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# APPENDIX 2. Subregions

| SUBREGION(1) [5] | WHO MEMBER STATES |
|---|---|
| AFR D | Algeria; Angola; Benin; Burkina Faso; Cameroon; Cabo Verde; Chad; Comoros; Equatorial Guinea; Gabon; Gambia; Ghana; Guinea; Guinea-Bissau; Liberia; Madagascar; Mali; Mauritania; Mauritius; Niger; Nigeria; Sao Tome and Principe; Senegal; Seychelles; Sierra Leone; Togo. |
| AFR E | Botswana; Burundi; Central African Republic; Congo; Côte d'Ivoire; Democratic Republic of the Congo; Eritrea; Ethiopia; Kenya; Lesotho; Malawi; Mozambique; Namibia; Rwanda; South Africa; Swaziland; Uganda; United Republic of Tanzania; Zambia; Zimbabwe. |
| AMR A | Canada; Cuba; United States of America. |
| AMR B | Antigua and Barbuda; Argentina; Bahamas; Barbados; Belize; Brazil; Chile; Colombia; Costa Rica; Dominica; Dominican Republic; El Salvador; Grenada; Guyana; Honduras; Jamaica; Mexico; Panama; Paraguay; Saint Kitts and Nevis; Saint Lucia; Saint Vincent and the Grenadines; Suriname; Trinidad and Tobago; Uruguay; Venezuela (Bolivarian Republic of). |
| AMR D | Bolivia (Plurinational State of); Ecuador; Guatemala; Haiti; Nicaragua; Peru. |
| EMR B | Bahrain; Iran (Islamic Republic of); Jordan; Kuwait; Lebanon; Libya; Oman; Qatar; Saudi Arabia; Syrian Arab Republic; Tunisia; United Arab Emirates. |
| EMR D | Afghanistan; Djibouti; Egypt; Iraq; Morocco; Pakistan; Somalia; South Sudan(2); Sudan; Yemen. |
| EUR A | Andorra; Austria; Belgium; Croatia; Cyprus; Czech Republic; Denmark; Finland; France; Germany; Greece; Iceland; Ireland; Israel; Italy; Luxembourg; Malta; Monaco; Netherlands; Norway; Portugal; San Marino; Slovenia; Spain; Sweden; Switzerland; United Kingdom. |
| EUR B | Albania; Armenia; Azerbaijan; Bosnia and Herzegovina; Bulgaria; Georgia; Kyrgyzstan; Montenegro; Poland; Romania; Serbia; Slovakia; Tajikistan; The Former Yugoslav Republic of Macedonia; Turkey; Turkmenistan; Uzbekistan. |
| EUR C | Belarus; Estonia; Hungary; Kazakhstan; Latvia; Lithuania; Republic of Moldova; Russian Federation; Ukraine. |
| SEAR B | Indonesia; Sri Lanka; Thailand. |
| SEAR D | Bangladesh; Bhutan; Democratic People's Republic of Korea; India; Maldives; Myanmar; Nepal; Timor-Leste. |
| WPR A | Australia; Brunei Darussalam; Japan; New Zealand; Singapore. |
| WPR B | Cambodia; China; Cook Islands; Fiji; Kiribati; Lao People's Democratic Republic; Malaysia; Marshall Islands; Micronesia (Federated States of); Mongolia; Nauru; Niue; Palau; Papua New Guinea; Philippines; Republic of Korea; Samoa; Solomon Islands; Tonga; Tuvalu; Vanuatu; Viet Nam. |

Notes: (1) The subregions are defined on the basis of child and adult mortality as described by Ezzati *et al.* [5]. Stratum A = very low child and adult mortality; Stratum B = low child mortality and very low adult mortality; Stratum C = low child mortality and high adult mortality; Stratum D = high child and adult mortality; and Stratum E = high child mortality and very high adult mortality. The use of the term 'subregion' here and throughout the text does not identify an official grouping of WHO Member States, and the "subregions" are not related to the six official WHO regions, which are AFR = African Region; AMR = Region of the Americas; EMR = Eastern Mediterranean Region; EUR = European Region; SEAR = South-East Asia Region; WPR = Western Pacific Region.

