Harmonization of Guidelines between Office of Prevention, Pesticides and Toxic Substances and Organization for Economic Cooperation and Development

Science Oversight Group

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Harmonization of Guidelines between Office of Prevention, Pesticides and Toxic Substances and Organization for Economic Cooperation and Development

I. Introduction

International harmonization of ecotoxicity test guidelines may reduce the burden of repeated testing from chemical companies attempting to satisfy similar data requirements. Further, if the various nations review comparable data in a comparable way, reviews can be shared. Shared data and data reviews save resources for participating nations and eliminate redundant waiting periods for chemical companies.

All data submission guidelines can be harmonized, where regulatory questions are similar. Within this assumption, OPPTS has given staff members two goals: harmonization and continued support of regulatory needs. OPP and OPPT have resolved most harmonization issues except test species and the age of test birds. These two issues also can be harmonized, but will require additional steps.

Harmonization has been undertaken to increase regulatory efficiency and multi-lateral communication, while reducing non-tariff trade barriers. Specifically, with toxic chemicals and pesticides, four advantages of harmonization have emerged:

- decreased market-entry, financial and time burden on industry;
- improved international efficiency of information exchange;
- common review of comparable data; and
- increased confidence that common conclusions are reached.

To meet regulatory needs, all submitted data must answer scientific questions applied to informed risk management decisions. The four primary risk management needs for toxic chemicals and pesticides are:

- identification of hazard and risk;
- comparative assessments of alternative pesticides;
- evaluation of risk reduction for mitigation options; and
- scientific defense of regulatory decisions.

The purpose of this meeting is twofold. The first is to respond to the July 15, 1993 Firestone memo that followed the July 14, 1993 meeting of the Science Oversight Group (SOG). The second is to raise for consideration the remaining issue in Organization for Economic Cooperation and Development (OECD) guidelines harmonization: the age of birds in avian dietary studies.

II. Issue I: Test Species

A. Regulatory utility

OPP and OPPT have resolved most of the harmonization issues except test species. Differences in test species selection is a generic issue between OPPTS and OECD guidelines. OPPTS testing guidelines currently designate a limited number of species. For pesticide registration, LC_{50} tests are required for rainbow trout (cold-water species) and bluegill sunfish (warm-water species). Similarly, avian LC_{50} tests are required for the mallard duck and bobwhite quail. In contrast, OECD guidelines allow selection from among a broader group of test animals which includes non-native and less sensitive species. (Figure 7 compares OPP and OECD species for four tests: avian dietary, avian reproduction, fish acute toxicity and freshwater invertebrate.)

When OPP presented the species issue to the SOG on July 14, some questions were raised. Principally, SOG members asked OPP to demonstrate whether species variation is actually great enough to affect regulatory decisions. Specifically, the Firestone memo of July 15, 1993 asked OPP to:

- analyze the distribution of species differences;
- use case studies to demonstrate how alternative species would affect regulatory decisions;
- identify international testing policies; and
- assess OECD reaction to changes in choosing test species for ecotoxicity testing.

Species selection

Species selection is important in the guideline harmonization effort because it critically affects OPP's ecological risk assessment and risk management processes. Test species selection has a substantial impact on identification of risk, comparison of chemicals and defense of risk assessment and risk management decisions of the pesticide program. OPPT guidelines and data needs are less affected, as test species selection is a less critical issue in their regulatory program.

Ecological risk identification

Ecological risk identification is partially based on the relative sensitivity of the species tested. If insensitive test species are used, pesticide risk may be underestimated. This problem can be partially solved by an assessment factor such as that utilized in OPPT assessments. In the pesticide program, where a large proportion of the substances pose significant risk to non-target species, this concern is somewhat less central to the programs operation than chemical comparison, which allows us to set priorities among many risk targets.

Defending decisions

The use of native game species in ecotoxicology is a long-standing practice that aids in defending decisions. Historically, risk management decisions have been based on risk to native species that are likely to be exposed and are of concern to the public. The importance of this native species factor depends heavily on the audience, however. It may mean very little to those who are accustomed to dealing only with human health risk assessments, where interspecies extrapolation is almost always required. Professional ecologists and wildlife and fisheries biologists in North America favor the continued use of native species to address the concerns of those who hunt, fish or engage in other outdoor activities.

Comparative ecological risk assessments are an important aspect of the pesticide program. Alternative comparisons for the same pesticide use are prepared for:

- all special reviews where ecorisk triggers are included,
- RED reviews where ecorisk levels of concern have been exceeded,
- new pesticide or new use reviews where ecorisk levels of concern have been exceeded, and
- new pesticide reviews under the safer pesticide policy.

The above OPP activities are very important because numerous pesticides pose high risks to non-target species. Given the agricultural need for pesticides, it will be a long time before we can eliminate pesticide risks to ecosystems. We can reduce them, however, and comparisons of different pesticide alternatives are central to pesticide risk reduction.

For the foreseeable future, comparative risk assessments for pesticide alternatives will be made with laboratory data, rather than incident reports. Incident reports can confirm risk, but rarely allow direct comparisons of one pesticide to another. This is particularly true since comparison of potential use rather than current use is most needed. For example, Diazinon has a long list of bird kills. But the mere absence of bird incidents for its alternatives does not indicate that they will be safer if used in place of Diazinon. The alternatives may lack incident reports because they are not used much (or at all, if the alternative chemical is new) or because they are used where fewer birds are exposed or where incidents are unlikely to be detected and reported.

Because chemical comparisons are the most crucial OPP task affected by the species issue, specific case studies (Section II-A.2, page 8) demonstrate how the species tested may affect OPP decisions.

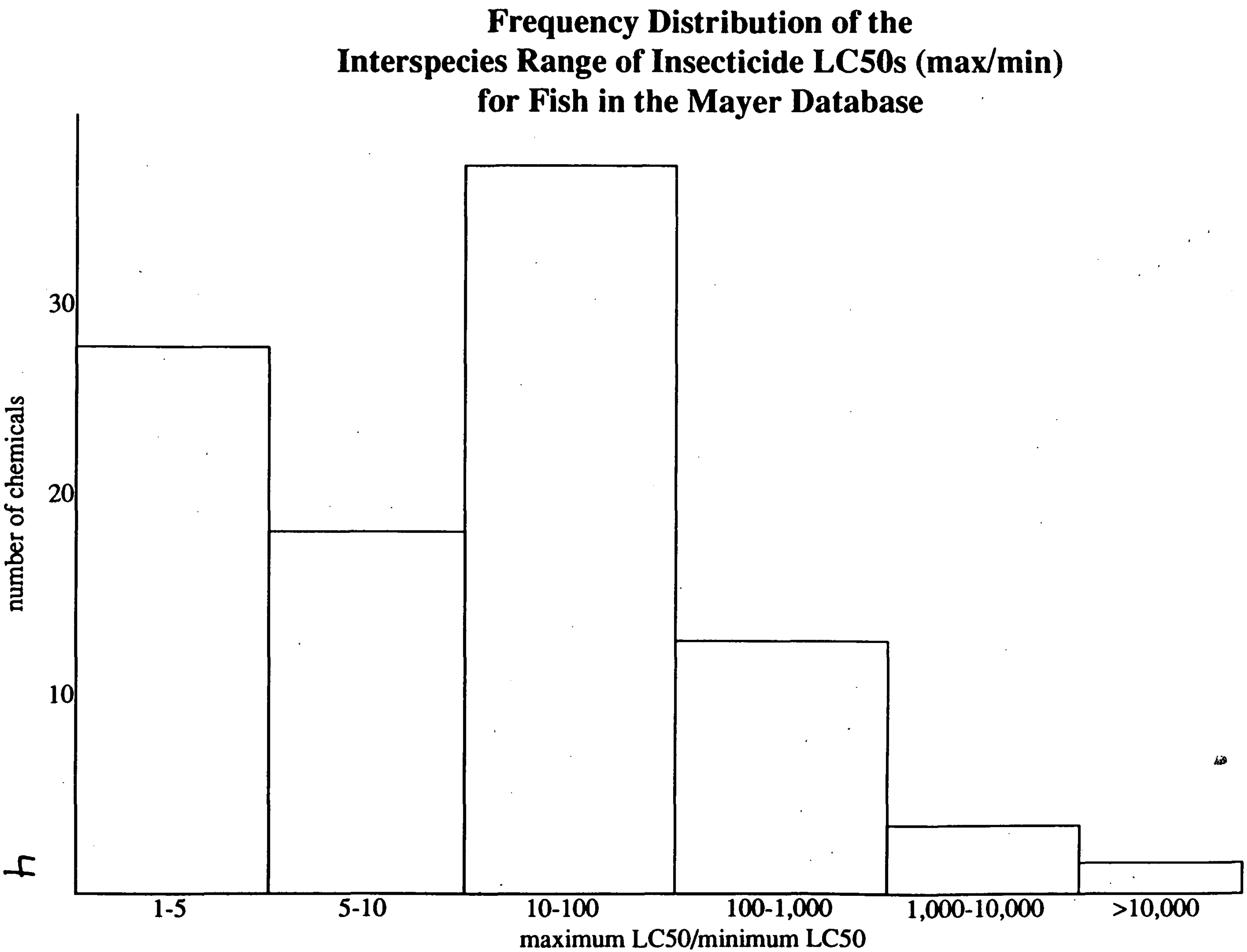
1. Species data

Species variation in the susceptibility of organisms to pesticides is well documented (Department of Health, Education and Welfare, 1969; Macek and McAllister, 1970; Hill *et al.*, 1975; Kenaga, 1978, 1979; Tucker and Leitzke, 1979; Doherty, 1983; LeBlanc, 1984; Suter and Vaughan, 1985; Thurston *et al.*, 1985; Mayer and Ellersieck, 1986; Mayer *et al.*, 1987; Joermann, 1991; Hill, 1992; Suter, 1985). LeBlanc (1984) reported that taxonomic relationships have a much greater influence on comparative sensitivities to pesticides than to other chemicals. He reasoned that pesticides kill target organisms by specific modes of action, and responses vary more among all taxa than among related species.

