The acute reference dose (ARfD)

When setting ARfDs, the WHO panel of the JMPR uses the most appropriate data from the available toxicology database. For some compounds such as those which have specific investigations of acute toxic endpoints the ARfD that is set will have a relatively low level of uncertainty associated with it. For other compounds such as those with ARfDs based on repeat dose studies with large margins between NOAELs and LOAELs the degree of uncertainty will be large and the resulting ARfD will be conservative.

Further uncertainty and potential conservatism can occur in the ARfD if the default safety/uncertainty factor of 100 (10× for interspecies extrapolation, 10× for variability of responses in the human population) is used in the absence of specific data which support the application of chemical specific adjustment factors (CSAFs).

Attention is drawn to the fact that when the ARfD is conservative, because of a lack of appropriate toxicological data, this will be clearly stated in the relevant section of the JMPR report, together with an indication of the types of data needed to refine the estimate. The Meeting notes that since the introduction of the acute reference dose concept at the national and international level in the late 1990s, a number of conservative ARfDs which were set initially have subsequently been amended on the basis of recently generated acute toxicity data and improved guidance on the establishment of ARfDs.

Conclusions

It is recognized that the IESTI and the ARfD values are not absolute numbers but are associated with uncertainty and variability. While it is possible to reduce uncertainty, biological variability[9,10] can only be characterized. Both are set conservatively and the degree of conservatism reflects the level of uncertainty and variability in the data The IESTI calculation should assist the decision making process rather than be the sole determinant of acceptable or unacceptable risk. The calculation takes into account only the parameters presented to it. At present, the decision making process does not take into account important qualitative influences, e.g. the nature of the toxicological endpoint.

In order to improve the estimation process the uncertainty of the individual components of the estimation should be examined and possible ways of improvements be identified.

The Meeting recommended that FAO and WHO address the issues identified in this document, with the participation of all relevant stakeholders. The main objectives would be the improvement of the estimation of the short-term dietary intake of pesticides and of the interpretation of the outcome of the short-term assessment conducted by the JMPR. The discussion should include *inter alia* the following specific issues:

- Uncertainty and variability of the parameters used in the estimation;
- Ways to improve the consumption, unit weight and body weight data provided to the JMPR;
- Identification of additional subgroups of the population for which the assessment should be conducted, e.g., toddlers;
- The adequacy of the IESTI equations when residues from monitoring/enforcement data are used or the need of a specific methodology for this application;
- How to improve communication between the JMPR and the risk managers and the public on the output of the risk assessment conducted by the Meeting

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[9] Uncertainty: Imperfect knowledge concerning the present or future state of an organism, system, or (sub) population under consideration. (IPCS Risk Assessment Terminology, WHO Geneva 2004).

[10] Variability: Heterogeneity of values over time, space, or different members of a population, including stochastic variability and controllable variability. Variability implies real differences among members of that population. National Resource Council, Science and Judgement in Risk Assessment (National Academy Press, Washington, DC, 1994).

②　WHO で IESTI 評価に使用されている数値の例

http://www.who.int/foodsafety/chem/acute_data/en/index.html　より

HIGHEST REPORTED 97.5th PERCENTILE CONSUMPTION FIGURES (EATERS ONLY) FOR VARIOUS COMMODITIES BY THE GENERAL POPULATION AND CHILDREN AGES 6 AND UNDER (Updated April 2008 - Note latest changes in bold)

(表の一部)

Codex Code	Commodity	General Population (g/kg bw/day)	Reporting Country	Children ≥ 6 Years (g/kg bw/day)	Reporting Country
AP 1	Honey	0.86	Australia	2.26	Australia
CF 1210	Wheat germ	3.33	France	0.53	USA
CF 1211	Wheat flour	**9.17**	**France**	**12.95**	**France**
CF 1212	Wheat wholemeal	2.39	USA	4.91	USA
CF 1250	Rye flour	1.84	France	1.18	USA
CF 1251	Rye wholemeal	0.51	USA	0.68	USA
CF 1255	Maize flour	**2.04**	**France**	3.16	Australia
CM 81	Bran, unprocessed	0.55	Australia	0.67	Australia
CM 649	Rice, husked	6.07	Japan	**6.40**	**France**
CM 654	Wheat bran, unprocessed	1.23	USA	1.98	USA
CM 1205	Rice, polished	7.70	Thailand	12.49	Japan
CM 1206	Rice bran, unprocessed	0.75	Australia	0.21	USA
CP 179	Bread & other cooked cereal products	7.19	Japan	14.27	Japan
CP 1211	White bread	**9.08**	**France**	19.00	S. Africa
CP 1212	Wholemeal bread	7.10	S. Africa	16.90	S. Africa
CP1250	Rye bread	3.60	Australia	10.63	Australia
	Water chestnut *(Eleocharis tuberose* Schult)	5.10	Thailand	7.85	Thailand
DF 14	Dried prunes	4.66	USA	8.95	Australia
DF 167	Dried fruits	2.22	France	5.67	France
DF 226	Apple, dried	0.14	Australia	0.23	Australia
DF 240	Apricots, dried	0.47	Australia	1.29	Australia
DF 247	Peach, dried	0.75	Australia	1.82	USA
DF 295	Dates, dried or dried & candied	**2.15**	**Australia**	**3.30**	**Australia**
DF 297	Figs, dried or dried and candied	2.15	Australia	3.30	France
DF 301	Nectarines, dried	0.19	Australia		
DF 302	Pineapple, dried	0.42	Australia		
DF 303	Pear, dried	0.32	Australia	0.41	Australia
DF 269	Raisins (=currants, raisins & sultanas)	**1.08**	**USA**	3.95	USA
DH 170	Herbs, dried	**0.29**	**France**	**0.50**	**Australia**
DH 1100	Hops, dry	**0.25**	**France**	0.03	Japan
DM 305	Olives, processed	1.19	Australia	**1.32**	**France**
DM 659	Sugar cane molasses	3.19	Australia	8.85	Australia
DM 1215	Cocoa butter	0.36	USA	0.62	USA
DT 171	Teas (tea and herb tea)	3.13	France	4.02	France
DT 1114	Tea, green, black	0.30	Japan	0.64	Japan
FB 18	Berries and other small fruits	11.20	Australia	11.63	Australia