
<td>3. End of October 2011</td>
</tr>
<tr>
<td>Arsenic</td>
<td>Utilize JECFA report, updates with systematic review to evaluate contribution of As in food to BoD</td>
<td>End of 2012</td>
</tr>
<tr>
<td>Methylmercury</td>
<td>Develop ToRs for commissioning</td>
<td>November 2010</td>
</tr>
<tr>
<td>Organophosphates (OPs)</td>
<td>1. Identify the use of OPs in different countries</td>
<td>1. March 2011</td>
</tr>
<tr>
<td></td>
<td>2. Systematic review of the literature to identify acute OP poisoning from misuse on food</td>
<td>2. March 2011</td>
</tr>
<tr>
<td></td>
<td>4. Evaluate exposure and effect from foodborne OPs</td>
<td>4. March 2011</td>
</tr>
</tbody>
</table>

#### 4.6 Country Studies Task Force (CSTF) – Burden of Disease group

#### 4.6.1 Progress to date and issues arising

Since its inaugural meeting in June 2009, the CSTF Burden of Disease Group (BoDG) has focused on preparing the necessary steps to startup the pilot studies, which will eventually lead to the full country studies. The first progress towards these pilots was presented during the CSTF March 2010 task force meeting in Atlanta. At FERG 4, the names of the first four selected countries were presented.

In addition to the preparation of the pilot studies’ launch, the plenary discussions focused on the development of a FBD Burden protocol and on the possible establishment of a specific workgroup that would focus on the methodological issues arising from the
pilot and full country studies.

The progress of the priority activities of the BoDG is summarized in Table 8.

<table>
<thead>
<tr>
<th>Activity</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Define criteria to select countries for burden studies</td>
<td>Finalized</td>
</tr>
<tr>
<td>Describe data gaps arising from the work of each FERG TF</td>
<td>Finalized</td>
</tr>
<tr>
<td>Link FERG country studies with relevant networks</td>
<td>Finalized</td>
</tr>
<tr>
<td>Map existing National Burden of Disease studies</td>
<td>Finalized</td>
</tr>
<tr>
<td>Map existing FBD Burden studies</td>
<td>Finalized</td>
</tr>
<tr>
<td>Development of a FBD Burden protocol</td>
<td>In progress</td>
</tr>
<tr>
<td>Select countries for pilot studies</td>
<td>First four countries selected</td>
</tr>
</tbody>
</table>

Table 8: Summary of CSTF/BoDG activities and progress

The following sub-sections summarize the BoDG sessions on the pilot studies, the presentation on the burden of FBD in Greece, the discussions on the methodological protocol for the national burden of FBD studies, and the recommendations regarding the establishment of a methodological workgroup. The CSTF/BoDG section is concluded by presenting the endorsed work plan for the coming year and beyond.

4.6.2 Pilot Studies

Pilot studies are designed as a pre-assessment phase before starting the actual national FBD Burden study, during which the actual data collection and burden assessment will take place. The pilot studies therefore aim at:

1. Testing the ability of countries to conduct full studies;
2. Testing the FBD Burden protocol;
3. Testing mechanisms and procedures for overseeing the studies; and
4. Testing if the country selection criteria actually are appropriate (i.e., did they lead to a representative selection of countries?).

After the first call for expression of interest was launched in September 2010, eleven countries, from four WHO regions, filed an application, all of which were of exceptional quality. Based on the earlier formulated selection criteria, the following countries were selected to conduct an official pilot study:

1. Albania (EURO)
2. Japan (WPRO)
3. Thailand (SEARO)
4. Uganda (AFRO)
4.6.3 National Burden of Foodborne Disease study: the example of Greece

The burden of illness due to foodborne pathogens in Greece was quantified using publicly available surveillance data, hospital statistics and literature (Gkogka et al., 2011). Results were expressed both as the incidence of different disease outcomes and as DALYs. It was estimated that, each year, approximately 370,000 illnesses per million inhabitants in Greece are likely caused by eating contaminated food; 900 of these illnesses are severe and 3 fatal, corresponding to 896 DALYs per million inhabitants. Brucellosis, echinococcosis, salmonellosis and toxoplasmosis were found to be the most important known causes of foodborne illnesses, being responsible for 70% of the DALYs and 89% of Years of Life Lost. Ill-defined intestinal infections accounted for the greatest part of reported cases and 27% of the DALYs. Overall, the DALY metric provided a quantitative perspective on the burden of foodborne illness, which may be useful for prioritizing food safety management targets, different from incidence estimates that do not consider severity or duration of disease.