Evaluation of interspecies sensitivity differences must compare data from a large number of chemicals and species tested under identical or substantially similar conditions. For fish, data compiled in Mayer and Ellersieck (1986) include results from 4,902 tests performed with 66 species and 410 chemicals. (See Figure 1 for fish species tested on insecticides.) For the graphs presented here, the data were narrowed to obtain the four most frequently tested fish species (rainbow trout, bluegill sunfish, channel catfish and fathead minnow). The data were further selected to include only those tests conducted with technical-grade materials, similar environmental conditions, and generally conformed to ASTM standard methods. Although this analysis covers many North American test species, it fails to include some OECD species (carp, Japanese medaka, zebrafish and guppy). Data were not available to evaluate the variation that might be introduced by the use of these species. Given these specified conditions, 42 chemicals were compared.

For birds, the data set is limited to chemicals for which test data are available on the avian test species of interest. The avian data used in the OPP sensitivity analyses were LC_{50} values on 50 pesticides from Hill *et al.* (1975), LD_{50} values for six avian species with 16 pesticides from Tucker and Haegele (1971), and bobwhite quail and mallard duck LD_{50} values for 18 pesticides from Hudson *et al.* (1984). For data from Hudson *et al.*, an attempt was made to match toxicity values on birds of the same age, same sex, and same chemical purity. When more than one toxicity value was available or the toxicity value was a range, the mean value was used in the comparison.

Figures 2, 3 and 4 compare species response across the test compounds (X axis) against the log of the LC_{50} (Y axis). The chemicals are ranked by decreasing toxicity for a given species (the lower the LC_{50}, the greater the toxicity). The chemicals are identified by numbers in the key on appendix page 1-7.



Frequency Distribution of the
Interspecies Range of Insecticide LC50s (max/min)
for Fish in the Mayer Database
number of chemicals
30
20
10
1-5
5-10
10-100
100-1,000
1,000-10,000
>10,000
maximum LC50/minimum LC50

Figure 1

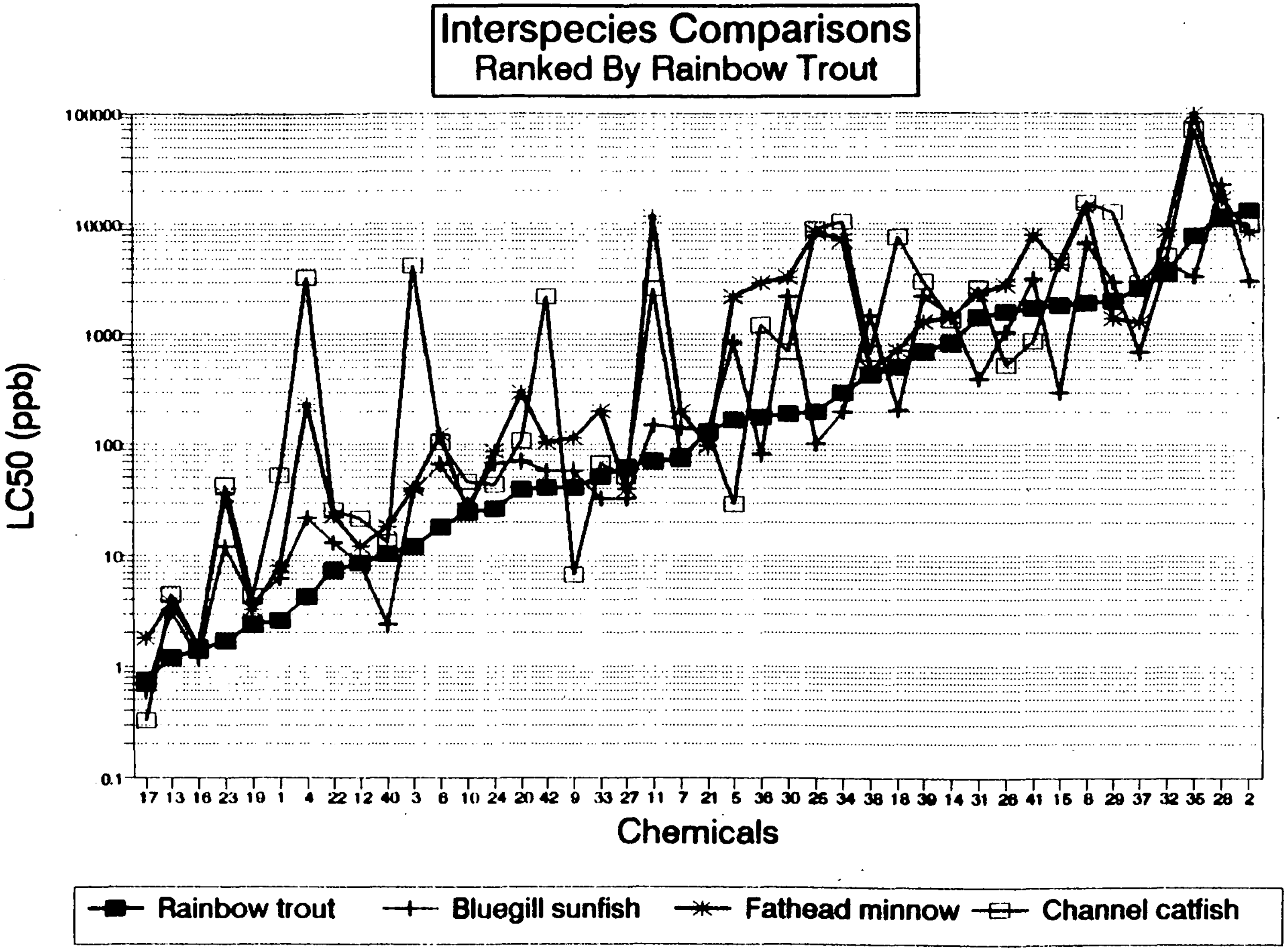
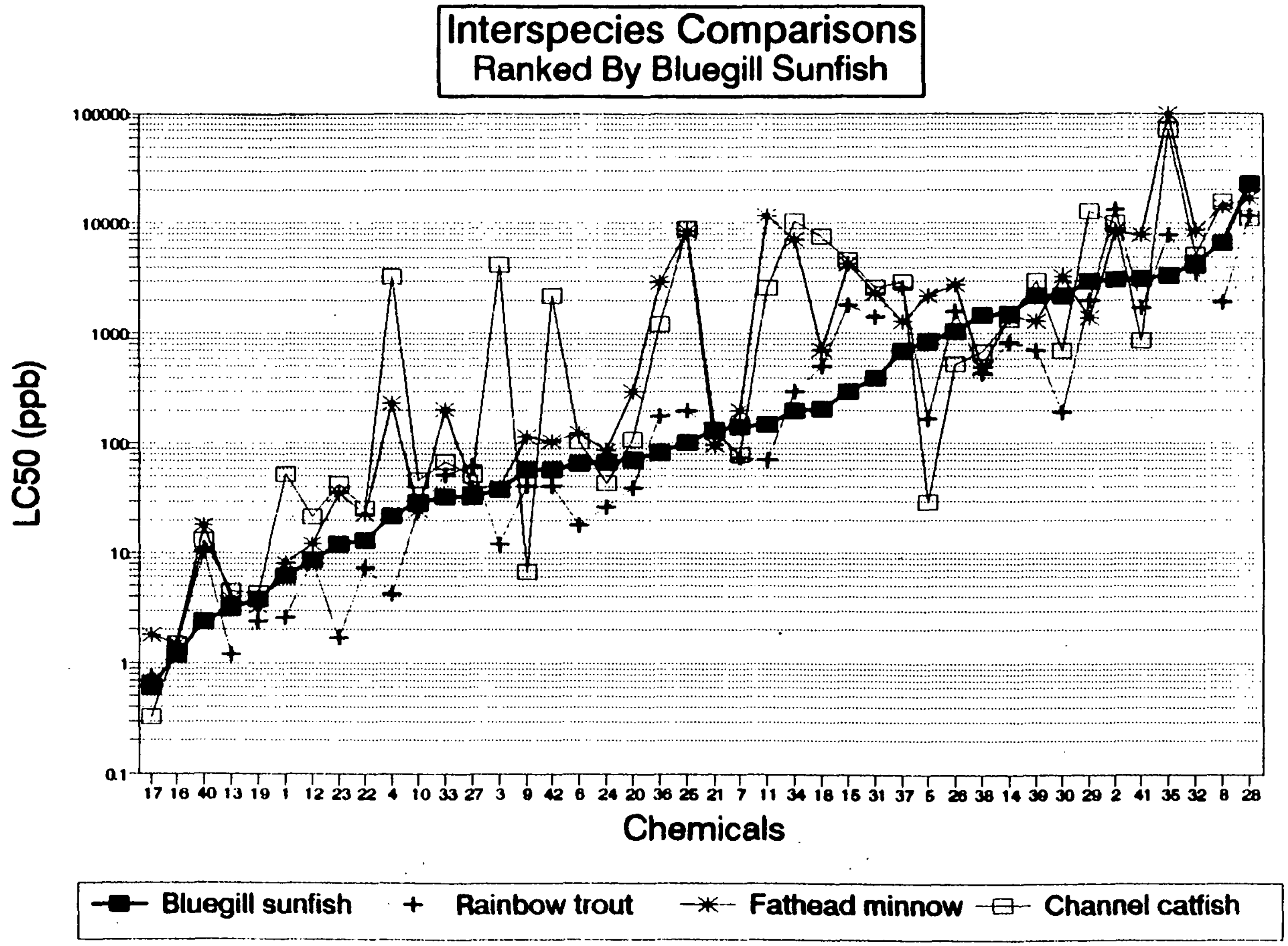

