資料８

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Pesticide residues in food 2006

Joint FAO/WHO Meeting on Pesticide Residues

2.4 SHORT-TERM DIETARY INTAKE ASSESSMENT: UNCERTAINTIES IN THE INTERNATIONALESTIMATED SHORT-TERM IN TAKE (IESTI) CALCULATION AND ITS INTERPRETATION.

Introduction

The JMPR uses the deterministic method for the International Estimated of Short-Term Intake (IESTI) of a particular pesticide from the consumption of a food commodity. This calculation was first introduced by a WHO Consultation on exposure assessment in 1997 and further developed by the JMPR in subsequent meetings (Chapter 3; 2005 JMPR Report).

In characterizing the risks associated with the short-term dietary exposure to a pesticide from the consumption of a certain food, the IESTI is compared with the established acute reference dose (ARfD) of the compound, and the intake expressed as a percentage of the ARfD. This value can then be used to make a judgment about the potential risk associated with the consumption of that food commodity.

In a case where an IESTI calculation, for a crop/pesticide combination, results in an intake higher than 100% ARfD, the Meeting will state according to current practice: "The information provided to the JMPR precludes an estimate that the short-term dietary intake would be below the ARfD for the consumption of the commodity". Due to the uncertainties in the assessment, arising from the uncertainties in each of the parameters or assumptions used, an exceedance of the ARfD does not necessarily represent a health risk to the consumers. The establishment of an ARfD which is necessarily conservative and/or a conservative assessment of exposure will lead to an overly conservative estimate of acute dietary risk.

Some governments, regional authorities, the CCPR and the JMPR have discussed the possibilities for improvement in the methodology currently used by the JMPR in assessing the short-term dietary intake of pesticide residues.

International Estimated Short-Term Intake (IESTI)

The equations below show the IESTI calculation used currently by the JMPR for raw agricultural commodities and when post-harvest treatment of the pesticide was used in grains, oil seeds and pulses:

Case 1: U < 25 g $$IESTI = \frac{HR \times LP}{bw}$$

Case 2: U ≥ 25g

Case 2a: LP > U $$IESTI = \frac{HR \times \nu \times U + (LP - U) \times HR}{bw}$$

Case 2b: LP < U $$IESTI = \frac{HR \times \nu \times LP}{bw}$$

Where:

HR = highest residue in composite samples from supervised trials conducted according to GAP, in mg/kg

ν = variability factor, which gives the relationship between the 97.5th percentile of the residues in crop units and the average residue in the sampled lot of the commodity

LP = highest large portion provided (97.5th percentile of eaters), in kg of food per day

U = median unit size unit weight of the crop unit examined, in kg

Bw = mean body weight, of the selected population, in kg.

The information on each of these parameters and the limitations attached to the data provided to the Meeting are described below.

---- *For processed commodities, Case 3:*

$$IESTI = STMR\text{-}P \times LP/bw$$

Highest residue

The highest residue (HR) is estimated from supervised trials evaluated by the Meeting that have been conducted according to GAP. The uncertainties in these values are mainly associated with the residue dataset available to the JMPR. For major commodities moving in trade, a minimum of eight residue trials are necessary for recommendations to be made, but for minor or specialty crops, as low as three trials could be acceptable. When only limited residue data is available, and the distribution of the residue population is not known, the resulting MRL recommendation can be substantially higher than the HR.

The HR used in the IESTI calculation refers to the residues of toxicological concern present in the edible portion of the crop, while the MRL refers to a residue definition relevant for enforcement purposes related to the commodity in trade. There is a concern that conducting the assessment using the HR value instead of the MRL might not assure the safety of consumers, mainly when the MRL is much larger than the HR. The incorporation of statistical calculation in the recommendation process in 2006 (General Consideration 2.10), will improve the consistency in the estimations of the MRL made by the JMPR based on the available data.

