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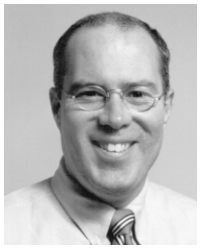
Risk in Perspective

THE PRECAUTIONARY PRINCIPLE IN PRACTICE: COMPARING US EPA AND WHO PESTICIDE RISK ASSESSMENTS



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"If further work confirms these findings, this analysis would seem to confirm that, at least for Acceptable Daily Intakes for pesticides in foods, the US is indeed more precautionary."

Overview

Although the Precautionary Principle (PP) (Risk In Perspective, vol. 7, issues 3 and 6) describes a general approach to confronting risks, it is less clear on how to use the PP to make specific management decisions ranging from product bans to the setting of exposure standards. In the debate over the implementation of the PP, the United States government has argued for several years and multiple presidential administrations that American approaches to risk management already embody precaution. The presence of "conservative" assumptions and choices in the risk assessment process, it is argued, make US decisions "precautionary."

This article describes a study of actual risk management decisions informed by specific risk assessment methods and choices, focusing on Acceptable Daily Intakes (ADIs) set by the U.S. Environmental Protection Agency (EPA) and the World Health Organization (WHO) . We show that U.S. standards, at least in this instance, are indeed more precautionary on average than those set by the WHO and that the difference is likely due to conservative choices made in the risk assessment process.

Introduction

Organizations around the world establish standards for pesticide exposure. Referred to as Reference Doses, Acceptable Daily Intakes, or Tolerable Intakes, these standards are used to establish a level of pesticide residues on food products that will pose a negligible risk to consumers. These approaches are used in addressing non-cancer risks, types of toxicologic outcomes that are not related to potential increases in cancer rates. In most cases, tools of risk assessment are used to establish these levels. Epidemiologic and toxicologic data are evaluated to determine a "critical effect" that is used in dose response evaluation. In most cases, the No-Observed-Adverse-Effect-Level (NOAEL) dose for the critical effect is adjusted by factors, alternatively known as safety factors or uncertainty factors or adjustment factors, to establish an acceptable dose of exposure that

is usually 100 times or more below the dose causing no effect in animals. A *de minimus* level of risk is then used in setting specific pesticide/crop tolerances. These dose levels are then converted into the ADI metric by establishing estimates of intake based on the different crops on which the pesticides are used and the consumption patterns of foods derived from those crops.

In this study, Acceptable Daily Intakes (ADIs) established by the United States EPA and the WHO, for the same pesticides, are compared through calculation of the ratio of the EPA ADI to the WHO ADI. There are two questions addressed by such an evaluation. First, is one organization or the other more stringent, on average, in the setting of ADIs? Second: Do the organizations differ in the stringency of ADIs when a compound is a suspected carcinogen. While both US EPA and WHO principally focus on non-cancer effects when setting ADIs (W. Burnam, personal communication) it may be that knowledge of possible carcinogenicity plays a role.

Here an important difference arises. If a compound is a suspected carcinogen the U.S., EPA uses a conservative linear no-threshold approach in deriving a probabilistic estimate of risk for use in risk management. The WHO specifically rules out the use of probabilistic methods for risk assessment of carcinogens (International Program on Chemical Safety, 1990). To investigate whether the two groups might assess the non-cancer risks of suspected carcinogenic compounds differently, the ratios were examined separately for potential carcinogens and non-carcinogens. Finally, possible reasons for differences in stringency between US EPA and WHO are discussed, as are the implications of our findings for discussions about the role of precaution in risk assessment and management.