Given the lack of country specific data for source attribution, underreporting and case fatality, multipliers based on a review of existing data from other developed countries were used to correct for uncertainty due these phenomena. The plausible range of these multipliers was wide and resulted in DALY estimates with similarly wide credible intervals. However, despite this limitation, estimates were still useful for risk ranking purposes.

This study could be used as an example for the FERG national burden of FBD studies and is rather encouraging for the FERG initiative since only one person has conducted it. It has been highlighted that there is a lot of uncertainty around the final estimates, underlining the important role of the CSTF in supporting the FERG national burden of FBD to deal with data gaps.

4.6.5 Methodological choices of National Burden of Foodborne Disease study protocols

An update was given on the progress on the development of protocols that will guide the selected countries to conduct their own national burden of FBD study.

For the country studies, researchers will undertake burden of foodborne disease studies. To estimate the burden of foodborne disease the DALY metric will be used. A variety of methods may be used to calculate DALYs. To ensure a uniform method to assess FBD burden, it is necessary to establish the methods of choice.

The aim of the presentation was to discuss ten key methodological choices and establish recommendations for each of these. These methodological choices were:

1. Incidence or prevalence based approach?
2. Should age weighting and discounting be applied?
3. Which life expectancy should be used?;
4. Which disability weights should be used?;
5. Agent-based or outcome-based approach?;
6. How to obtain incidence/prevalence data and how to correct for underreporting?;
7. What strategy should be used to deal with data gaps?;
8. Which uncertainty analysis should be performed?;
9. Which software is recommended?; and
10. Should there be a correction for co-morbidity?

The available options were explained for all methodological choices. Some of the choices were not up for discussion, because the lead of the Global Burden of Disease (GBD) study will be followed. In the recommendations, it was clearly stated for which choices this is the case. The recommendations will be incorporated in the Country Studies Methodology protocol.

The national burden of FBD protocol development is based on existing peer-reviewed and grey literature addressing FBD burden estimations. PubMed and Google Scholar search engines were used, respectively. Some of the scientific publications used to develop the protocol are in other languages than English and Dutch. Four papers are written in Chinese and one in Spanish. FERG members that can deal with these languages could help in translating these references. In the case of diseases caused by chemicals and toxins, specific studies will be provided to the CSTF.

Based on the national burden of FBD study protocol, study training material should be developed in the near future.

4.6.5.1 Incidence versus prevalence approaches

Using the incidence for the burden estimations is important for diseases having a long time-period between exposure and appearance of clinical signs. An incidence-based approach for the burden estimations fits better with an agent-based approach. However, incidence figures are not always available. For example, in the case of peanut allergy, only prevalence figures are available.

An incidence-based approach will be used in the framework of the national burden of FBD studies. When only prevalence figures are available, incidence will be estimated based on the prevalence figures and on the duration of the disease.

4.6.5.2 Age weighting and discount rate

The national burden of FBD studies will follow the GBD methodology. In the framework of the GBD 2010 study, age will not be weighted. However, both calculations may be done since changing the age weighting parameter does not ask much extra work and more information will be available. Moreover, par-
Participating countries may also give their point of view depending on the national context.

4.6.5.3 Life expectancy

In order to allow comparison between countries, it was recommended to use the West level 25 and 26 life tables developed by WHO. However, it was emphasized that this could lead to an overestimation of the FBD burden making the study results not trustable for decision makers.

It was argued that the West level 25 and 26 life tables have to be considered as optimal life expectancies, and that a lower national life expectancy is due to a disease that should be identified. The derived Standard Life Expectancy used in the GBD approach is therefore a needed standard to really show how much health is lost. However, national life expectancies may be used to explore how results are affected by competing causes of death, and could therefore be a potential approach to account for co-morbidity (see also 4.6.5.8).

4.6.5.4 Disability weights

The question arose as to whether specific disability weight should be developed for diseases caused by chemicals and toxins and other diseases that do not have one yet. Specific TFs should map FBD health outcomes and related available GBD disability weights. Missing disability weights should be listed, extrapolated from comparable GBD disability weights, or extracted from another disability weight list.

As mentioned in 3.2.1, the GBD 2010 study is reconsidering the disability weights using an innovative approach. More disability weights will be made available, but it is still unclear to what extent these will cover the FBD-related symptoms. An interaction between FERG and the GBD group will be established to handle missing disability weights.

4.6.5.5 Disease model

An agent-based approach was recommended because:
- it allows a complete estimate of the BoD due a specific agent;
- it includes all related sequelae; and
- it is the natural choice since there has to be thought in function of prevention of FBD.