Interspecies Comparisons
Ranked By Rainbow Trout
100000
10000
1000
100
10
1
0.1
LC50 (ppb)
17 13 16 23 19 1 4 22 12 40 3 6 10 24 20 42 9 33 27 11 7 21 5 36 30 25 34 38 18 39 14 31 26 41 15 8 29 37 32 35 28 2
Chemicals
Rainbow trout
Bluegill sunfish
Fathead minnow
Channel catfish

Figure 2

5



Interspecies Comparisons
Ranked By Bluegill Sunfish
LC50 (ppb)
100000
10000
1000
100
10
1
0.1
17 16 40 13 19 1 12 23 22 4 10 33 27 3 9 42 6 24 20 36 25 21 7 11 34 18 15 31 37 5 26 38 14 39 30 29 2 41 35 32 8 28
Chemicals
Bluegill sunfish
Rainbow trout
Fathead minnow
Channel catfish

Figure 3

Interspecies Comparisons
Ranked by Bobwhite Quail

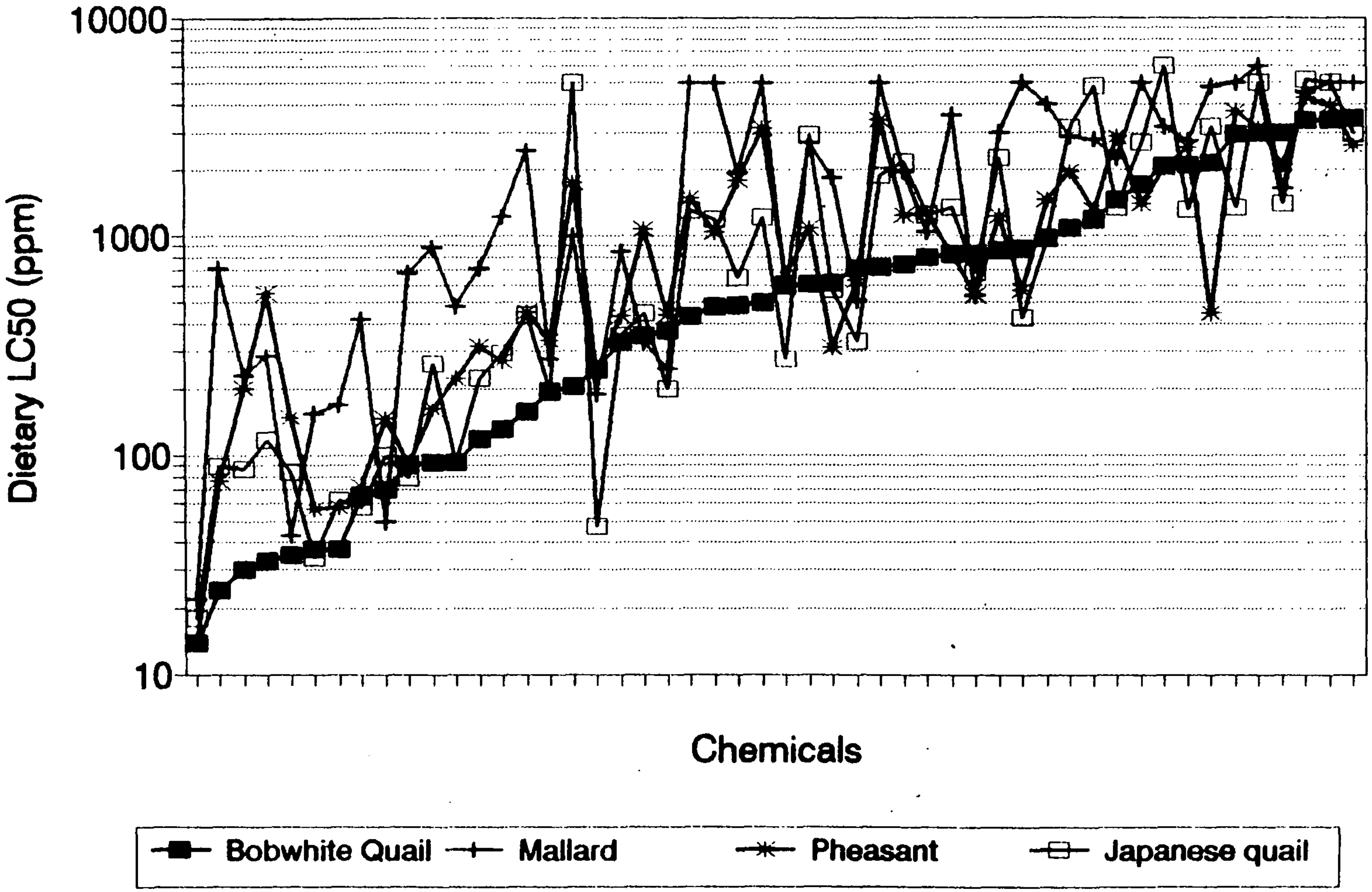


Figure 4

7

The figures show that there is a rough correlation among a wide range of toxicities; that there are large differences in sensitivity between species; and that some species tend to be more sensitive to pesticides than others.

2. Case Studies: Clusters and "Safer Chemicals"

The cluster approach to reviewing existing pesticides focuses on a specific crop use pattern. Chemicals having the same use pattern are reviewed simultaneously. Using the cluster approach, OPP can compare risks if one or more pesticides are canceled or restricted, since the probable alternatives are evaluated at the same time.

OPP intends to promote the registration of safer pesticides. One way to achieve this goal is by easing the registration process for pesticides that appear to be safer than those currently registered. Often, pesticides proposed as safer by their manufacturers have fairly high toxicity to non-target species other than mammals. However, they still may pose substantially less risk than the chemicals currently on the market. Hazard and risk comparisons evaluate the degree to which these pesticides are "safer."

Case Study I: Corn Insecticide Cluster

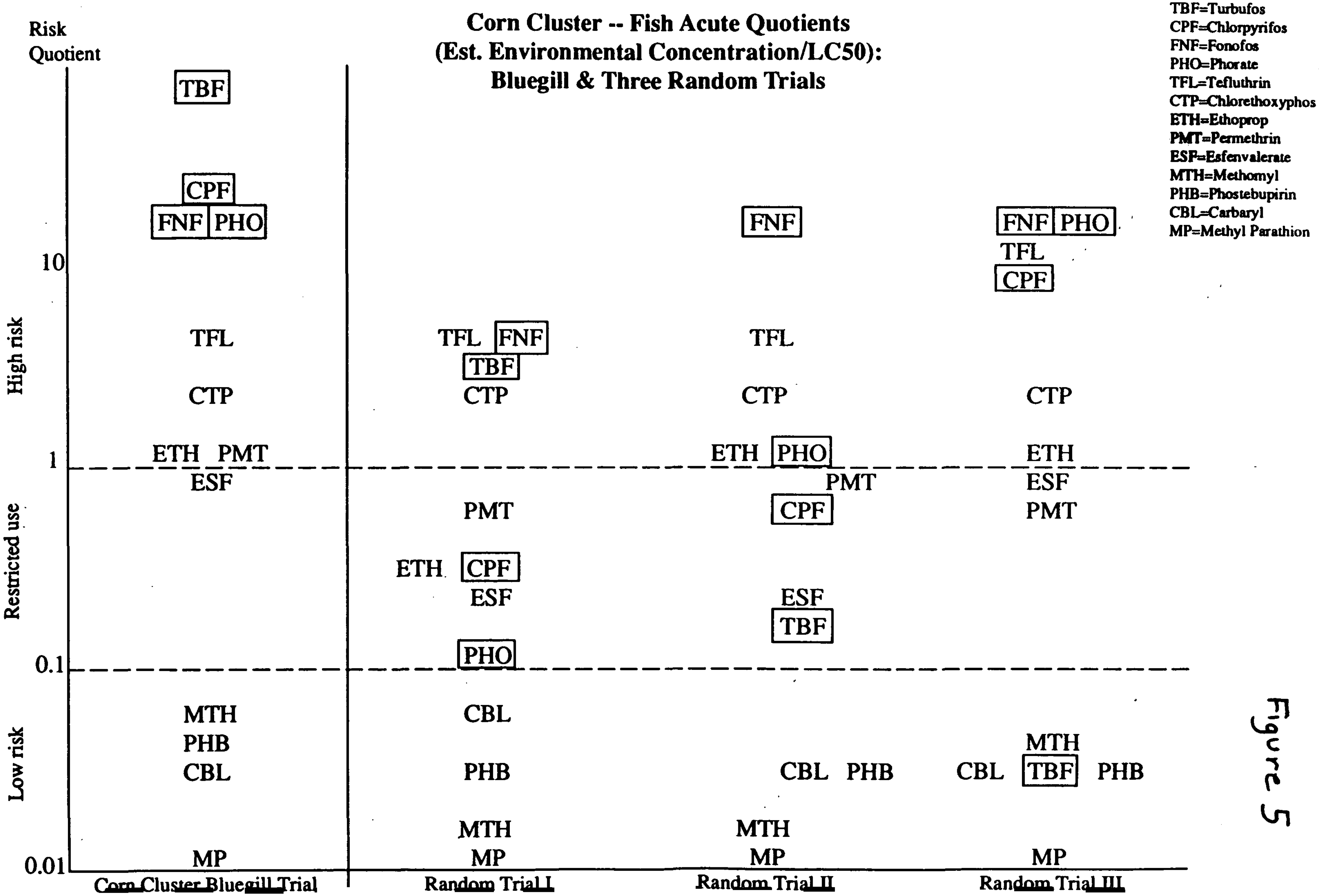
The first cluster analysis was conducted for all 14 corn insecticides used at the time of planting (see appendix page 2-1). The purpose of this phase of the analysis was to select the most problematic alternatives for in-depth review. By definition, the pesticides selected for in-depth review will be those posing the greatest risk to human health and the environment. The program can then be assured that any restrictions on their use will result in reduced risk, since the remaining alternatives will be generally safer.