(2) South Sudan was re-assigned to the WHO African Region in May 2013. As this study relates to time periods prior to this date, estimates for South Sudan were included in the WHO Eastern Mediterranean Region.

# APPENDIX 3.
# Preliminary hazards considered by each task force

At the FERG 1 meeting (26–28 November 2007), each of the hazard-based TFs considered a comprehensive list of potential foodborne hazards for the development of burden estimates. During the course of the project these lists had to be reduced, largely for practical reasons concerning the ability to generate burden estimates. For reference, the complete list is given here.

### EDTF

Adenovirus
*Aeromonas* spp.
Astrovirus
Bacterial toxins (*B. cereus*)
Bacterial toxins (*C. perfringens*)
Bacterial toxins (*S. aureus*)
*Brucella* spp.
*Campylobacter* spp.
*Clostridium botulinum*
Enteroaggerative *E. coli* (EAggEC)
Entero-pathogenic *E. coli* (EPEC)
Entero-toxigenic *E. coli* (ETEC)
Enterovirus
*Helicobacter pylori*
Hepatitis A virus
Hepatitis E virus
*Leptospira* spp.
*Listeria monocytogenes*
*Mycobacterium bovis*
Non cholera Vibrios
Norovirus
Prions
Rotavirus
*Salmonella* (non-typhoidal) spp.
*Salmonella* (typhoid) spp.
Shiga-toxin producing *E. coli* (STEC)
*Shigella* spp.
*Vibrio cholerae* 01/0139
*Yersinia* spp.

### PDTF

*Ancylostoma duodenale*
*Angiostrongylus cantonensis*
*Angiostrongylus costaricensis*
*Anisakis simplex*
*Ascaris* spp.
*Blastocystis hominis*
*Capillaria philippinensis*
*Clonorchis sinensis*
*Cryptosporidium* spp.
*Cyclospora* spp.
*Dicrocoelium dendriticum*
*Dientamoeba fragilis*
*Diphyllobothrium latum*
*Echinococcus* spp.
*Echinostoma* spp.
*Entamoeba histolytica*
*Fasciola* spp.
*Fasciolopsis buski*
*Gastrodiscoides hominis*
*Giardia* spp.
*Gnathostoma spinigerum*
*Heterophyes heterophyes*
*Hymenolepis nana*
*Isospora belli*
*Linguatula serata*
*Metagonimus yokogawai*
*Nanophytes salmincola*
*Opisthorchis felineus*
*Opisthorchis viverrini*
*Paragonimus* spp.
*Sarcocystis hominis*
*Taenia saginata*
*Taenia solium*
*Toxocara* spp.
*Toxoplasma gondii*
*Trichinella* spp.
*Trichostrongylus* spp.
*Trichuris trichiura*

### CTTF

Elemental contaminants (e.g. lead, mercury, cadmium, manganese, arsenic)
Mycotoxins (e.g. aflatoxins, ochratoxins, fumonisin, trichothocenes)
Food additives (e.g. sulphites, nitrites/ nitrates, benzoic acid)
Pesticides (e.g. organophosphates, carbamates, DDT, pyrethrins)
Organic industrial pollutants (e.g. persistent organic pollutants)
Veterinary drugs/residues (e.g. antibiotics, hormones–but not antimicrobial residues)
Seafood toxins (e.g. tetrodotoxin, ciguatera, shellfish toxins, DSPs, PSPs, histamines)
Process contaminants (e.g. acrylamide, PAHs, choropropanol)
Allergens (e.g. peanuts)
Natural toxicants (e.g. cyanide in cassava, aminoglycosides)
Radionuclides and depleted uranium

