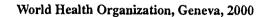
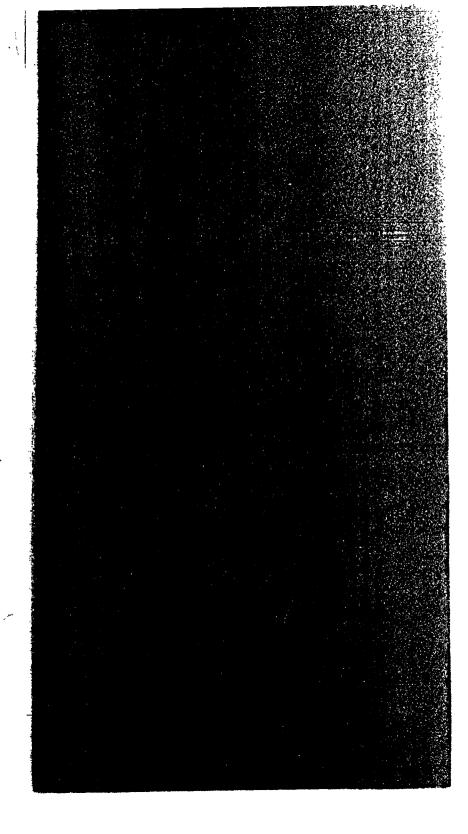
WHO FOOD ADDITIVES SERIES: 44

Safety evaluation of certain food additives and contaminants

Prepared by the Fifty-third meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA)



IPCS - International Programme on Chemical Safety



METHYLMERCURY

First draft prepared by
Dr D.C. Bellinger¹, Dr M. Bolger², Dr C. Carrington², Dr E. Dewailly³,
Dr L.P.A. Magos⁴ and Dr B. Petersen⁵

¹Harvard Medical School, Boston, Massachusetts, USA; ²US Food and Drug Administration, Washington DC, USA; ³Centre de Sante Publique du Québec, Québec, Canada, ⁴TNO BIBRA International Ltd, Carshalton, Surrey, United Kingdom; and ⁵Novigen Sciences Inc., Washington DC, USA

Explanation	314
Biological data	315
Pharmacokinetics	315
Absorption	315
Distribution	315
Transfer from mother to offspring	317
Placental transfer	317
Lactation	318
Clearance	319
Biochemical aspects	321
Cleavage of carbon-mercury bond	321
Complexes with thiol radicals	322
Interaction with selenium	323
Toxicological studies	325
Acute toxicity	325
Renal and hepatic toxicity	325
Anorexia	326
Neurotoxicity	326
Small rodents	326
Non-human primates	328
Domestic animals	329
Reproductive and developmental toxicity (other than	
neurotoxicity)	329
Developmental neurotoxicity	333
Exposure in utero	333
Exposure in utero and postnatally	334
Exposure after parturition	335
Carcinogenicity	336
Immunomodulation	, 337
Extrapolation between species	337
Observations in humans	338
/ Case series	338
/ Childhood development	341
Neurological status	341
Developmental milestones	343
Early development	345
Development later in childhood	348
Sensory, neurophysiological and other end-points	351

Adult neurological, neurophysiological, and	
sensory function	352
Bias: Covariates, confounders and effect modifiers	354
Study in the Faroe Islands	354
Study in the Seychelles	359
Study in the Amazon Basin	361
Study in New Zealand	361
Study in Peru	363
Reanalysis of the study in Iraq	363
Estimates of dietary intake	364
Environmental mercury	364
Biomarkers of exposure	365
Intake assessment	367
Residues	367
National intake estimates	368
Estimates based on WHO GEMS/Food diets	370
Estimates of intake by fish consumers at the	
95th percentile	370
Comments	372
Evaluation	377
References	377

1. EXPLANATION

The Committee first evaluated methylmercury at its sixteenth meeting (Annex 1, reference 30), when it established a provisional tolerable weekly intake (PTWI) of 300 μg of total mercury per person, of which no more than 200 μg should be present as methylmercury. At its twenty-second and thirty-third meetings (Annex 1, references 47 and 83), the Committee confirmed the PTWI of 200 μg of methylmercury (3.3 $\mu g/kg$ bw) for the general population. At its thirty-third meeting, the Committee noted that pregnant women and nursing mothers may be at greater risk than the general population from the adverse effects of methylmercury. The Committee considered the available data insufficient to recommend a specific intake for this population group, and it recommended that more detailed studies be undertaken.

At its present meeting, the Committee reviewed information that had become available since the previous evaluation. The PTWI was not reconsidered and was maintained at its present value. Two other WHO publications have dealt with the effects of mercury and methylmercury on human health (WHO, 1976, 1990). Relevant information from those documents and the studies published since the report of the thirty-third meeting are summarized and discussed in this monograph, and the data were used to estimate the risks associated with exposure to methylmercury. It should be noted that the doses given refer to the mercury constituent of the organic mercury compound,

M

2 2

m st pι s∈ m

et (R inç

al 2.

co ery bio

of e rap oth

bra cor blo rats

(Sw

0.5

con ratic nea al., et a Sun (Ho (Ulfv

grea sust incre

high

rat h