Methods

EPA and WHO ADI values were taken from the 1997 US EPA Reference Dose Tracking Report (US EPA, 1997). A selection of the WHO values was checked against the International Program on Chemical Safety Inventory of IPCS and WHO Pesticide Evaluations through 2001 (International Program on Chemical Safety, 2003). Only compounds with both EPA and WHO ADI values were compared. Banned pesticides were removed. There were a total of 111 pesticides in

Table 1: EPA and WHO Acceptable Daily Intake Values for Pesticides

Name	CASRN*	EPA ADI (mg/kg/day)	WHO ADI (mg/kg/day)
2,4-D (acid+salts)	94-75-7	0.0100	0.3000
Acephate	30560-19-1	0.0040	0.0300
Aldicarb (Tern ik)	116-06-3	0.0010	0.0030
Anilazine (Dyrene)	101-05-3	0.0004	0.1000
Avermectin B1	65195-55-3	0.0004	0.0001
Azinphos-methyl (Guthion)	86-50-0	0.0015	0.0050
Baycor (Bitertanol)	55179-31-2	0.0063	0.0100
Baygon (Propoxur)	114-26-1	0.0050	0.0200
Bendiocarb	22781-23-3	0.0050	0.0040
Bentazon (Basagran)	25057-89-0	0.0300	0.1000
Biferthrin (Talstar)	82657-04-3	0.0150	0.0200
Bromorn ethane	74-83-9	0.0014	1.0000
Captan	133-06-2	0.1300	0.1000
Carbaryl	63-25-2	0.0140	0.0100
Carbofuran	1563-66-2	0.0050	0.0100
Carbophenothion	786-19-6	0.0001	0.0005
Carbosulfan (FMC 35001)	55285-14-8	0.0100	0.0100
Chlorobenzilate	510-15-6	0.0200	0.0200
Chlorothalonil	1897-45-6	0.0200	0.0300
Chlorpyrifos	2921-88-2	0.0030	0.0100
Chlorpyrifos-methyl	5598-13-0	0.0100	0.0100
Clofentezine (Apollo)	74115-24-5	0.0130	0.0200

Table 1: EPA and WHO Acceptable Daily Intake Values for Pesticides — continued

Name	CASRN*	EPA ADI (mg/kg/day)	WHO ADI (mg/kg/day)
Cyfluthrin (Baythroid)	68359-37-5	0.0250	0.0200
Cyhalothrin/Karate	68085-85-8	0.0010	0.0200
Cyhexatin (TCTH)	13121-70-5	0.0008	0.0010
Cypermethrin (Ammo)	52315-07-8	0.0100	0.0500
Cyrom azine (Larvadex)	66215-27-8	0.0075	0.0200
Deltamethrin (Deca-)	52918-63-5	0.0100	0.0100
Diazinon	333-41-5	0.0001	0.0020
Dichlorvos (DDVP)	62-73-7	0.0050	0.0040
Dicloran (DCNA/Botran)	99-30-9	0.0250	0.0300
Dicofol (Kelthane)	115-32-2	0.0012	0.0020
Difubenzuron (Dimilin)	35367-38-5	0.0200	0.0200
Dimethipin (Harvade)	55290-64-7	0.0200	0.0200
Dimethoate	60-51-5	0.0005	0.0100
Dinocap (Karathane)	39300-45-3	0.0040	0.0010
Diphenylamine	122-39-4	0.0300	0.0200
Diquat dibromide	85-00-7	0.0050	0.0020
Disulfoton	298-04-4	0.0003	0.0003
Dodine acetate	(NA)	0.0040	0.0100
Ebufos Icadusafos/Apache)	95465-99-9	0.0000	0.0000
Endosulfan	115-29-7	0.0060	0.0060
Ephephon	16672-87-0	0.0180	0.0500
Ethion	563-12-2	0.0005	0.0020
Ethofenprox (Etofenprox)	80844-07-1	0.0500	0.0300
Ethoprop (Ethoprophos)	13194-48-4	0.0001	0.0003
Ethoxyquin	91-53-2	0.0300	0.0600
Ethylene thiourea (ETU)	96-45-7	0.0001	0.0040
Fenamiphos (Nemacur)	22224-92-6	0.0001	0.0005
Fenbutatin oxide (Vendex)	13356-08-6	0.0500	0.0300
Fenitrothion (Sumithion)	122-14-5	0.0013	0.0050
Fenpropathrin (Danitol)	39515-41-8	0.0250	0.0300
Fensulfothion	115-90-2	0.0003	0.0003
Fenthion	55-38-9	0.0007	0.0010
Fenvalerate (Pydrin)	51630-58-1	0.0250	0.0200
Flusilazole (Nustar)	85509-19-9	0.0007	0.0010
Folpet	133-07-3	0.0090	0.0100
Glufosinate-ammonium	77182-82-2	0.0200	0.0200
Glyphosate (+salts)	1071-83-6	2.0000	1.7500
Hexaconazole (Anvil)	79983-71-4	0.0200	0.0050
Hexythiazox (Savey)	78587-05-0	0.0250	0.0300
Imazalil	35554-44-0	0.0250	0.0300
Iprodione (Glycophene)	36734-19-7	0.0600	0.2000
Isofenphos (Amaze)	25311-71-1	0.0005	0.0010
Lindane (gamma BHC)	58-89-9	0.0047	0.0080
Malathion	121-75-5	0.0200	0.0200
Maleic hydrazide	123-33-1	0.2500	0.5000
Mancozeb	(NA)	0.0030	0.0300
Maneb	12427-28-2	0.0050	0.0500
Metalazyl	57837-19-1	0.0740	0.0300
Mthamidophos (Monitor)	10265-92-6	0.0010	0.0040
Methidathion	950-37-8	0.0015	0.0010
Methiocarb (Mesurol)	2032-65-7	0.0050	0.0010
Methomyl	16752-77-5	0.0080	0.0300
Methoxychlor	72-43-5	0.0050	0.1000
Methyl parathion	298-00-0	0.0003	0.0200
Metiram	9006-42-2	0.0003	0.0300
Mevinphos (Phosdrin)	7786-34-7	0.0003	0.0015
Monocrotophos (Azodrin)	6923-22-4	0.0001	0.0006
Myclobutanil (Systane/Rally)	88671-89-0	0.0250	0.0300
Oxamyl (Vydate)	23135-22-0	0.0002	0.0300
Oxydemeton-methyl	301-12-2	0.0005	0.0003
Oxythioquinox (Morestan)	(NA)	0.0060	0.0060
Paclobutrazol	76738-62-0	0.0250	0.0100
Paraquat dichloride	1910-42-5	0.0045	0.0040