# APPENDIX 4.
# Hazard-specific input parameter sources and methods

## A4.1 Brucellosis

### Incidence

There were 32 countries identified as "free of brucellosis in livestock", using 2006–2012 data reported to the World Organisation for Animal Health (OIE) [248], and a list of European countries recognized by the European Union as "officially brucellosis free" in cattle, sheep and goats in 2010 [249]. Using 2001–2004 OIE data, a previous review [250] estimated human brucellosis incidence for 9 of the countries identified as free of brucellosis in livestock. The median human brucellosis incidence from these 9 countries free of brucellosis in livestock was used as the estimated human brucellosis incidence for each of the 32 countries free of brucellosis in livestock. A FERG-commissioned systematic review was then used to screen 2385 articles [251] and a literature review for national human brucellosis incidence estimates [174, 175, 187, 188, 252, 253], to extract brucellosis national incidence estimates for 17 countries (Argentina, Canada, Chad, China, Egypt, France, Greece, Iraq, Iran, Italy, Kyrgyztan, Jordan, Mexico, Oman, Saudi Arabia, Turkey, and the United States of America). The human brucellosis incidence estimates in each of these countries were compared with human brucellosis incidence estimates in the same country in a previous review, which used 2001–2004 OIE data [250], to estimate a multiplier (mean=5.4, range 1.6–15.4) to account for under-reporting. This multiplier was used to estimate national human brucellosis incidence for countries with OIE human brucellosis data in the previous review but without national human brucellosis incidence estimates identified in the current systematic review or literature review. By multipling the human brucellosis incidence reported to OIE by the multiplier, there were 32 such countries. These steps yielded human brucellosis incidence estimates for 81 countries. The FERG Computational Task Force imputation model was then used to impute an incidence of human brucellosis in all countries with missing incidence.

### Clinical Outcomes

The FERG-commissioned systematic review assisted in determining the clinical outcomes for human brucellosis [254]. These were: acute brucellosis (severe); acute brucellosis (moderate); chronic brucellosis; brucellosis orchitis; and brucellosis death. For acute brucellosis, it was assumed that 50% of cases were severe, 50% of cases were moderate, 40% of brucellosis cases resulted in chronic brucellosis, and 10% of brucellosis cases in males resulted in orchitis [254].

### Duration

Acute brucellosis: duration 14 days (min. 7 days–max. 21 days). Chronic brucellosis: duration 6 months (min. 3 months– max. 24 months). Brucellosis orchitis: duration 6 months (min. 3 months–max. 24 months) [254].

### Disability weight

Acute brucellosis (severe): GBD2010 disability weight of 0.210 (95% UI 0.139–0.298) for infectious disease, acute episode, severe. Acute brucellosis (moderate): GBD2010 disability weight of 0.053 (95% UI 0.033–0.081) for infectious disease, acute episode, mild. Chronic brucellosis: GBD2010 disability weight 0.079 (95%UI 0.053–0.115) for musculoskeletal problems, legs, moderate. Brucellosis orchitis: GBD2010 disability weight of 0.097 (95% UI 0.063–0.0137) for epididymo-orchitis [82].

### Mortality

Acute brucellosis and chronic brucellosis case fatality ratio 0.5% (min. CFR 0.25%–max. CFR 0.75%) [255, 256].

### Age distribution

Acute brucellosis, chronic brucellosis, brucellosis orchitis and brucellosis death age distribution: 3% <15 years; 29% 15–24 years; 24% 25–34 years; 16% 35–44 years; 13% 45–54 years; 12% 55–64 years; and 3% >65 years [257].

### Sex distribution

Acute brucellosis, chronic brucellosis and brucellosis deaths sex distribution: 55% male (95% UI 50%–60% male) [254]. Brucellosis orchitis: 100% male.

## A4.2 Mycobacterium bovis infections

### Incidence

There were 51 countries identified as "free of *Mycobacterium bovis* in cattle" using 2005–2012 data reported to OIE [248] and a list of European countries recognized by the European Union as "officially free of bovine tuberculosis" in 2010 [249]. A FERG-commissioned systematic review screened 1203 articles [258] with data from 91 countries, and estimated the median proportion of human tuberculosis cases due to *M. bovis* at the region level as 2.8% for AFR, 0.4% for EUR and 0.3% for AMR; the overall median proportion from studies in the review (1.0%) was used in the three other regions. These proportions were applied to all countries in each respective region except for the 51 countries free of *M. bovis* in cattle. The lowest observed proportion (0.3%) was assigned to the 51 countries free of *M. bovis* in cattle. Country-level human tuberculosis incidence was abstracted from the WHO Global Tuberculosis Report [165] and multiplied by population estimates and the proportion of human tuberculosis cases due to *M. bovis* to estimate human *M. bovis* cases.