Variability factor

For crops with unit weight > 25 g (Case 2), a variability factor of 3 applied to the HR value will represent a unit with the highest residue value. The variability factor reflects the variability of residues in individual units and is defined as the 97.5^{th} percentile of residue data within a lot divided by the mean of the lot. The factor of 3 represents the mean of variability factors estimated from a dataset of residue data from over 22000 crop units in single plots from 13 countries representing 13 crops and 25 pesticides (2005 JMPR Report). Further improvement on this estimation may be made based on new data or new approaches.

Large portion, unit weight and body weight

Data on the consumption of large portions (LP), unit weight (U) and body weight used currently by the JMPR were provided by the governments of Australia, France, The Netherlands, Japan, Sweden, South Africa, the UK and the USA and compiled by GEMS/Food. The large portion value from each country represents the 97.5^{th} percentiles of consumers; however, the information provided to GEMS/Food does not include the method used to collect the data neither the size of the dataset which was the base of the estimated LP. Consequently, the uncertainty behind the consumption data is unknown.

In the IESTI calculation, the unit weight value (U) will determine whether a variability factor is to be applied to the HR and whether the LP will be composed by more than one crop unit (Case 2a) or will be a portion of the unit (Case 2b). The Meeting does not know whether the U values provided represent the median of units consumed in a country or a different estimation. Also, it is not clear in all cases whether that value refers to the whole commodity or the edible portion.

The body weight (bw) data provided represent the mean body weight for children and for the general population in each country. However, the correlation between the large portion and body weight of each population should be established.

The IESTI was primarily developed to assess the short-term exposure arising from the consumption of food containing residues at levels found in supervised residue trials conducted according to GAP. Some countries have been applying the IESTI equations to assess the safety of food containing residues at levels found in monitoring and/or enforcement programs. The adequacy of such an approach needs to be discussed further.

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

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

Mean Body Weights and Age Distributions for Countries Reporting 97.5th Percentile Consumption

Country	Weight (kg)		Age (years)	
	General	Children	General	Children
Australia	67	19	2 and above	2 to 6
France	52.2	18.9	3 and above	3 to 6
Netherlands	63	17	All	6 and under
Japan	52.6	15.9	All	6 and under
South Africa	55.7	14.2	10 and above	1 to 5
Thailand	53.5	17.1	3 and above	3 to 6
United Kingdom	70.1	14.5	16 to 64	1.5 to 4.5
USA	65	15	All	1 to 6

As of April 2008

Unit weight, Edible portion （表の一部）

Check unit wts Code	Commodity	Mean/ Median Unit Wt (g)	Edible Portion (%)	Net Edible Portion Wt (g)	Reporting Country	Remarks
DF14	Prunes, dried	6	83	5	France	Commodity changed from 'Plums, including prunes'
FB269	Grapes	125	94	118	France	
		150			Japan	
		456	96	438	Sweden	New data
FB275	Strawberry	14	96	13	France	
		15			Japan	
		13	95	12	UK	
		16	94	15	Belgium	New data
FC4	Oranges	190	72	137	France	Old net edible - 134 g
		200			Japan	
		229	70	160	UK	
		131	73	96	USA	
		251	71	178	Sweden	New data
		205	68	140	Belgium	New data
FC5	Shaddocks or pomelos	210	60	126	France	
		230	70	161	UK	New data
FC203	Grapefruit	400			Japan	
		340	47	160	UK	
		256	49	125	USA	
		340	49	167	Sweden	New data
		300	70	210	Belgium	New data
FC204	Lemon	100	64	64	France	
		70			Japan	
		108	67	72	USA	
		173	53	92	Sweden	New data
		115	62	70	Belgium	New data
FC205	Lime	67	84	56	USA	
FC206	Mandarins	100	72	72	France	Old net edible - 64 g
		70			Japan	
		133	75	100	UK	Old net edible - 10 g
		168	74	124	USA	
		90	67	60	Belgium	New data
FI326	Avocado	300	60	180	France	
		201	75	151	USA	
		187	67	125	Sweden	New data
		230	70	160	Belgium	New data
FI327	Banana (hand of six)	900	68	612	France	
		720			Japan	
		900	66	594	UK	
		708	68	481	USA	
		1218	63	767	Sweden	New data
FI336	Guava	90	97	87	USA	
FI341	Kiwifruit	75	86	64	France	
		120			Japan	
		76	97	74	USA	
		90	85	75	Belgium	New data
FI345	Mango	207	67	139	USA	
		339	69	234	Sweden	New data
		300	68	200	Belgium	New data