During the data collection process, both approaches may be used and finally translated into an agent-based approach.
4.6.5.6 Data gaps

Pilot national burden of FBD studies will allow identifying the main data gaps. The CSTF may then provide tools to deal with these gaps. However, the CSTF should also provide some tools in advance, even though it is very difficult to be prepared for all possible data gaps. Clustering issues and extrapolation problems from limited field studies will probably appear. A clear understanding of the risk factors should allow avoiding over- or underestimations.

Discussions on the data gap issues from the European Centre for Disease Prevention and Control (ECDC) initiative aiming at estimating the burden of disease of at least 18 foodborne diseases in nearly 30 countries may be useful in the framework of FERG activities. The ECDC initiative is developing a protocol to take underreporting into account. For this purpose, it could be interesting to organize a joint meeting between ECDC, WHO and FERG. This meeting should take place in January 2011 before the start of pilot national burden of FBD studies.

4.6.5.7 Uncertainty analyses

Uncertainty analyses should be included in the national burden of FBD study protocol in order to inform decision makers on where the major data gaps were located. A clear distinction has to be made between data gaps due to underreporting, and estimate differences related to value choices such as discount rate, age weighting and life tables.

The question arose as to whether uncertainty analyses should be conducted by external statisticians and/or experts, or by the countries themselves if technical assistance is provided.

4.6.5.8 Co-morbidity adjustment

The question arose as to whether co-morbidity adjustment should be used in the framework of the national burden of FBD studies and how to conduct it. Two examples were raised: (1) the impact of malnutrition on diarrheal diseases, and (2) the immunosuppressing effect of aflatoxins favoring the establishment of infections. Researchers from the Johns Hopkins University School of Public Health and the London School of Hygiene and Tropical Medicine developed a methodological framework to deal with co-morbidity (Fenn et al., 2005). It was suggested to consult this group to know if the described framework may be applicable to the national burden of FBD studies. The issue of co-morbidity should be considered in the national burden of FBD estimates since it may considerably influence the DALY estimations.
4.6.6 Methodological Workgroup

During the pilot studies and the subsequent full country studies, methodological problems might arise that require a high level of technical expertise to resolve. These issues might relate to the methodological aspects of data collection and disease burden assessment.

To tackle this problem, the CSTF recommended to form a specific workgroup under its aegis, which would focus on these methodological issues through brainstorm sessions and technical notes. This workgroup would be composed of technical experts in the areas of data collection, extrapolation, modeling, DALY calculation and uncertainty and sensitivity analysis, and would be made up by members of the different task forces and, possibly, supplemented by external advisers.

Textbox 5:
Summary of CSTF/BoDG discussions, recommendations, and action points

- Albania, Japan, Thailand, and Uganda are the first four selected countries to conduct a pilot study;
- Decisions have been made regarding the methodological aspects of the national burden of FBD study protocol. The lead of the GBD will be followed, but countries will be given maximum flexibility in performing their national FBD studies;
- The CSTF recommended to establish a specific methodological workgroup, which would deal with any technical issue arising from the pilot and full country studies.

4.6.7 CSTF/Burden of Disease Group work plan 2010-2011

The 2010–2012 work plan for the BoDG is summarized in Table 9.

<table>
<thead>
<tr>
<th>Priority activities</th>
<th>Specific associated activities</th>
<th>Timeframe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Development of a FBD Burden protocol (to be used in the full Country Studies)</td>
<td>1. Draft a “burden of foodborne disease protocol”, based on the choices regarding FBD Burden protocols that were made at FERG 4; 2. Evaluate and complete the FBD Burden protocol.</td>
<td>1. End 2010 2. FERG 5</td>
</tr>
<tr>
<td>Training material</td>
<td>1. Review and map training materials for countries wishing to undertake burden of foodborne disease studies; 2. Evaluation and completion of training material.</td>
<td>1. March 2011 2. FERG 5</td>
</tr>
<tr>
<td>Full country studies</td>
<td>Initiate the full country studies</td>
<td>After FERG 5</td>
</tr>
</tbody>
</table>

Table 9:
CSTF/BoDG work plan for 2010–2012
4.7 Country Studies Task Force (CSTF) – Knowledge Translation and Policy Group (KTPG)

4.7.1 Progress to date and issues arising

The first formal meeting of the KTPG took place in Atlanta from 17-20 March 2010. Since March, the group has been working on developing the products outlined in its initial work plan. The group’s discussions and plenary presentations at FERG 4 focused on finalizing its first technical outputs. Furthermore, as this was the first time the group convened with FERG as a whole, a key objective of the meeting was to increase the KTPG members’ insight into the work and progress of the other FERG TFs, and enhance interaction with other FERG members.