### Clinical Outcomes

Clinical outcomes were *M. bovis* tuberculosis and *M. bovis* death.

### Duration

*M. bovis* tuberculosis duration was estimated using data in the 2014 WHO Global Tuberculosis Report on incidence and prevalence of human TB infections [165]; these data yielded a duration of 1.5 years in all regions except AFR, where the duration was 1 year.

### Disability weight

*M. bovis* tuberculosis: GBD2010 disability weight of 0.331 (95% UI 0.222–0.450) for tuberculosis without HIV infection [82].

### Mortality

Deaths from *M. bovis* were estimated following the same approach for estimating *M. bovis* cases after reducing the mortality by 20% due to the recognition from another FERG-commissioned review that *M. bovis* infections are more likely to result in extrapulmonary infections [259] and that extrapulmonary infections have a lower case-fatality ratio (CFR) than pulmonary tuberculosis infections; a 20% reduction in mortality was based on a review of the United States of America national surveillance data from 2009–2010, which found that the CFR for extrapulmonary tuberculosis infections was approximately 20% lower than the CFR for pulmonary tuberculosis infections. Therefore, country-level human tuberculosis mortality rates of tuberculosis among persons not infected with HIV were abstracted from the WHO Global Tuberculosis Report [165], reduced by 20%, and then multiplied by population estimates and the proportion of human tuberculosis cases due to *M. bovis* to estimate *M. bovis* deaths.

### Age distribution

It was assumed that the age distribution of *M. bovis* cases and *M. bovis* deaths was the same as the age distribution of human tuberculosis cases and deaths, and therefore used the age distribution from Table 3.2 of the WHO Global Tuberculosis Report: 2% <15 years; 60% 15–44 years; 28% 45–64 years; 10% >65 years [165].

### Sex distribution

It was assumed that the sex distribution of *M. bovis* cases and *M. bovis* deaths was the same as the sex distribution of human tuberculosis cases and deaths, and therefore used the sex distribution from Table 3.2 of the WHO Global Tuberculosis Report: 65% male [165].

## A4.3 Typhoid

### Incidence

FERG reviewed available burden of disease estimates for typhoid fever [6, 260] before selecting the IHME Global Burden of Disease 2010 (GBD2010) estimates because these estimates were published in peer-reviewed literature and were available for all countries. At the request of FERG, IHME provided GBD2010 data with country-specific, age-standardized prevalence (per 100 000 population) of "typhoid and paratyphoid fever", and "typhoid and paratyphoid liver abscesses and cysts" [6]. Assuming a steady disease state, prevalence of typhoid and paratyphoid fever was converted to incidence by dividing by duration; similarly for typhoid and paratyphoid abscesses and cysts. Typhoid fever incidence was determined using a ratio of 1.0 *Salmonella* serotype Typhi cases to 0.23 *Salmonella* serotype Paratyphi A cases observed in national laboratory-based surveillance in the United States of America and in a global survey in 1997 [262]; similarly for typhoid abscesses and cysts. We used the GBD2010 range of estimates around the mean estimate of global deaths due to typhoid and paratyphoid fevers (190 242 with UI 23 786–359 075) to derive a range of estimates for typhoid incidence.

### Clinical Outcomes

Clinical outcomes were typhoid fever, typhoid liver abscesses and cysts, and typhoid death [6].

### Duration

Typhoid fever: duration 28 days (min. 7 days–max. 42 days). Typhoid liver abscesses and cysts: duration 42 days (min. 28 days–max. 56 days). Duration was estimated based on median duration before hospitalization for typhoid fever or typhoid abscesses/cysts of 10 days, recommended treatment duration for typhoid fever of 10–14 days and for typhoid abscesses/cysts of 28–112 days, and presumed longer duration in patients with typhoid fever or typhoid abscesses/cysts who are not hospitalized [263].