Table 1: EPA and WHO Acceptable Daily Intake Values for Pesticides — continued

Name	CASRN*	EPA ADI (mg/kg/day)	WHO ADI (mg/kg/day)
Parathion (Ethyl pararthion)	56-38-2	0.0003	0.0050
Pentachloronitrobezene	82-68-8	0.0030	0.0070
Permethrin	52645-53-1	0.0500	0.0500
Phorate (Thimet)	298-02-2	0.0005	0.0002
Phosalone	2310-17-0	0.0025	0.0010
Phosmet (Imidan)	732-11-6	0.0100	0.0200
Phosphamidon	13171-21-6	0.0002	0.0005
Piperonyl butoxide	51-03-6	0.0175	0.0300
Pirimiphos-methyl	29232-93-7	0.0100	0.0300
Prochloraz	67747-09-5	0.0075	0.0100
Procymidone (Sumilex)	32809-16-8	0.0350	0.1000
Profenofos (Curacron)	41198-08-7	0.0001	0.0100
Propargite (Omite)	2312-35-8	0.0400	0.1500
Propiconazole (Banner/Tilt)	60207-90-1	0.0130	0.0400
Pyrethrins	121-21-1	0.0640	0.0400
Sumithrin(Phenothrin)	26002-80-2	0.0710	0.0700
Terbufos	13071-79-9	0.0001	0.0002
Thiabendazole (+salt)	148-79-8	0.1000	0.1000
Thiodicarb (Larvin)	59669-26-0	0.0300	0.0300
Thiophanate-methyl	23564-05-8	0.0800	0.0800
Thiram	137-26-8	0.0080	0.0100
Triadimenfon (Bayleton)	43121-43-3	0.0400	0.0300
Triadimenol (Baytan)	55219-65-3	0.0380	0.0500
Triforine(Funginex)	26644-46-2	0.0250	0.0200
Triphenyltin hydroxide	76-87-9	0.0003	0.0005
Vindozolin (ronilan)	50471-44-8	0.0120	0.0700

(* CHEMICAL ABSTRACT SERVICE REGISTRATIOIN NUMBER)

The ADIs were compared by constructing the ratio of the US EPA ADI to the WHO ADI. The distribution of ratios was then plotted and evaluated.