4.7.2 Finalizing the terms of reference for global context mapping

Global policy context mapping describes the international forces that affect research-policy interactions at the global level and influence national food safety decision-making, prevention and control at the country level. According to the Terms of References (ToRs) submitted to the KTPG and discussed at FERG 4, the mapping process will involve two main elements:

1. Analysis of the policy context and dynamics of food safety; and
2. A stakeholder analysis.

In order to finalize the ToRs, the chair raised three points for discussion at the outset:

1. Should the document focus on policy only or should it also include a political component?
2. How comprehensive should the document be, e.g., should it include a media analysis?
3. Should the global context mapping process go beyond document review, and, for example, also use interviews or focus group discussions?

In summary, the global policy context mapping document will focus on a few key questions only: what exists as policy, who is setting the policies, and what are the drivers as well as barriers for evidence-informed food safety decision-making? The analysis will be kept to a desk review to be executed within a timeframe of two to three months. Numerous documents on policy, prepared by countries, stakeholders and other international organizations (in particular FAO), already exist and should be included into the desk review. In particular, a context mapping tool already developed by a PAHO partnership was recommended as a potential template for the analysis.

The global context mapping exercise is a public good which will, beyond being an internal tool for FERG’s use and guidance, also be shared with countries complementing and informing their national food safety policy context mapping activities.
4.7.3 Finalizing the guidance manual for national context mapping

National level policy context mapping of food safety aims to identify and elaborate on the dominant national forces that shape food safety policy formulation and implementation. The guidance manual will assist countries in reviewing and documenting their food safety policy context at the local, regional and national levels, using approaches that are appropriate to the locality being mapped. Discussions on finalizing this document focused on the content and structure of both the guidance manual and the proposed food safety committee to steer the country studies work.

4.7.3.1 Content and structure of the country policy context mapping guidance manual

The guidance manual will comprise a section on the background and rationale for the country policy context mapping, a chapter on clearly defined expected outputs to be presented by the countries participating in the FERG country studies, it will outline the purpose of the context mapping as well as listing suggested methodologies (including detailed guidance on items for key informant interviews and focus group sessions) to be applied by the countries, and finally key resources to further guide the countries in view of useful methods and tools.

4.7.3.2 Food safety committee

The national food safety committee will overview and monitor the planning and execution of the country studies. It will be composed of burden of disease researchers, context mapping experts and other key stakeholders such as representatives from media, civil society and the trade sector. If not yet existent in the country, the committee will ideally be established prior to the launch of the country studies. Countries will be provided with a reference list of key stakeholders to guide the membership of their committees.

The first committee meeting will consist of a briefing session to orient all committee members. Following this, the burden of disease and context mapping teams will work together to validate the timelines and context mapping guidance document. The latter is not to be considered as a blueprint, but will be modified according to country-specific requirements. In order to guarantee the comparability of the research process and its results, consistent context mapping methods are, however, to be applied across countries. The aim of the second meeting is to provide information on the timeframe and resources required to the entire food safety committee. Research work will then commence (a general timeframe of three months was suggested for the context mapping), the results of which will be presented at the third committee meeting.
4.7.3.3 Principles

Principles for developing the guidance manual were addressed by the KTPG:

- The importance of keeping questions in the manual as simple and clear as possible as well as relevant to country needs was stressed.
- Orientation should be provided on how to find data and what tools to use to undertake the national context mapping.

4.7.4 Finalizing the terms of reference for issue briefs and standard operation procedures for developing an issue brief

4.7.4.1 Terms of reference for issue briefs

An issue brief is an important communication tool to catalyze the demand for relevant FERG data acquisition among specific target audiences. In some situations, issue briefs may be used to also raise awareness of other pertinent issues experienced by the FERG such as lack of chemical contamination data.

The issue brief ToRs are targeted towards the FERG Task Forces whose role is to identify the needs and lead the issue brief development, including the specification of target audiences (which comprise one or more of the following: senior national policy-makers, international organizations and donors, NGOs, and researchers).

4.7.4.2 Standard operating procedures for preparing an issue brief

The standard operating procedures (SOPs) for FERG issue briefs provide guidance to all actors involved in developing an issue brief. They specify the roles, tasks and procedures linked to the preparation of an issue brief. SOPs should be updated regularly to improve operational processes and include lessons learned.