Updated 1 May 2003

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JMPR による IESTI 評価例 （2005, アセフェート，小児）

The Meeting concluded that the short-term intake of residues of acephate from uses considered by the 2003 JMPR is unlikely to present a public health concern, with the exception of pome fruit (e.g. apple, pear) flowerhead brassicas (e.g. broccoli, cauliflower), mandarin, nectarine, peach and peppers.

ACEPHATE (95) International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS** ARfD = 0.1 mg/kg bw Maximum % of ARfD: 390%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Variability factor	Case	IESTI µg/kg bw/day	%ARfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight (g)	Country	Unit weight, edible portion (g)				
FP 0226	Apple	-	6.6	USA	15.0	679	110	FRA	100	3	2a	386.74	390
JF 0226	Apple juice	1.31	-	-	-	ND	-	-	ND	ND	ND	ND	-
VS 0620	Artichoke globe	-	2.8	FRA	17.8	89	230	FRA	99	3	2b	42.00	40
VP 0061	Beans except broad bean & soya bean (green pods & immature seeds)	-	8.3	FRA	17.8	203	-	-	ND	ND	1	63.78	60
VB 0400	Broccoli	-	4.5	USA	15.0	164	608	USA	474	3	2b	147.83	150
VB 0404	Cauliflower (head)	-	4.5	NLD	17.0	209	1733	UNK	780	3	2b	166.19	170
MO 0105	Edible offal (mammalian)	-	0.022	FRA	17.8	203	-	-	ND	ND	1	0.25	0
PE 0112	Eggs	-	0.01	-	-	ND	-	-	ND	ND	1	ND	-
FP 0228	Loquat	-	6.6	-	-	ND	-	-	ND	ND	ND	ND	-
FC 0206	Mandarin	-	5.2	JPN	15.9	353	70	JPN	70	3	2a	161.33	160
MM 0095	Meat from mammals other than marine mammals: 20% as fat	-	0.022	AUS	19.0	52	-	-	ND	ND	1	0.06	0
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	-	0.022	AUS	19.0	208	-	-	ND	ND	1	0.24	0
ML 0106	Milks	0.011	-	USA	15.0	1286	-	-	ND	ND	3	0.94	1
FS 0245	Nectarine	-	4.9	AUS	19.0	302	110	FRA	99	3	2a	128.97	130
FS 0247	Peach	-	4.9	AUS	19.0	315	110	FRA	99	3	2a	132.43	130
FP 0230	Pear	-	6.6	UNK	14.5	279	100	FRA	89	3	2a	208.00	210
VO 0444	Peppers, chili	-	19.7	AUS	19.0	31	45	USA	43	3	2b	94.87	90
VO 0445	Peppers, sweet (incl. pim(i)ento)	-	19.7	AUS	19.0	60	172	UNK	160	3	2b	186.76	190
PM 0110	Poultry meat: 10% as fat	-	0.01	AUS	19.0	22	-	-	ND	ND	1	0.01	0
PM 0110	Poultry meat: 90% as muscle	-	0.01	AUS	19.0	201	-	-	ND	ND	1	0.11	0
PO 0111	Poultry, edible offal of	-	0.01	USA	15.0	37	-	-	ND	ND	1	0.02	0
FP 0231	Quince	-	6.6	NLD	17.0	1	92	USA	56	3	2b	1.19	1
VD 0541	Soya bean (dry)	0.105	-	JPN	15.9	88	-	-	ND	ND	3	0.58	1
OR 0541	Soya bean oil, refined	0.045	-	USA	15.0	35	-	-	ND	ND	3	0.11	0

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厚生労働科学研究費補助金（食品の安心・安全確保推進研究事業）
平成１８年度分担研究報告書