In the pilot analysis, the four compounds selected, based on ecological and health risk, were Terbufos, Phorate, Chlorpyrifos and Fonofos. EFED staff feels very comfortable with these four because:

- they were selected based on tests in species that are at risk and of concern;
- the choice agrees with the judgment of experienced OPP biologists; and
- the choice is consistent with what we know about adverse field effects.

As shown in the first ranking (Figure 5), the bluegill sunfish risk quotients for these four chemicals rank at the top and substantially higher in acute risk to freshwater fish than the remaining alternatives. The bluegill sunfish was chosen for use in this analysis because the largest number of corn cluster chemicals included LC_{50} values for this species.

We simulated the effect of using OECD species on our regulatory process with three random trials. In each trial, one species was randomly selected from among those with appropriate LC_{50} values for each pesticide (appendix page 2-4). The risk quotient determined by the LC_{50} for that species was calculated for each of the three trials. The resultant ranking is shown to the right of the original bluegill sunfish ranking in Figure 5. We would not necessarily expect a single risk index to select the four compounds as well as the bluegill sunfish ranking did. A useful index would, however, show these four pesticides above the concern level and among the five to six highest-risk compounds. The actual results for random species are very different. In fact, random species use sometimes ranks the most problematic pesticides below what our judgement and experience tell us.



Corn Cluster -- Fish Acute Quotients
(Est. Environmental Concentration/LC50):
Bluegill & Three Random Trials
Risk Quotient
High risk
Restricted use
Low risk
10
1
0.1
0.01
TBF=Turbufos
CPF=Chlorpyrifos
FNF=Fonofos
PHO=Phorate
TFL=Tefluthrin
CTP=Chlorethoxyphos
ETH=Ethoprop
PMT=Permethrin
ESF=Esfenvalerate
MTH=Methomyl
PHB=Phostebupirin
CBL=Carbaryl
MP=Methyl Parathion
TBF
CPF
FNF
PHO
TFL
CTP
ETH
PMT
ESF
MTH
PHB
CBL
MP
Corn Cluster Bluegill Trial
Random Trial I
Random Trial II
Random Trial III

Figure 5

Case Study II: Turf Insecticide Cluster and NTN

The turf insecticide cluster was used in the second case study. The pilot study selected several turf insecticides for in-depth review based on all the areas of risk.

Diazinon clearly emerged as the chemical of greatest concern for birds among the turf cluster insecticides. The available information on field effects and the judgement of OPP biologists support this concern.

In comparison, NTN is a new chemical claimed to be safer for turf. Although this claim seemed to be supported for mammals and some other non-target species, NTN appears to be very persistent. As such, a chronic risk concern was identified for aquatic and bird species. Also, there appears to be an acute risk to marine invertebrates and small birds. Only the acute avian risk had sufficient cross-species data, so although it is not the endpoint of greatest concern, it is used in this case study. Only those turf cluster pesticides considered alternatives to NTN were used in this analysis (appendix page 2-5).

The analysis was conducted like that for the corn cluster case study. The first ranking shows results for a single species (bobwhite quail; see Figure 6). This puts Diazinon at the top and NTN far below. Of the three randomized species rankings, all place NTN at the bottom, but not necessarily with a clear distance between it and the others. Two of the three place Diazinon at the top. However, in one case (randomized trial I), Diazinon and NTN are fairly close together. Faced with this result, we would be reluctant to categorize NTN as safer, and would wonder whether a large number of incidents would occur if NTN replaced Diazinon.

Based on these analyses, we therefore conclude that species variability is sufficient to affect OPP regulatory decisions.

B. Harmonization

A survey of other countries, regulatory authorities and multi-national industry (appendix page 3-1) shows that the ecotoxicological test species in actual use internationally are generally very close to those used in the U.S. Figure 7 lists the test species used by OPP and those of the EC and compares them with species recommended by OECD.

Other authorities typically use safety factors with ecotoxicological hazard data. The size of the safety factor is generally adjusted to take into account the number of species for which test data re available and any differences in sensitivity between the species tested and those ecologically or commercially important native species potentially at risk. Thus, when high potential risk is indicated, other countries are likely to require an additional round of tests in native species. The OPP approach, in contrast, gives direct results.

C. Options to Resolve Issue 1: Test Species

Option 1. Develop correction factors based on round-robin testing, as well as existing data, to compare species.

Testing would be performed to insure results on all OECD recommended species for chemicals representing many structural classes.

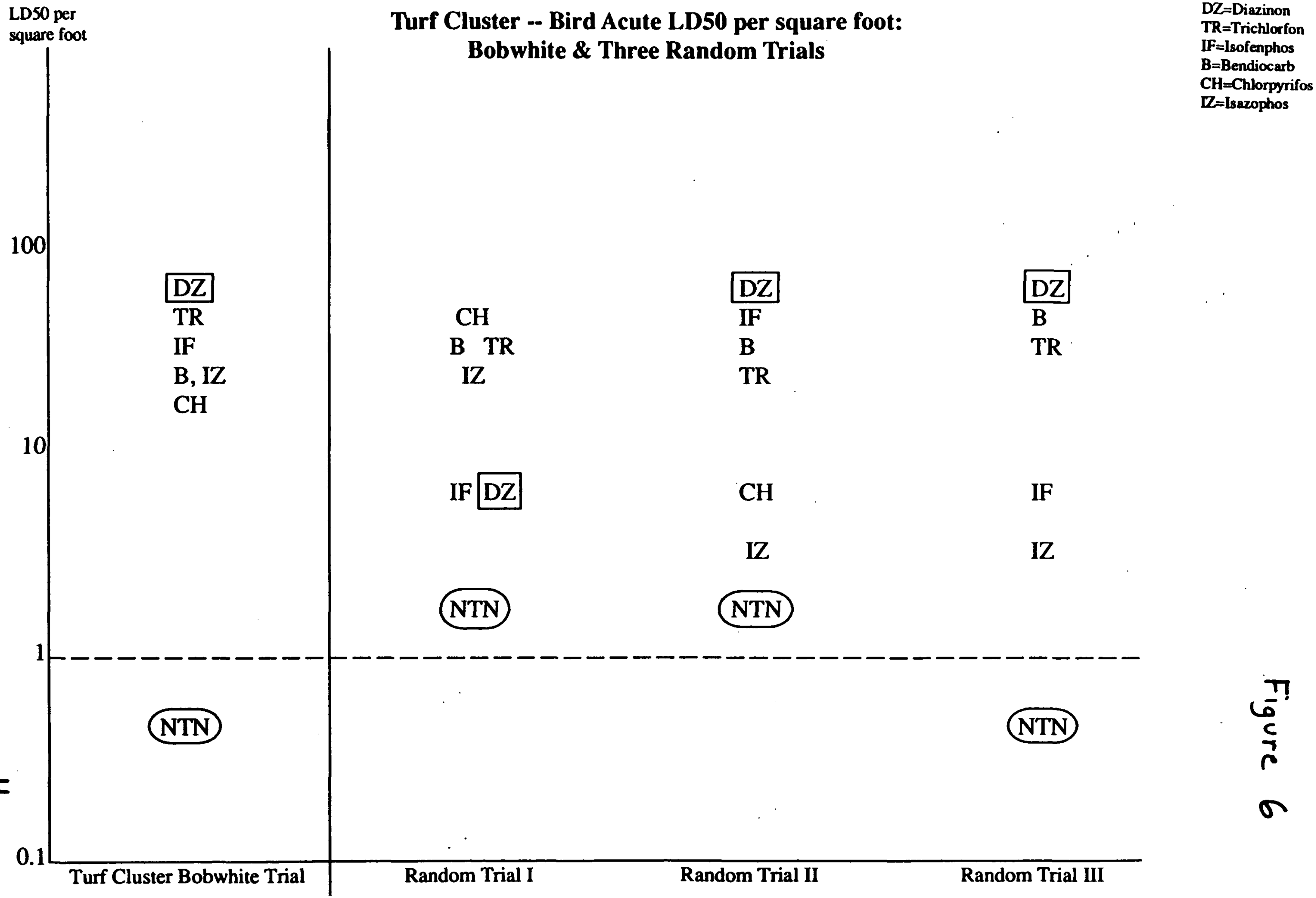

Turf Cluster -- Bird Acute LD50 per square foot:
Bobwhite & Three Random Trials
LD50 per square foot
DZ=Diazinon
TR=Trichlorfon
IF=Isofenphos
B=Bendiocarb
CH=Chlorpyrifos
IZ=Isazophos
100
10
1
0.1
DZ
TR
IF
B, IZ
CH
NTN
CH
B TR
IZ
IF DZ
NTN
DZ
IF
B
TR
CH
IZ
NTN
DZ
B
TR
IF
IZ
NTN
Turf Cluster Bobwhite Trial
Random Trial I
Random Trial II
Random Trial III

Figure 6

11

Comparison of International Recommendations for Test Species

Test Guidelines	OPP	EC (for pesticides)	OECD
Avian dietary test (LC_{50})	Bobwhite quail Mallard duck	Bobwhite quail Japanese quail Mallard duck	Bobwhite quail Japanese quail Mallard duck Common pigeon Ring-necked pheasant Red-legged partridge
Avian reproduction test	Bobwhite quail Mallard duck	Japanese quail Mallard duck	Bobwhite quail Japanese quail Mallard duck
Fish acute toxicity test (LC_{50})	Bluegill sunfish Rainbow trout	Bluegill sunfish Rainbow trout	Bluegill sunfish Rainbow trout Zebrafish Fathead minnow Common carp Guppy Japanese medaka
Freshwater invertebrate test	Daphnia magna	Daphnia magna	Daphnia magna and other species; OECD expert panel recommends Daphnia magna

Figure 7

Pros:

- Enables U.S. to accept data on OECD species.
- Correction factors derived from testing will be based upon studies specifically designed for this purpose.
- Risk assessment is less likely to be driven by test species selection.