The following three actors, internal to the Initiative, need to be identified at the outset and fully briefed on the purpose and procedures of developing an issue brief in the context of the Initiative:

1. a KTPG Focal Point;
2. a FERG Task Force Focal Point; and
3. the WHO Secretariat.

A fourth actor involved is the external expert to whom the work will be commissioned. The steps that are required to prepare an issue brief are outlined in Figure 8:
4.7.4.3 Additional guidance to FERG TFs and external contractors

1. Sample issue brief
   A sample issue brief should be provided for further guidance to the FERG Task Forces and external contractors.

2. Inclusion of additional step into the SOPs
   It was recommended that an additional step on devising specific TORs for the commissioning of a particular issue brief should be included in the SOPs.

3. Dissemination of the issue brief
   The mode of dissemination of issue briefs will be dictated by the publication policies in place at WHO. However, the KTPG will support the process by identifying the most effective routes of dissemination to reach each target group.

4.7.5 Pilot country studies

4.7.5.1 Timeline requirements for the context mapping
Although an experienced social scientist or knowledge translation (KT) expert limiting the context mapping to the policy level (without assessing practices) could complete the mapping in one month, a timeframe of three months was considered more reasonable. Including predictions on future trends will increase the costs and time requirement of the context mapping exercise.

4.7.5.2 Comprehensiveness of the country studies

Questions arose on whether context mapping should be confined to the pilot phase only, and knowledge translation would take place in the full studies via the establishment of committees as described in the guidance document on context mapping (cf. 4.7.3). This approach was further reinforced as:

1. The context mapping will enable the identification of key stakeholders to be included into KT mechanisms; and
2. Time constraints will not allow the establishment of these committees before the pilot studies (it will take approximately three months to set up the committees in countries where they are non-existent). However, it was pointed out that in many countries (including, most likely, the pilot countries) these types of committees already operate or could potentially be easily established.

4.7.5.3 Monitoring and evaluation (M&E)

It was recommended to develop and apply a common framework for both the burden of disease assessment and the context mapping. When developing the M&E framework, the merits of prospective and retrospective evaluations need to be appraised and a decision taken for which approach to opt.

4.7.6 CSTF/Knowledge Translation and Policy Group work plan for 2010–2011

The 2010–2011 work plan for the KTPG is summarized in Table 10.
Table 10:
CSTF/KTPG work plan for 2010–2011

| Training for national context mapping | 1. Development of ToRs (including: identification of potential needs for training, provision of training modules for national context mapping, identification of evaluation tools, conducting the trainings) | 1. End of November 2010 |
| 2. Identifying contractor | 2. TBD |
| 3. Commissioning | 3. TBD |
| 5. Internal review of the provided training modules | 5. End of March 2011 |

| Global context mapping | 1. Finalization of the ToRs | 1. By 15 November 2010 |
| 2. Identification of contractor | 2. End of November 2010 |
| 3. Commissioning (implementation within 6 to 8 weeks) | 3. By 31 March 2011 |

| Issue brief (ToRs & SOPs) | 1. Designation of the KTPG focal points | 1. By 12 November 2010 |
| 2. Finalization of the SOPs | 2. Mid-December |
| 3. Format of the issue briefs to be included into the ToRs and issue brief example to be found | 3. Mid-December (including KTPG review) |
| 4. Review by key FERG TF members | 4. End of January 2011 |
| 5. Dissemination of the finalized documents to entire FERG electronically | 5. Mid February 2011 |
| 6. Briefing of the FERG TF | 6. Next FERG TF meeting |

4.8 FERG progress and future directions

As the Initiative has come half-way, an evaluation was commissioned of its progress thus far. The results of this Mid-term evaluation were presented at FERG 4 by the external evaluator, and were appraised by the FERG members. In addition, recommendations were made by the members concerning the future directions of the FERG, during the plenary session held on the closing day of the FERG 4 meeting.

4.8.1 FERG Mid-term evaluation

Regular monitoring and evaluations are critical for the success of any initiative. A specific FERG Monitoring and Evaluation framework was developed by the WHO Secretariat in 2008 and provided the foundation for the design, completion and analysis of the Mid-term Evaluation of the Initiative. The aims of this evaluation were to:

1. Provide an overall verdict of the progress made;
2. Identify what is going well and must continue; and
3. Identify what would benefit from improvements or change.