### Disability weight

Typhoid fever: GBD2010 disability weight of 0.210 (95% UI 0.139–0.298) for infectious disease, acute episode, severe. Typhoid liver abscesses and cysts: GBD2010 disability weight of 0.254 (95% UI 0.170–0.355) for infectious disease, post-acute consequences, severe [82].

### Mortality

GBD2010 country-specific mortality data for "typhoid and paratyphoid fevers" were obtained by sex and 20 age groups from the IHME website [58]. Typhoid mortality was determined using a ratio of 1.0 *Salmonella* serotype Typhi cases to 0.23 *Salmonella* serotype Paratyphi A cases observed in national laboratory-based surveillance in the United States of America and in a global survey in 1997

[262]. The GBD2010 range of estimates around the mean estimate of global deaths due to typhoid and paratyphoid fevers (190 242 with UI 23 786–359 075) were used to derive a range of estimates for paratyphoid deaths.

### Age distribution

Using data from IHME, the age distribution for typhoid fever, typhoid liver abscesses and cysts, and typhoid deaths was 5% <1 year; 16% 1–4 years; 22% 5–14 years; 19% 15–24 years; 14% 25–34 years; 9% 35–44 years; 6% 45–54 years; 3% 55–64 years; 3% 65–74 years; 1% 75–84 years; and 1% >85 years [6].

### Sex distribution

Using data from IHME, the sex distribution for cases of typhoid fever, and typhoid liver abscesses and cysts was 56% male, and the sex distribution for typhoid deaths was 58% male [6].

## A4.4 Paratyphoid

### Incidence

FERG reviewed available burden of disease estimates for typhoid and paratyphoid fever [6, 260] before selecting the IHME Global Burden of Disease 2010 (GBD2010) estimates because these estimates were published in peer-reviewed literature and were available for all countries. At the request of FERG, IHME provided GBD2010 data with country-specific, age-standardized prevalence (per 100 000 population) of "typhoid and paratyhoid fever", and "typhoid and paratyphoid liver abscesses and cysts" [6]. Assuming a steady disease state, prevalence of typhoid and paratyphoid fever was converted to incidence by dividing by duration; similarly for typhoid and paratyphoid abscesses and cysts. Paratyphoid fever incidence was determined using a ratio of 0.23 *Salmonella* serotype Paratyphi A cases to 1.0 *Salmonella* serotype Typhi cases observed in national laboratory-based surveillance in the United States of America and in a global survey in 1997 [262]; similarly for paratyphoid abscesses and cysts. We used the GBD2010 range of estimates around the mean estimate of global deaths due to typhoid and paratyphoid fevers (190 242 with UI 23 786–359 075) to derive a range of estimates for paratyphoid incidence.

### Clinical Outcomes

Clinical outcomes were paratyphoid fever, paratyphoid liver abscesses and cysts, and paratyphoid deaths [6].

### Duration

Paratyphoid fever: duration 28 days (min. 7 days–max. 42 days); paratyphoid liver abscesses and cysts: duration 42 days (min. 28 days–max. 56 days). Duration was estimated based on median duration before hospitalization for paratyphoid fever or paratyphoid abscesses and cysts of 10 days, with a recommended treatment duration for paratyphoid fever of 10–14 days and for paratyphoid abscesses and cysts of 28–112 days, and presumed longer duration in patients with paratyphoid fever or paratyphoid abscesses and cysts who are not hospitalized [263].

### Disability weight

Paratyphoid fever: GBD2010 disability weight of 0.210 (95% UI 0.139–0.298) for infectious disease, acute episode, severe. Paratyphoid liver abscesses and cysts: GBD2010 disability weight of 0.254 (95% UI 0.170–0.355) for infectious disease, post-acute consequences, severe [82].

### Mortality

GBD2010 country-specific mortality data for "typhoid and paratyphoid fevers" were obtained by sex and 20 age groups