Cons:

- Correction factors introduce additional uncertainty in comparative risk assessments.
- Correction factors are likely to be controversial.
- Requires more testing and analyses of data.
- Will take several years.
- May not accurately account for variabilities among important species (may underestimate or overestimate comparative risks).

Option 2. Use tests in OECD species for screening purposes.

OPPTS would accept test results with OECD species with correction factors or assessment factors, such as those currently used by OPPT. If a level of concern is reached, testing would be required with benchmark standard species to allow appropriate comparative analyses.

Pros:

- Stronger basis for defending regulatory decisions than Option 1.
- Flexible and politically appealing.
- Consistent with certain international approaches (New Zealand, Canada).
- Allows for partial comparison of pesticide alternatives.

Cons:

- Decisions likely to take longer, to require more data and to require more OPP resources.
- Database may lose its historical utility.
- Would require some changes in risk assessment and management process.
- May result in more testing of different species than other options.

Option 3. Continue to require U.S. benchmark species and seek to change the OECD guidelines.

With this option, the United States would work through the OECD to require native benchmark species which have databases. Additional species could vary from country to country.

Pros:

- Achieves international harmony if OECD guidelines change.
- U.S. ability to perform and defend risk assessments for North American ecology will be sustained.
- Reduces uncertainty in comparative risk assessment.
- Requires relatively few resources.

Cons:

- Potential repercussions within OECD.
- Implementation requires negotiations within OECD.

Recommendation:

OPPTS prefers option 3 (restrict species to U.S. species and seek to change the OECD guidelines). This option is consistent with the current trend in the European Community (EC), which is narrowing its range of species for pesticides and moving toward acceptance of U.S. species. With this option, OPP scientists will be able to make more reliable comparisons of incoming data, and they will not have to change their existing risk assessment policies and approaches, which have taken many years to formulate. Decisions based upon indigenous species will also be easier to defend than those based upon foreign species.

Although this option does not provide additional data on species differences, it encourages a faster resolution of the issue than other options will provide. With option 3, the U.S. will need to develop its position on the test species issue and take it to the OECD for resolution. As discussed in Appendix 3, the U.S. position is close to that of the EC, and has a good chance for being accepted, at least for pesticides. It is also an appropriate time to take this issue to the OECD because they are currently considering change for the pesticide guidelines.

III. Issue 2: Age of Test Birds

Avian dietary studies expose birds to a treated diet for five days. The age of the test birds greatly affects the reliability of the resultant toxicity endpoints. If birds are too young, they will rely on unabsorbed yolk to survive. If birds are too old, they will survive the five-day interval without feeding. Differences in biology between species are therefore critical to the optimal age for testing. Mallard ducks should be tested from five to seven days old at test initiation, and bobwhite quail should be from 10 to 14 days old. The OECD and OPPT guidelines recommend birds be tested from 10 to 17 days old at initiation.

Test animals must be susceptible to the conditions of the test so their response can be quantified with reasonable statistical certainty. This can be met only for species that can be maintained in captivity in good health and cannot survive for five days without eating (Hill, 1992). Mallard ducks more than 10 days old can survive the five-day test without eating and therefore are not susceptible to the test.

The importance of seemingly trivial difference in age on LC_{50}s has been well documented. For example, between seven and 14 days, LC_{50}s increased an average of 1.5-fold for three organophosphates and two carbamates tested with Japanese quail from a single hatch. This was demonstrated for 10-day-old ducklings. LC_{50}s increased by 1.5- to 3.8-fold between five and 10 days of age for all but fensulfothion (Hill, 1992).

Recommendation:

OPP believes that the age of test birds is especially crucial in the avian dietary study. In 1982, the program established age limits of 10 to 14 days for bobwhite quail and five to 10 days for mallard ducks. These age limits are based on available evidence in Hudson, *et al.* (1972) and on comments received by the FIFRA Science Advisory Panel in its 1980 review of OPP's Subdivision E Test Guidelines. These ages also are consistent with the 1980 scientific consensus of the American Society of Testing Materials on the avian dietary test.

We recommend taking this issue to OECD, as part of the workshop on avian testing, and recommend changing the age of test birds to 10 to 14 days for bobwhite quail and five to 10 days for mallard ducks.

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Appendix 1:

Species Variability

Frequency Distribution of the Interspecies Range of Insecticide

LC_{50}s (Max/Min) for Fish in the Mayer Database

1-5	5-10	10-100	100-1,000	1,000-10,000	More than 10,000
Allethrin	Akton	Acephate	Aminocarb	Azinphos-M	Malathion
AMDRO	Chlorphyrifos-M	Aldicarb	Carbaryl	Leptophos	
Chlordane HCS	DDE	Aldrin	Carbofenthion	Terbufos	
Chlordireform	Dichlofenthion	Azinphos-E	Chlordane		
Coumaphos	Dioxathion	Benzene HCL	Chlorpyrifos		
Dicrotophos	DNOC	Carbofuran	DDD		
Diflubenzuron	Fenthion	Chlordecone	Methomyl		
Dinethoate	Fenvalerate	Chlorfenvinphos	Parathion		
Dimtramine	Heptachlor	Crotoxyphos	Parathion-Diq.		
Endosulfan	Lindane	DDT	Phorate		
EPN	Mevinphos	Diazinon	Phosnet		
Ethylan	Ortho 11775	Dichlorvos	RU-11679		
Fonofos	Oxydemeton-M	Dieldrin	Temephos		
Fospirate	Propoxur	Dilan	Trichtorfon		
Heptachlor Ep.	Ronnel	Dimethrin			
Lethane	Ryania	Disulfuton			

1-5	5-10	10-100	100-1,000	1,000-10,000	More than 10,000
Methidathion	SD-7438	Dis-Trans Allethrin			
Methil Trithion	SD-17250	Endrin			
Oxamyl		Ethion			
Oxythioquinot		Fenitrothion			
Pernethrin		Jodphenphos			
Phosaloe		Landrin			
Proferofos		Methoprene			
Terpen Poly C		Methoxychlor			
Tetrachlorvin		Methyl Parathion			
Thianate		Mexacarbate			
Trichloronate		Monocrotophos			
		Naled			
		Phosphamidon			
		Phoxim			
		Pyrethrin			
		Resmethrin			
		Rotenone			
		S-Bioallethrin			
		SD-16898			
		TEPP			
		Toxaphene			

Frequency Distribution of the Interspecies Range

of LC_{50}s (Max/Min) for a Subset of Four Fish from the Mayer Database

1-4x	5-10x	10-100x	100-1,000x
Aminocarb	Benzene	Aldrin	Antimycin A
Captan	Carbaryl	Benomyl	Azinphos methyl
Chlordane HCS	Endrin	Chlordane	Crotoxyphos
DDT	Folpet	Ethion	
Dieldrin	MON-0818*	Houghto-safe*	
Dinitramin	Methomyl	Malathion	
Endosulfan	Parathion ethyl	Naled	
Fenitrothion	PCP	Phosmet	
Glyphosate	Toxaphene	Phosphamidon	
Heptachlor	Trichlorphon	Phoxim	
Lindane		Trifluralin	
Methoxychlor			
Mexacarbate			
Parathion methyl			
Pthalic acid esters*			
Purifloc C-31*			
Pydraul 50E			