An external evaluator designed and performed the Mid-term Evaluation using a two-pronged approach, incorporating response data from survey questionnaires and semi-structured interviews with FERG members and stakeholders. Survey questionnaires were piloted for question clarity prior to their distribution (full report available upon request). Out of 46 FERG experts approached, 23 experts completed the questionnaire. Fifteen FERG experts and 5 stakeholders took part in the semi-structured interview.
Chapter 4: Summary of discussions and outcomes

The overall verdict of this evaluation of the WHO Initiative to Estimate the Global Burden of Foodborne Diseases is that it is making good progress. FERG experts and stakeholders consider it to be a very important initiative and are in agreement with its goals and objectives. They recognize that information on the burden of foodborne diseases is required in country, regional and global level in order to prioritize food safety interventions. The leadership and management of the Initiative by the WHO Secretariat is highly praised by the FERG experts and has been described very favorably in comparison with other international advisory bodies in which some of the experts are involved.

FERG experts recognize the complexity of the Initiative and some reported that at the outset they had doubts about whether it was possible to achieve. However, they have found that challenges have been overcome and continue to be addressed, many products are being produced and some have already been finalized. The project is being managed very energetically and they expect successful outcomes in due course.

There is also a high satisfaction level with the guidance and direction of the FERG and Task Force Chairs. The global and regional representation of the FERG membership is valued and FERG experts have reported that through their involvement, many of them have increased their own capacity. Stakeholder involvement is valued by FERG experts and the stakeholders themselves. Continued expansion of stakeholder constituencies was also suggested by both groups.

High quality of all outputs is considered very important by FERG experts and must be maintained. Most FERG experts are satisfied with the outputs that have already been produced – pathogen and hazard specific mortality and morbidity reports – though there is acknowledgement that there have been delays (some of which may not have been avoidable) and there is a lot more work to be done. These delays occurred initially, were mostly considered inevitable and were dealt with, and FERG experts consider that the Initiative is progressing according to plan. Stakeholders were satisfied with the results presented at stakeholder meetings to date and they look forward to the production of more results.

The advocacy efforts of the coordinator of the Initiative were praised and considered to be very effective.

FERG experts and stakeholders advised that there are some improvements that can be made to the Initiative. Some of these are in response to ongoing issues that may not be easily overcome by the WHO Secretariat but at some point, opportunities to solve these may arise. These include: administrative delays particularly in relation to funding; poor service from the WHO’s travel agency; understaffing in the WHO/FOS Secretariat; unclear support given from senior management within WHO; and the need for more collaborations with relevant WHO and United Nations departments and agencies.

Some of the improvements advised may be more amenable to implementation by the...
WHO Secretariat and include: maximizing the engagement of some FERG experts; not increasing the already high workload of FERG and Task Force chairs; balancing information needs with avoiding information overload; responding to feedback in the scheduling and planning of meetings; providing more frequent updates to stakeholders; and expanding the communication strategy with the purpose of communicating FBD information in the popular media.

The main challenge to the Initiative is how to deal with the expansion to the scope of the Initiative. The need to plan to collect primary data, overcome methodological challenges, integrate knowledge translation and respond appropriately to the 63rd World Health Assembly resolution on food safety are part of the expanded scope of the Initiative. FERG experts are in agreement that the expansion of the scope is necessary and appropriate. Because quality must be maintained, adjustments must be made to timelines and resources. Timelines can be reviewed, but FERG experts and stakeholders state that there is a limitation on timeline extension due to the risk of loss of momentum, and also the need to fulfill Member State and donor expectations for initial estimation of the global burden of foodborne diseases. Therefore, increasing the Initiative’s resources is the most appropriate change that can be made – both human and financial resources.

FERG experts are concerned about a major threat to the Initiative – the dependence of the Initiative and its success on such a small number of key personnel at the WHO Secretariat. These few key people are considered excellent in terms of technical expertise, enthusiasm, energy, dedication and motivation and much of the success so far is ascribed to these qualities. FERG experts are concerned that if there were any changes to personnel, the Initiative would be very vulnerable and could fail. They are concerned about sustainability and lack of a ‘safety net’ and therefore request an expanded team at the Secretariat with more of the existing skills. FERG experts would like high level senior management at WHO to reiterate their support for the Initiative through providing the necessary resources to ensure the success of the Initiative and the considerable investment that has been made.

There have been missed opportunities already because of resource issues: delays in commissioning work have occurred because of delayed access to financial resources. These missed opportunities are a source of frustration to FERG experts and the negative impact of these obstacles and delays is borne by the FERG experts and the Initiative. Work that should have been carried out by WHO Secretariat has sometimes been carried out by FERG experts as volunteers because of Secretariat understaffing. This is not sustainable and cannot be taken for granted.