食物摂取量調査から見た残留農薬等の暴露評価の精密化手法及び残留農薬等の短期暴露評価法の検討

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研究要旨

2006 年 10 月に公表された最新の国民健康・栄養調査データ（1次 DB）を加えて、2001～04 年分合わせて 43,839 日・人（約 236 万フードアイテム）のデータセットを整えた。短期暴露評価の目的に最も適うように、加工食品等を農薬が使用される個々の農作物に分解するとともに、コモディティーの大きさ、バルク等に応じて分類整理した（食品（群）として 125 グループに分類）。

農薬については、2006 年度 に JMPR で評価された物質のうちから、Endosulfan と Fenamiphos を選び、各農作物の残留濃度データを抽出した。これらのデータベースに基づき、モンテカルロ法によるリスクシミュレーションツール *@RISK* を使用して、シミュレーションを試行し、わが国においてもこのような手法が適用できることを確認した。しかし、ブロッコリ中の Endosulfan とトマト中の Fenamiphos は予想に近い結果となったが、ピーマン中の Fenamiphos は予想から大きく外れた結果となった。ユニット重量と97.5 パーセンタイル消費量が大きく違うため、一点推定法との差が大きくなった可能性がある。これらのことを含めて、今後の課題を考察した。

表1　短期曝露量推定のための食品分類（国民健康・栄養調査データを基にして各群の摂取量を算出

1 米	41 だいこん	81 すいか
2 とうもろこし	42 たかな	82 すもも
3 小麦	43 たけのこ	83 プルーン
4 さつまいも	44 玉ねぎ	84 なし＋洋ナシ
5 さといも	45 チンゲンサイ	85 *その他の核果類
6 じゃがいも	46 とうがらし	86 パインアップル
7 *その他の豆類	47 とうがん	87 バナナ
8 いんげん	48 トマト	88 パパイア
9 ささげ	49 白菜	89 びわ
10 そらまめ	50 なす	90 ぶどう
11 大豆	51 菜花	91 ブルーベリー
12 アーモンド	52 にがうり	92 ぽんかん
13 栗	53 にら	93 マンゴー
14 *その他のナッツ	54 人参	94 メロン
15 その他のねぎ系統作物	55 にんにく	95 もも
16 アスパラガス	56 瓜	96 ゆず
17 枝豆	57 ピーマン	97 ライチー
18 *その他の葉菜	58 ブロッコリー	98 りんご
19 さやえんどう	59 ほうれんそう	99 レモン
20 グリンピース	60 *その他の茎葉菜	100 さくらんぼ
21 *その他のアブラナ科葉菜	61 もやし	101 しいたけ
22 おくら	62 落花生	102 しめじ
23 かぶ	63 らっきょう	103 たもぎたけ
24 かぼちゃ	64 ねぎ	104 なめこ
25 *その他の果菜類	65 レタス	105 エリンギ
26 カリフラワー	66 れんこん	106 ひらたけ
27 *その他の根菜・地下茎野菜	67 わけぎ	107 まいたけ
28 キャベツ	68 アボガド	108 マッシュルーム
29 きゅうり	69 いちご	109 すだち
30 クワイ	70 いちじく	110 人参ジュース
31 *その他のアブラナ科野菜*葉菜を除く	71 うめ	111 みかん果汁
32 ごぼう	72 みかん	112 オレンジ果汁+その他の果汁
33 こまつな	73 オレンジ	113 ぶどう果汁
34 ししとうがらし	74 *その他のかんきつ類	114 りんご果汁
35 しゅんぎく	75 柿	115 レモン果汁
36 しょうが	76 キウイフルーツ	116 ごま油
37 しろうり	77 *その他のトロピカルフルーツ	117 とうもろこし油
38 ズッキーニ	78 *その他のベリー類	118 オリーブ油
39 せり	79 グレープフルーツ	119 米ぬか油
40 セロリー	80 さくらんぼ	120 大豆油
		121 なたね油
		122 ひまわり油
		123 綿実油
		124 *その他の植物油
		125 落花生油