* Non-pesticides

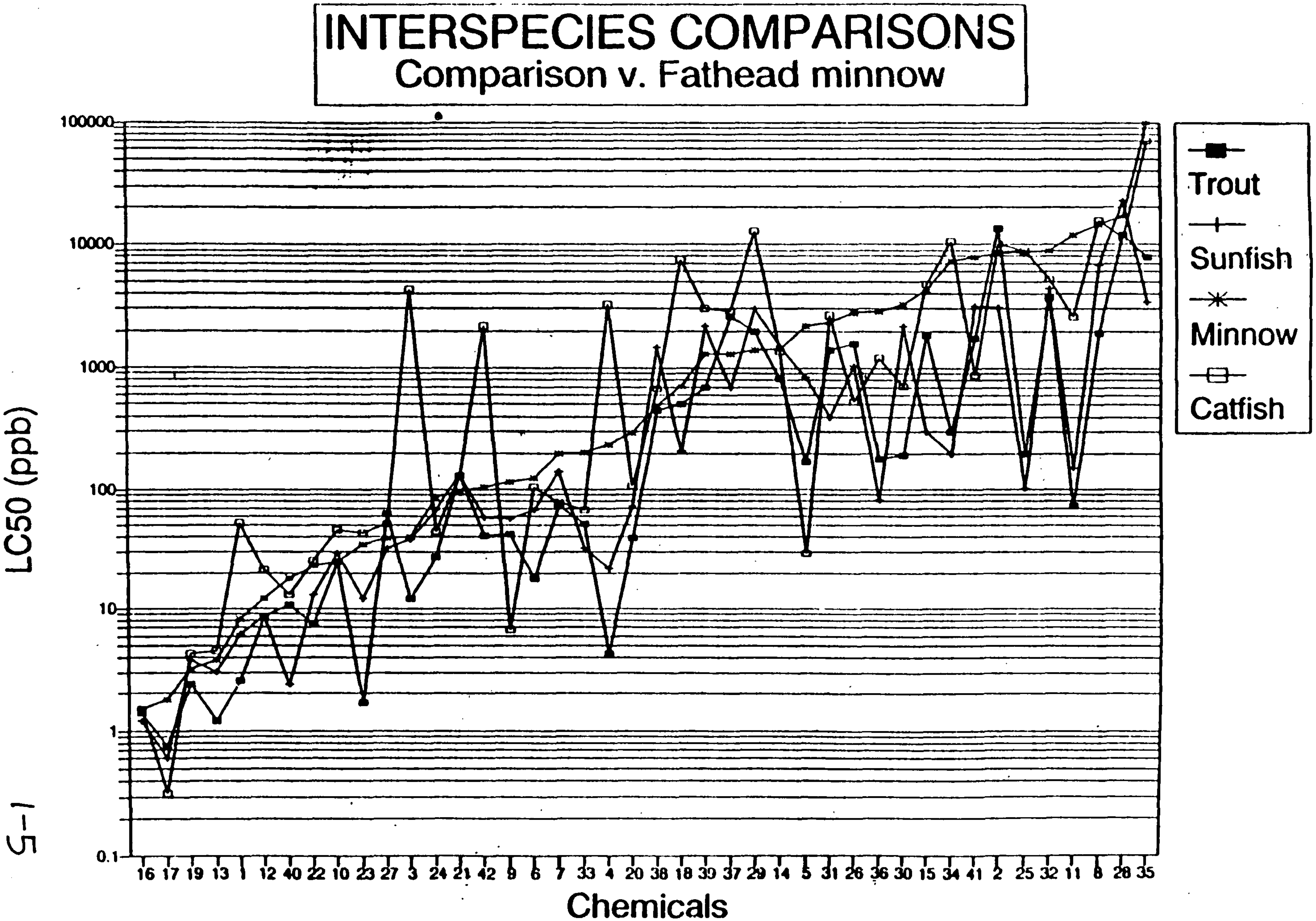
OECD Species vs. Comparison Graphs

Freshwater Fish

Family	Species	OECD	Species Reported in OPP Graphs
Salmonidae	Rainbow trout	√	+
Cyprinidae	Fathead minnow	√	+
	Zebrafish	√	
	Carp	√	
Ictaluridae	Channel catfish		+
Centrarchidae	Bluegill sunfish	√	+
Oryziidae	Japanese medaka	√	

Birds

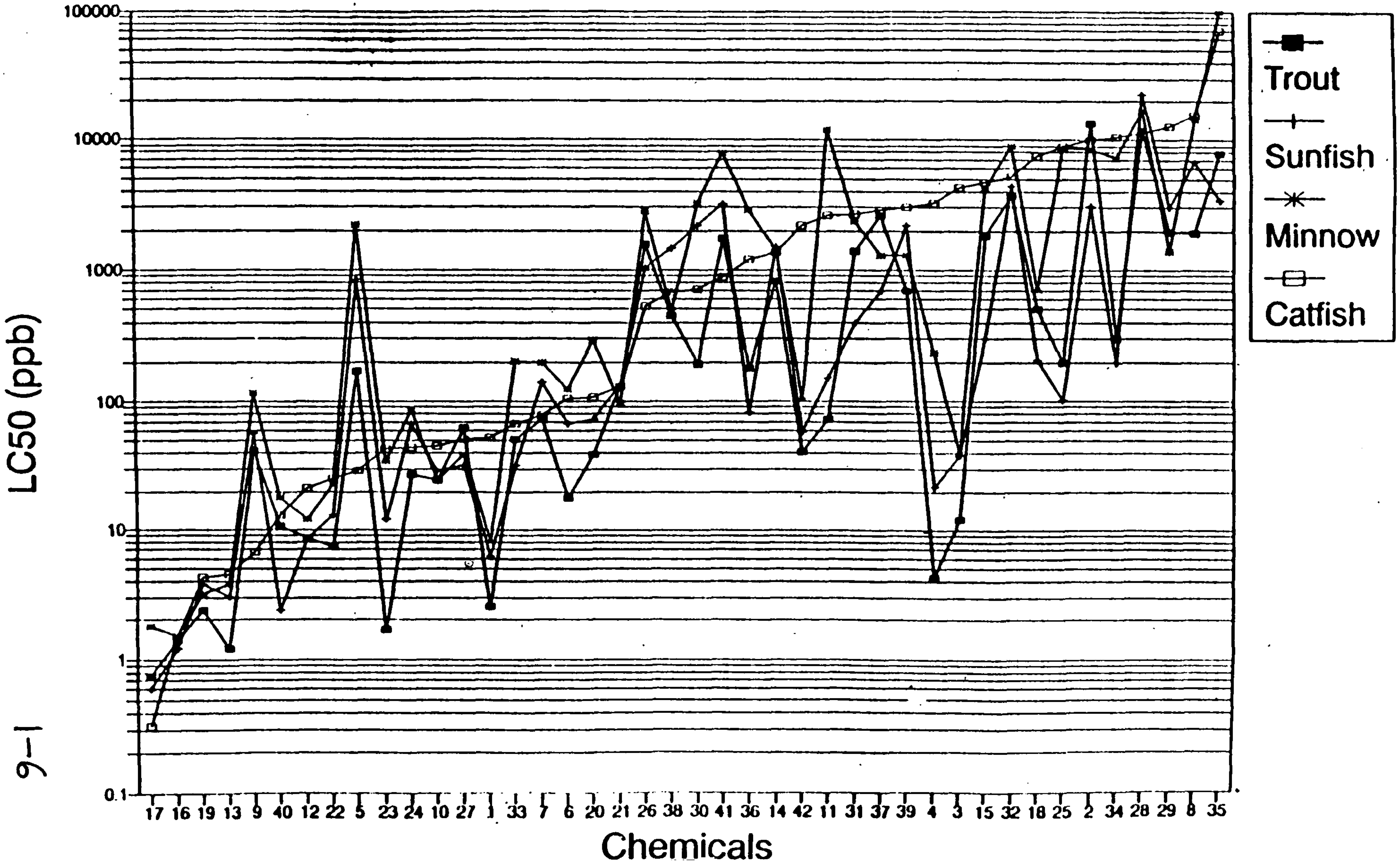
Family	Species	OECD	Species Reported in OPP Graphs: LC50	LD50
Anatinae	Mallard duck	√	+	+
Phasianidae	Bobwhite quail	√	+	
	Japanese quail	√	+	+
	Chukar		+	
	Ring-necked pheasant	√	+	+
	Red-legged partridge	√		
Columbidae	Common pigeon	√		+
Placeidae	House sparrow			+



INTERSPECIES COMPARISONS
Comparison v. Fathead minnow
100000
10000
1000
100
10
1
0.1
LC50 (ppb)
16 17 19 13 1 12 40 22 10 23 27 3 24 21 42 9 6 7 33 4 20 38 18 39 37 29 14 5 31 26 36 30 15 34 41 2 25 32 11 8 28 35
Chemicals
Trout
Sunfish
Minnow
Catfish

5-1

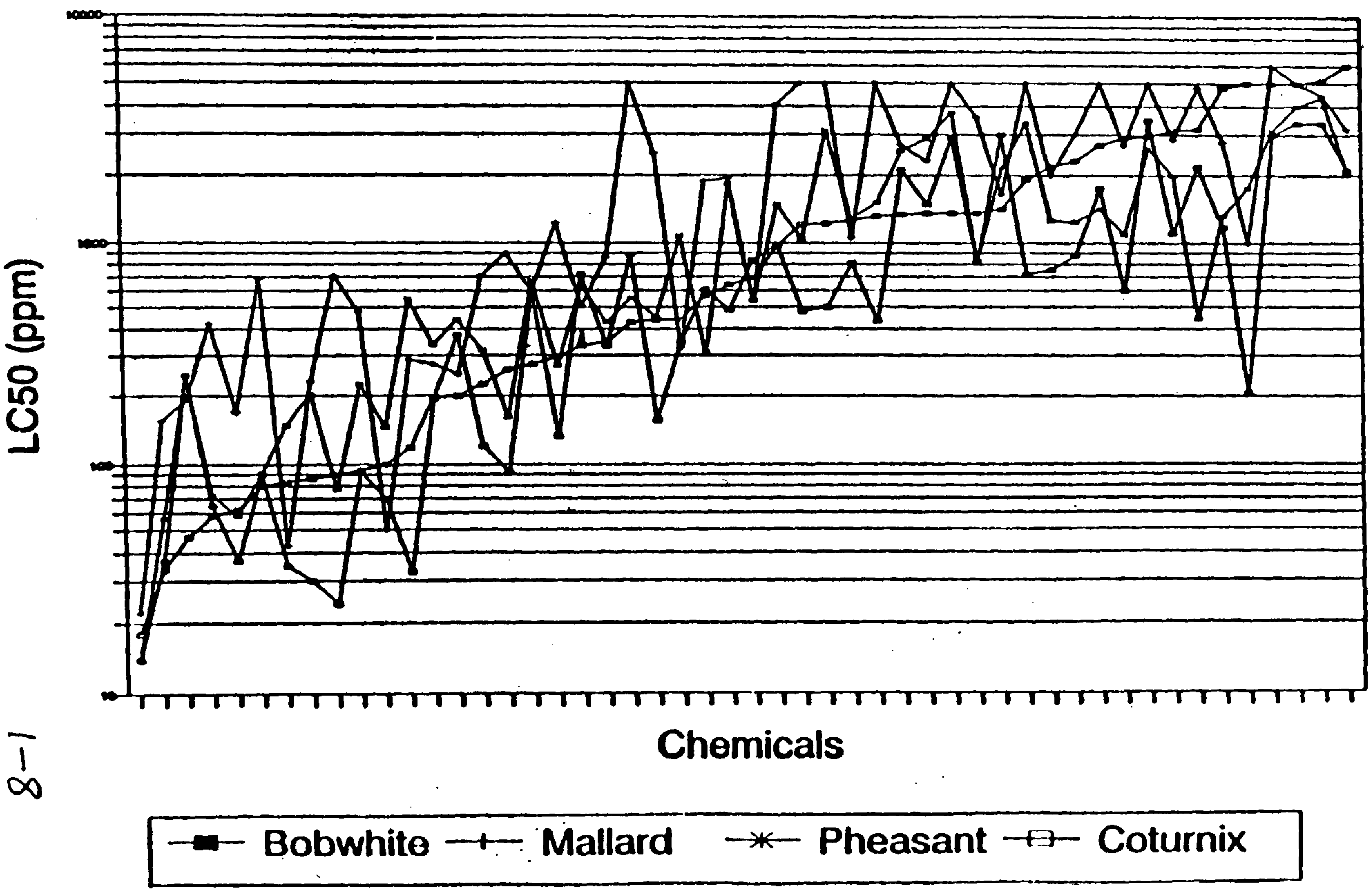
INTERSPECIES COMPARISONS
Comparison v. Channel catfish