If increased resources are not provided to implement the Initiative, there are several scenarios that may occur: continued progress (though this is unlikely because it depends on all current activities to remain at high efficiency and there is no spare capacity for unforeseen events); progress may slow (this is more likely and would damage the enthusiasm of FERG experts and stakeholders and may result in serious loss of momentum);
the Initiative could fail (this could happen if there were major changes for one or two key personnel in the Secretariat). Initiative failure would result in serious loss of expectations for those waiting for results, including Member States and donors.

High level support from senior management to address the resources needs of the Initiative particularly in the Secretariat would prevent Initiative failure. In addition, high level and visible support from senior management at WHO would offer acknowledgement to the very considerable volunteer efforts expended on the Initiative and may further strengthen the involvement of FERG experts and stakeholders. High level support of senior management would also facilitate increased collaboration with appropriate WHO and UN departments and agencies, and would help to reinforce the advocacy efforts of the Initiative, which would have many important benefits for the Initiative and the WHO.

The FERG applauded the comprehensive and accessible work done by the external reviewer. The outcomes of the review were a voice to their mental images, and there was a general consensus to move further along the chosen path, but to remain critical and to evaluate possible improvements.

The director of FOS, Dr Maged Younes, lauded the impressive results the FERG had already accomplished, even though some constraints were there and possibilities were sometimes limited. The high level commitment of the WHO to this Initiative should be clear from its establishment itself, and is further emphasized by the recent inclusion of the Initiative in the 63rd World Health Assembly resolution on food safety. The integration of this Initiative with other WHO Initiatives should be further encouraged, and administrative issues should be dealt with to the most feasible extent.

**Textbox 7:**
Summary of FERG Mid-term evaluation

- The Initiative is progressing very well;
- FERG experts and stakeholders consider the Initiative to be very important;
- The leadership and management by the WHO Secretariat are perceived as exceptional;
- Some threats are identified which should be addressed (e.g., Secretariat staffing, administrative processes);
- Some areas could potentially be enhanced (many outside control of Secretariat).

**4.8.2 FERG future directions**

During the closing day of the FERG 4 meeting, the experts discussed the future direc-
tions of the FERG. Recommendations were made for updating the inclusion criteria for burden of disease assessments, and considerations were made regarding the economic impact of FBD.

4.8.2.1 Inclusion criteria for burden of disease assessments

Since all task forces are making good progress, the question was raised what the endpoint of the FBD burden estimation would be, and which diseases should be worth including in future burden assessments.

During the subsequent plenary discussion, a consensus was reached to include diseases based on their health burden and on their importance on the (inter)national food safety agenda. Therefore, diseases with a low health impact, but a high economic impact, may also become subject of FERG burden assessments. In order to justify the inclusion or exclusion of certain foodborne diseases, it was recommended to make qualitative assessments of the evaluated diseases, and to document these evaluation processes.

In addition, it was noted that some parasites have a very focal distribution, and may therefore have a high local, but low global burden. Therefore, nations will be given the option of adding in their national FBD burden assessment studies whatever agent would be relevant for them, irrespective of the list of agents set up by the FERG.

4.8.2.2 Economic impact of foodborne diseases

Besides a substantial health impact, FBD may also have a significant economic burden, due to various direct (e.g., human treatment costs, livestock production losses) or indirect (e.g., human inactivity, trade restrictions) monetary losses. As knowledge translation aims at setting policy and research priorities, this process could benefit from data on the economic burden of FBD. Therefore, the FERG decided to give a start for economic burden assessments, by commissioning a concept paper on this issue. The KTPG will take on this task.

Textbox 8:
Summary of plenary discussion on FERG future directions

- The FERG decided to include in their burden assessments those agents that are responsible for a high public health impact and/or a high financial burden. Country studies can include any relevant agent, irrespective of the FERG list of priority agents;
- The KTPG will draft a concept paper on the economic impact of FBD.
The fourth general meeting of the FERG again brought together a wide range of outstanding experts from various disciplines and backgrounds. The set meeting objectives were met, and the considerable progress made in all commissioned reviews and protocols was exchanged and lively discussed. The meeting was concluded with the endorsement of the updated work plans, and with a general re-affirmation of the commitment to the ultimate goal of the Initiative – the estimation of the global burden of foodborne disease.

During FERG 4, the conclusions of the Initiative’s mid-term evaluation were presented, and showed an overall positive picture of the Initiative’s progress and conceived importance. As assessing the global burden of FBD is extremely complex and involves the integration of different fields of expertise, these conclusions confirm the dedication and outstanding proficiency of the FERG members and resource advisers. Progress in the area of advocacy and fundraising is essential to the success of the Initiative, a sentiment reassured at senior-level during the meeting.