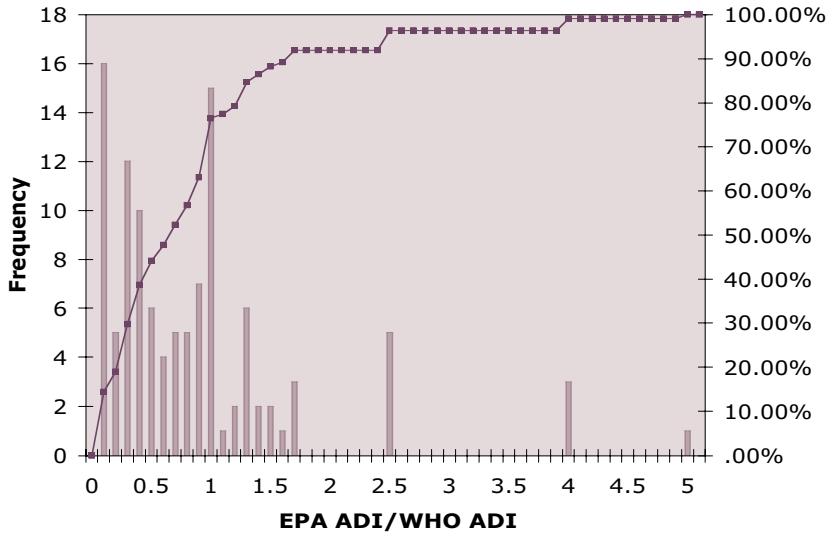
Findings

The distribution of ADI ratios is in Figure 1, illustrating more ratios below one (EPA value more stringent) than above. The geometric mean of the ratios is 0.44.

Also plotted are the distributions for pesticides designated as category B (probable human carcinogen) or C (possible human carcinogen-quantify) by the US EPA (Fig. 2) and those considered non-carcinogens (Fig. 3). The geometric mean for the potential carcinogens is 0.41 and for the non-carcinogens it is 0.46. Although there is no significant difference in the geometric means

FIGURE 1

Ratios of EPA/WHO ADI for 111 Pesticides



for the two distributions, for carcinogens only 6 out of 38 (16%) of WHO values are lower than the EPA values. For non-carcinogens only 20 out of 74 (27%) WHO values are lower – more stringent – than EPAs.

There are many compounds with the same ADI from both organizations, but it is clear that, on average, the EPA sets lower ADIs than does the WHO. It is likely that differences in risk assessment approaches play some role in this difference.

This finding is surprising in that both EPA and WHO use the same "safety factor" or "uncertainty factor" approach to non-cancer risk assessment in establishing ADIs (Barnes and Dourson, 1988). There are, however, additional important choices and assumptions in the risk assessment process that could explain more stringent assessments from US EPA. Perhaps the most likely explanation for the differences is the severity of endpoints chosen as the "critical effect" in evaluating the toxicological test results for a chemical. It may be that the EPA focuses on more subtle endpoints while the WHO process chooses toxicological effects with more direct correlation with clinical effects that occur at higher levels of exposure. These sorts of judgments are rarely dictated by formal procedures or guidelines but are more often part of the "culture"