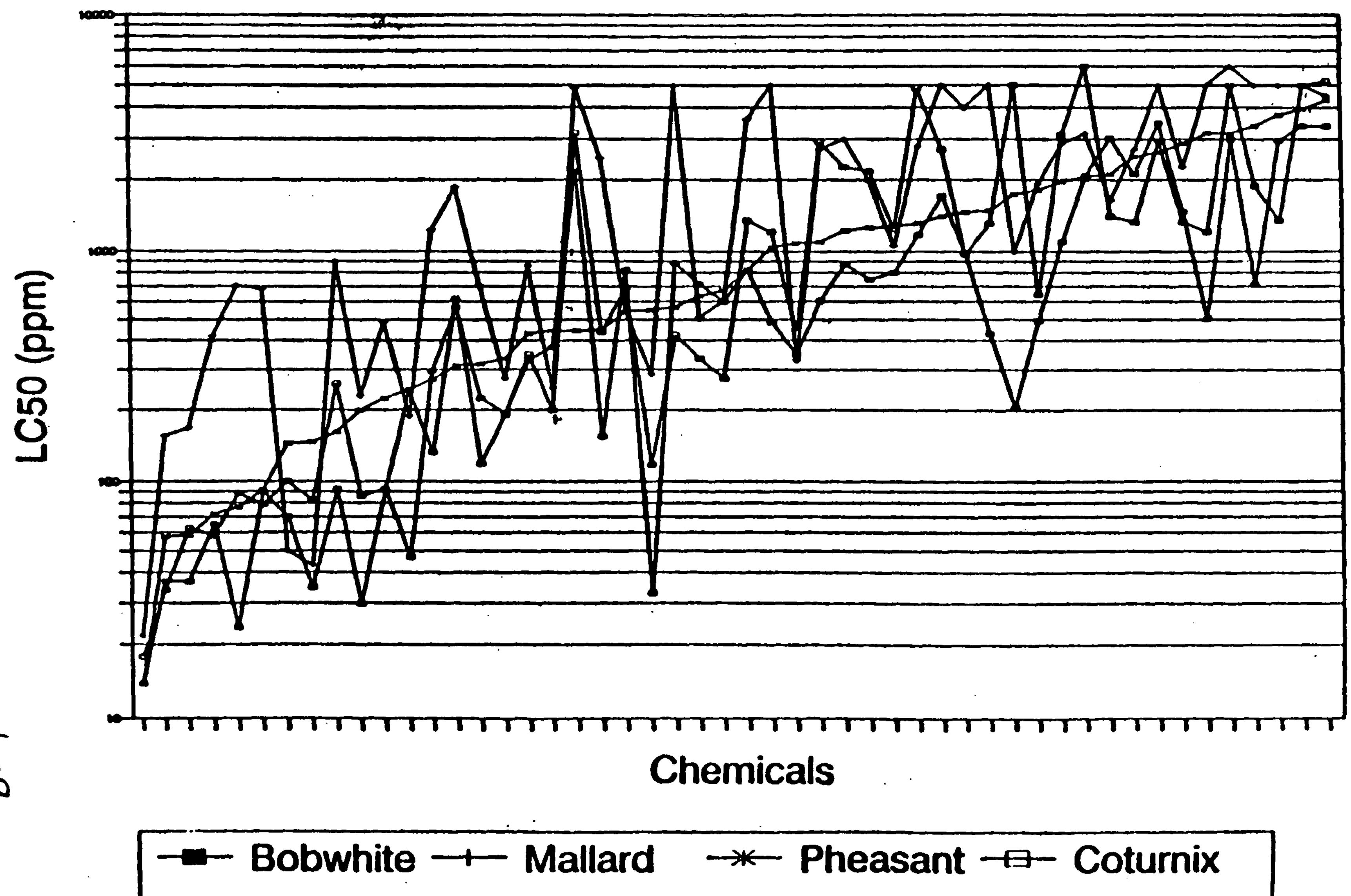
Key: Interspecies Comparisons of LC50s

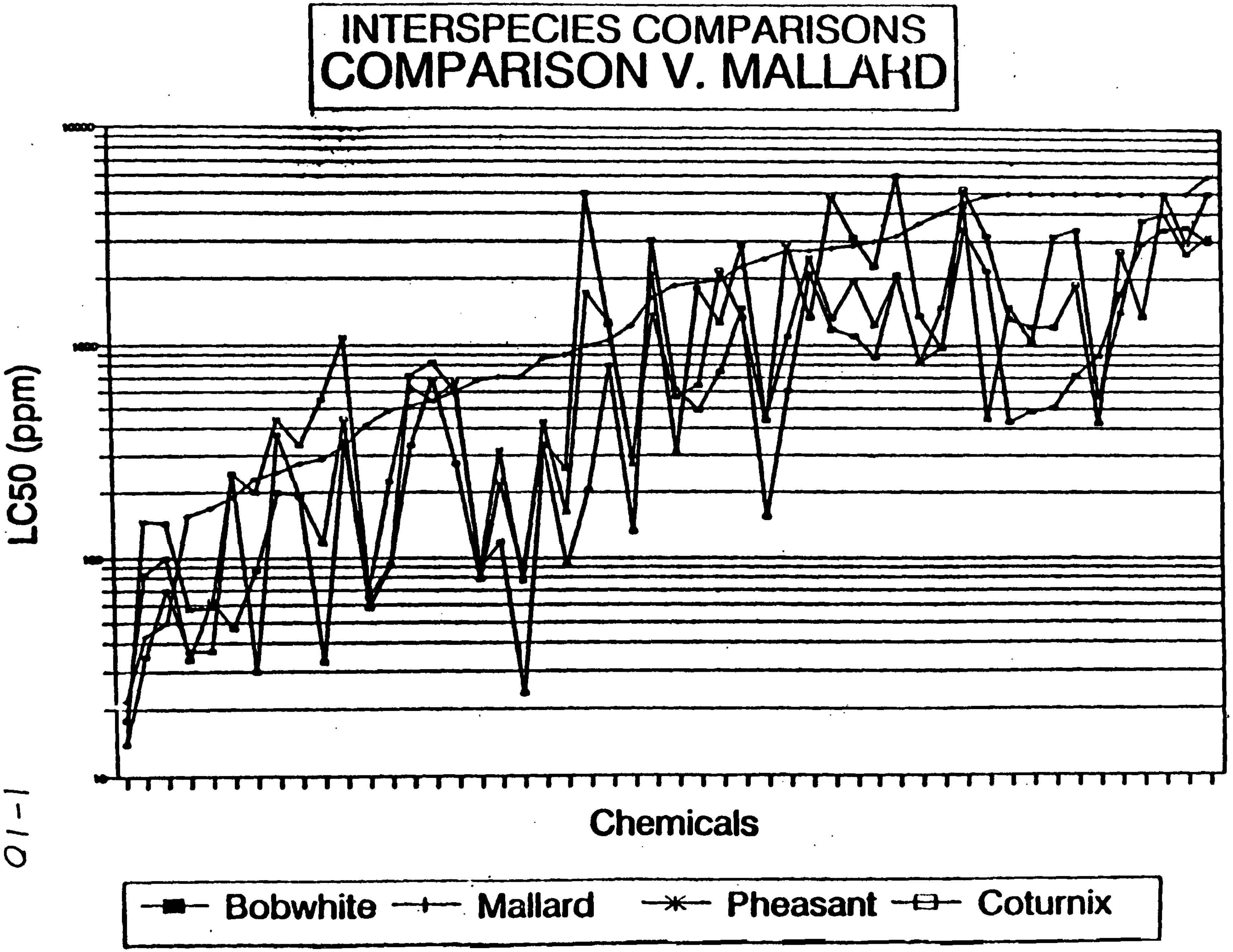
	Chemical	Rainbow trout	Bluegill sunfish	Fathead minnow	Channel catfish
1	Aldrin	2.6	6.2	8.2	53
2	Aminocarb	13500	3100	8500	10000
3	Antimycin A	12	38	40	4230
4	Azinphos methyl	4.3	22	235	3290
5	Benomyl	170	850	2200	29
6	Benzene hexachloride	18	67	125	105
7	Captan	73.2	141	200	77.5
8	Carbaryl	1950	6760	14600	15800
9	Chlordane	42	57	115	6.7
10	Chlordane HCS-3260	24.9	29.3	24.8	45.8
11	Crotoxyphos	72.4	152	11900	2600
12	DDT	8.7	8.6	12.2	21.5
13	Dieldrin	1.2	3.1	3.8	4.5
14	Dinitramine	820	1520	1440	1370
15	Disulfoton	1850	300	4300	4700
16	Endosulfan	1.4	1.2	1.5	1.5
17	Endrin	0.75	0.61	1.8	0.32
18	Ethion	500	210	720	7600
19	Fenitrothion	2.4	3.8	3.2	4.3
20	Folpet	39	72	298	108
21	Glyphosate	130	135	97	130
22	Heptachlor	7.4	13	23	25
23	Houghto-safe 1120	1.7	12	35	43
24	Lindane	27	68	87	44
25	Malathion	200	103	8650	8970
26	Methomyl	1600	1050	2800	530
27	Methoxychlor	62	32	39	52
28	Mexacarbate	12000	22900	17000	11400
29	MON-0818	2000	3000	1400	13000
30	Naled	195	2200	3300	710
31	Parathion ethyl	1430	400	2350	2650
32	Parathion methyl	3700	4380	8900	5240
33	Pentachlorophenol	52	32	205	68
34	Phosmet	300	200	7300	10600
35	Phosphamidon	7800	3400	100000	70000
36	Phoxim	180	82	2900	1210
37	Phthalic acid esters	2600	700	1300	2900
38	Purifloc C-31	446	1470	490	680
39	Pydraul 50E	700	2200	1300	3000
40	Toxaphene	10.6	2.4	18	13.1
41	Trichlorphon	1750	3170	7900	880
42	Trifluralin	41	58	105	2200