Continuing the trend set during the second general FERG meeting, a stakeholder event was successfully organized in conjunction with FERG 4. This event created the important opportunity to share the latest results with the global stakeholders and the general public, and to interact on the approach set out by the FERG. Looking forward to 2011 and beyond, with the further FERG progress and the launch and execution of the national burden of FBD studies, it seems clear that the next few years will be extraordinarily interesting for all those interested in food safety.
6. Outputs of FERG 4

At FERG 4, the following outputs were delivered:

Preliminary results on the:
- Global burden of diarrheal diseases;
- Global burden of foodborne trematodiasis;
- Global burden of cystic echinococcosis;
- Global burden of neurocysticercosis;
- Global burden of aflatoxicosis; and
- Global burden of cassava cyanide ingestion.

Recommendations for the further development of the currently ongoing commissioned systematic reviews of the:
- Source attribution methods;
- Global burden of foodborne hepatitis;
- Global burden of brucellosis;
- Global burden of bovine tuberculosis;
- Global burden of intestinal protozoa;
- Global burden of trichinellosis;
- Global burden of anisakiasis;
- Global burden of toxoplasmosis;
- Global burden of cadmium ingestion;
- Global burden of lead ingestion; and
- Global burden of dioxin ingestion.

Recommendations for new systematic reviews on:
- Source attribution for certain priority agents;
- Interventions and policy issues on reducing the FBD burden in developing countries;
- Outcome trees and chronic sequelae of priority enteric pathogens;
- The global burden of angiostrongyliasis;
- The global burden of capillarisis;
- The global burden of toxocariasis;
- The global burden of trichuriasis;
- The global burden of arsenic ingestion;
- The global burden of methylmercury ingestion; and
- The feasibility of assessing the global burden of organophosphate ingestion.

Agreements on the modalities for source attribution through expert elicitation, which will be worked out in a draft protocol and pre-tested on FERG members.

The further development of the interface between the SATF and CSTF and the other TFs.

A review and appraisal of the protocols developed for use in the forthcoming pilot country studies, both in the areas of burden of disease assessment and policy context mapping.
An update of the inclusion criteria for FBD burden assessments and a first step towards economic burden assessments, through the development of a concept paper.

The announcement of the first four countries to hold a FBD burden pilot study:

- Albania
- Japan
- Thailand
- Uganda


Appendix
FERG membership and roles

FERG Members
- Formally appointed by the WHO Director-General (DG), following selection procedure
- Allocation to Core Group and Task Forces
- Full participation in all technical discussions

Resource advisers
- Not formally appointed by the DG
- Allocation to Task Forces on ad hoc basis (as required)
- Full participation in technical discussions

WHO Secretariat and other UN Organizations
- Full participation in technical discussions
- Allocation to Task Forces on ad hoc basis

Observers
- Nominated by FERG members (one per member)
- No ‘formal’ right of intervention in plenary
- Participation in Task Forces, as appropriate

Stakeholders
- Invited by WHO to designated sessions
- Formal right of intervention in designated sessions
- No participation in technical discussions to avoid conflicts of interest
II. Appendix

List of participants

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## Appendix

### FERG 4 Meeting Agenda

<table>
<thead>
<tr>
<th>Time</th>
<th>Monday, 8 November</th>
<th>Lead</th>
<th>Tuesday, 9 November</th>
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<td>09:00</td>
<td>FERG PLENARY</td>
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<td>Source Attribution Task Force</td>
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<td>FERG going to countries</td>
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<td>Knowledge Translation &amp; Policy Group</td>
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<td>Workplan revisions - KTPG</td>
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**Colour Coding:**
- **PLENARY**
- **Task Force Meetings**
- **Specific KTPG Sessions**
- **Not relevant to the KTPG**
## Wednesday, 14 November

**Salle B**

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<td>Global burden of disease from exposure to arsenic (G. S. I. Bureau)</td>
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**Coffee break**

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**Lunch**

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**Coffee break**

## Thursday, 15 November

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**Lunch**

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## Friday, 16 November

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<tbody>
<tr>
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<td>Post TF Chair</td>
<td>Global burden of disease from exposure to lead and cadmium (M. &amp; S. Bureau)</td>
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**Coffee break**

<table>
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<td>Post TF Chair</td>
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**Colour Coding:**
- **Plenary:**
- **Test Force Meetings:**
- **Other Events:**