FIGURE 2

Ratios of EPA/WHO ADI for 38 Carcinogenic Pesticides

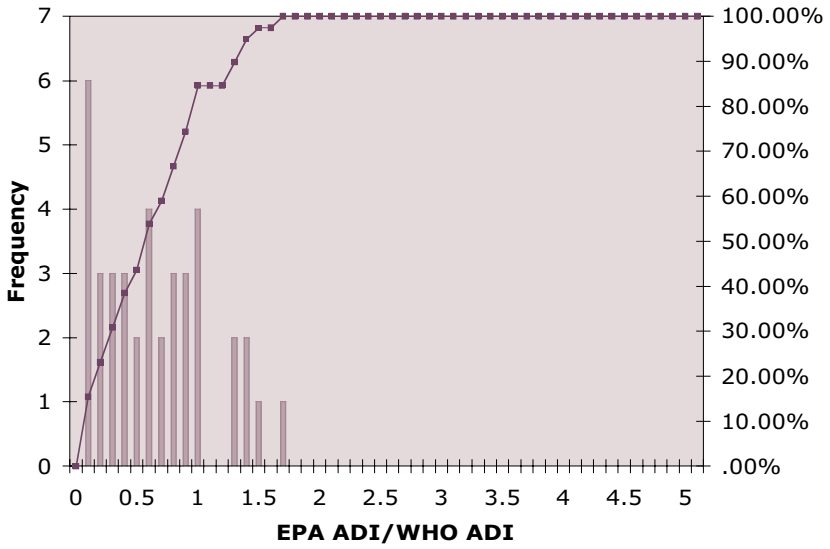
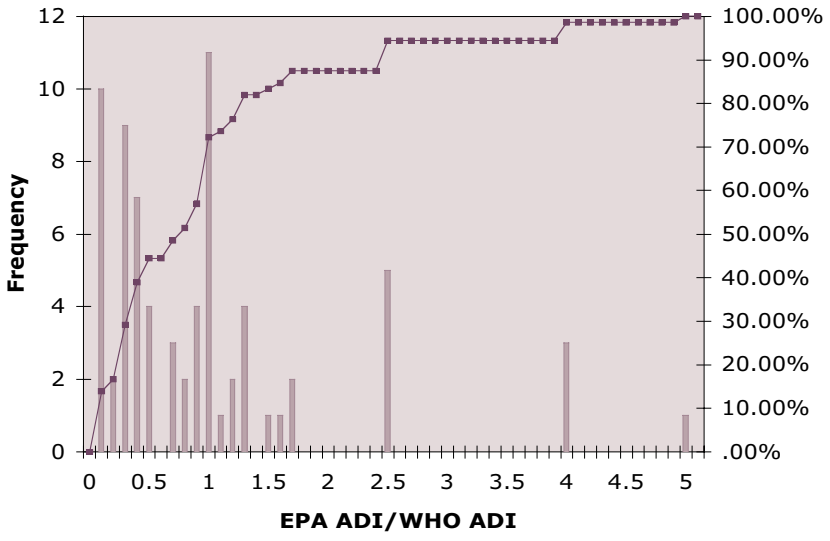


FIGURE 3

Ratios of EPA/WHO ADI for 74 Non-Carcinogenic Pesticides



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of a particular organization and, for this reason, may be less obvious to observers.

Although neither group uses potential cancer findings in setting ADIs it is conceivable that knowledge of potential carcinogenicity might influence setting of the ADI. While the geometric mean of the ADI ratios for carcinogens is similar to that for non-carcinogens (0.41 vs. 0.46), the distributions do suggest that US EPA may be even more stringent in setting ADIs (nominally based on non-cancer effects) if a compound is a suspected carcinogen.

A potential shortcoming of this analysis is the lack of control for the timing of ADI establishment. It is possible that the timing of pesticide review and ADI establishment (or revision) could differ between organizations. If new data and information become available there could be valid scientific reasons for different ADIs set at different times. However, there seems to be little reason to expect that either EPA or WHO has significantly more new (or old) values.

This preliminary analysis does identify several risk assessment issues that are likely to extend to other arenas of risk management. First, are different "safe" levels for the same compounds due to differences in risk assessment methods rather than differences in data? If variations in degrees of stringency are indeed due to different risk assessment techniques and choices, then it raises questions for harmonization of risk management across jurisdictions. The second issue is related to the U.S.-E.U. debate around the precautionary principle (Löfstedt, 2002). The U.S. government has argued that American approaches to risk management already embody precaution through conservative risk assessment approaches (e.g, Graham, 2002). If further work confirms these findings, this analysis would seem to confirm that, at least for Acceptable Daily Intakes for pesticides in foods, the US is indeed more precautionary.