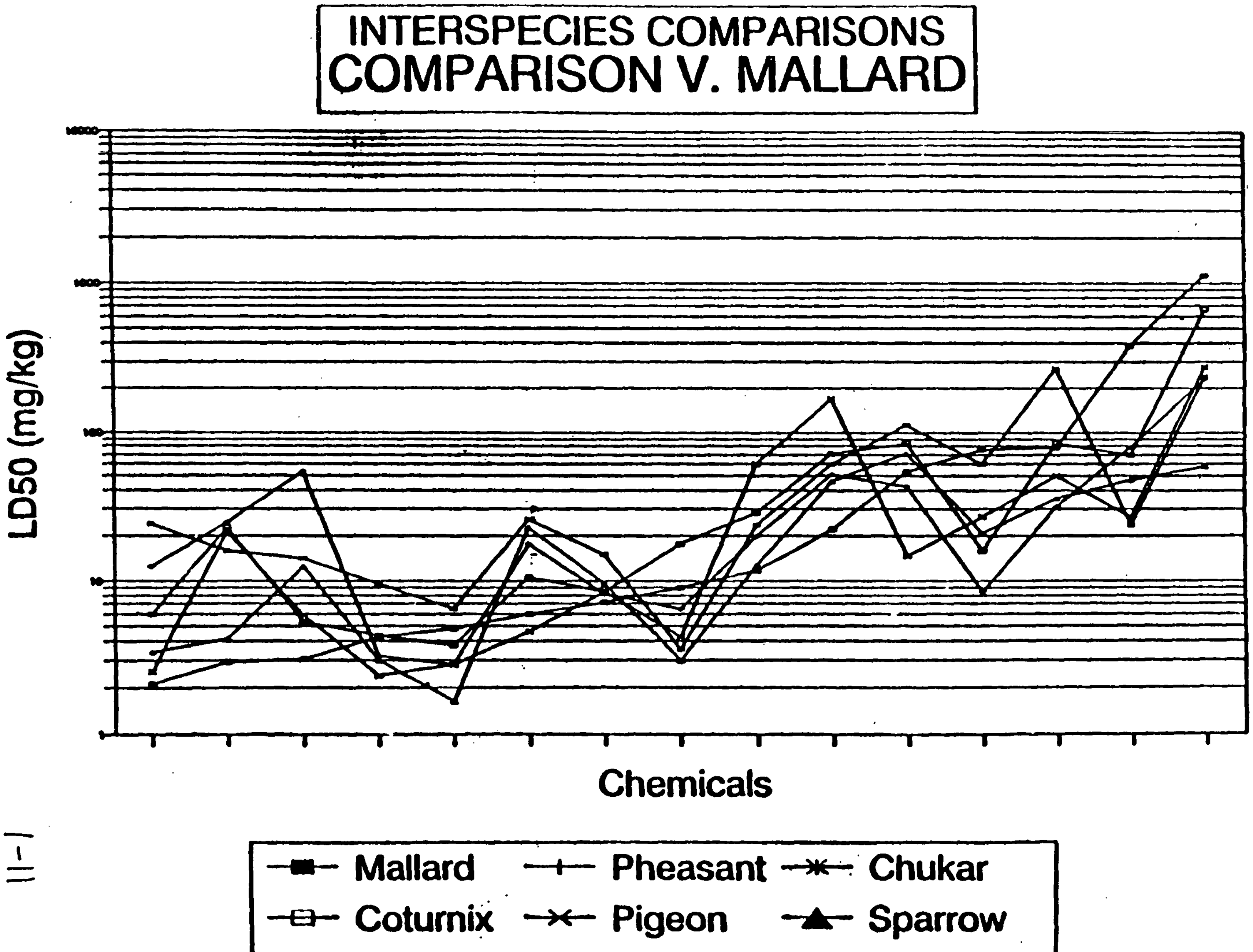
INTERSPECIES COMPARISONS
COMPARISON V. COTURNIX



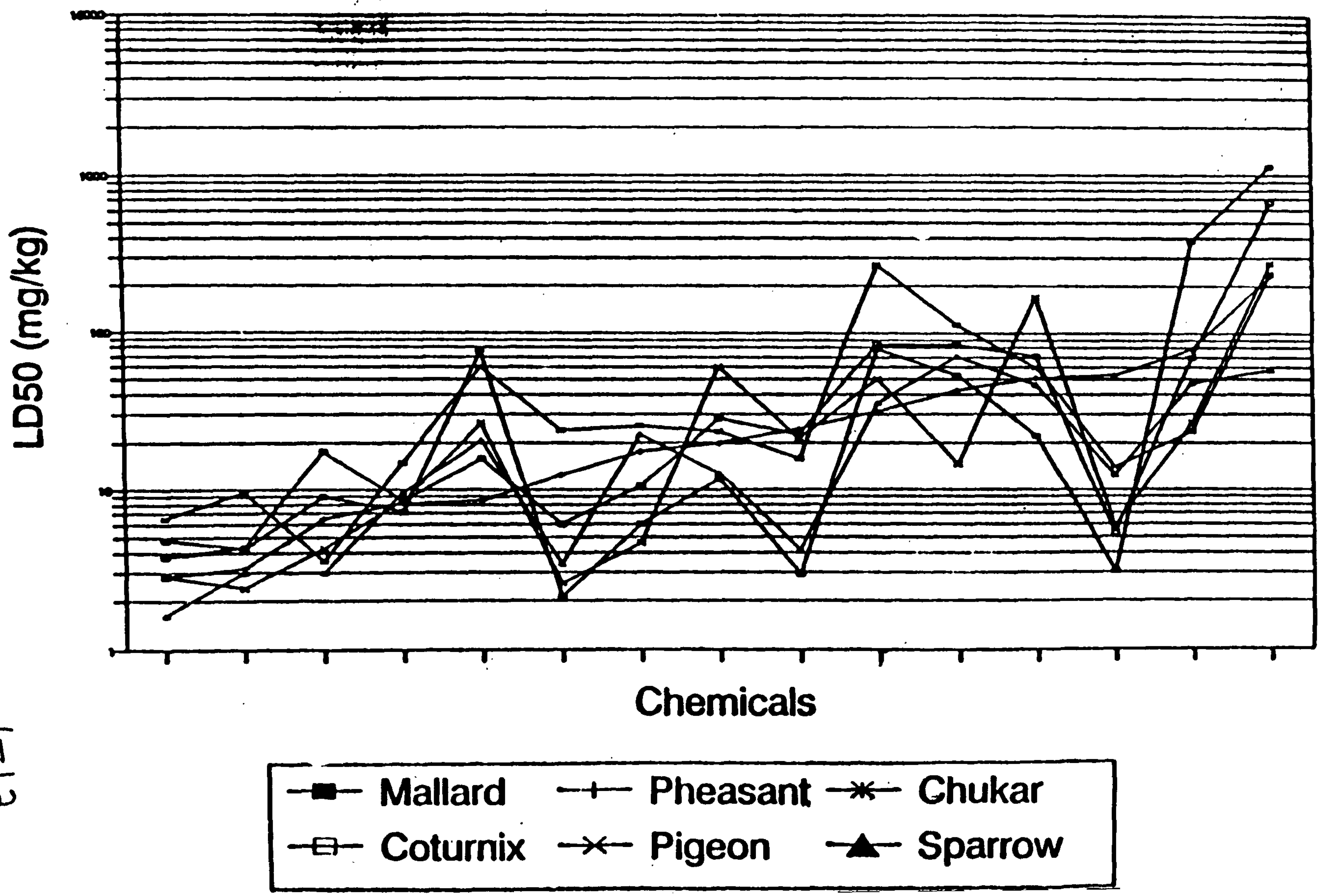
INTERSPECIES COMPARISONS
COMPARISON V. PHEASANT

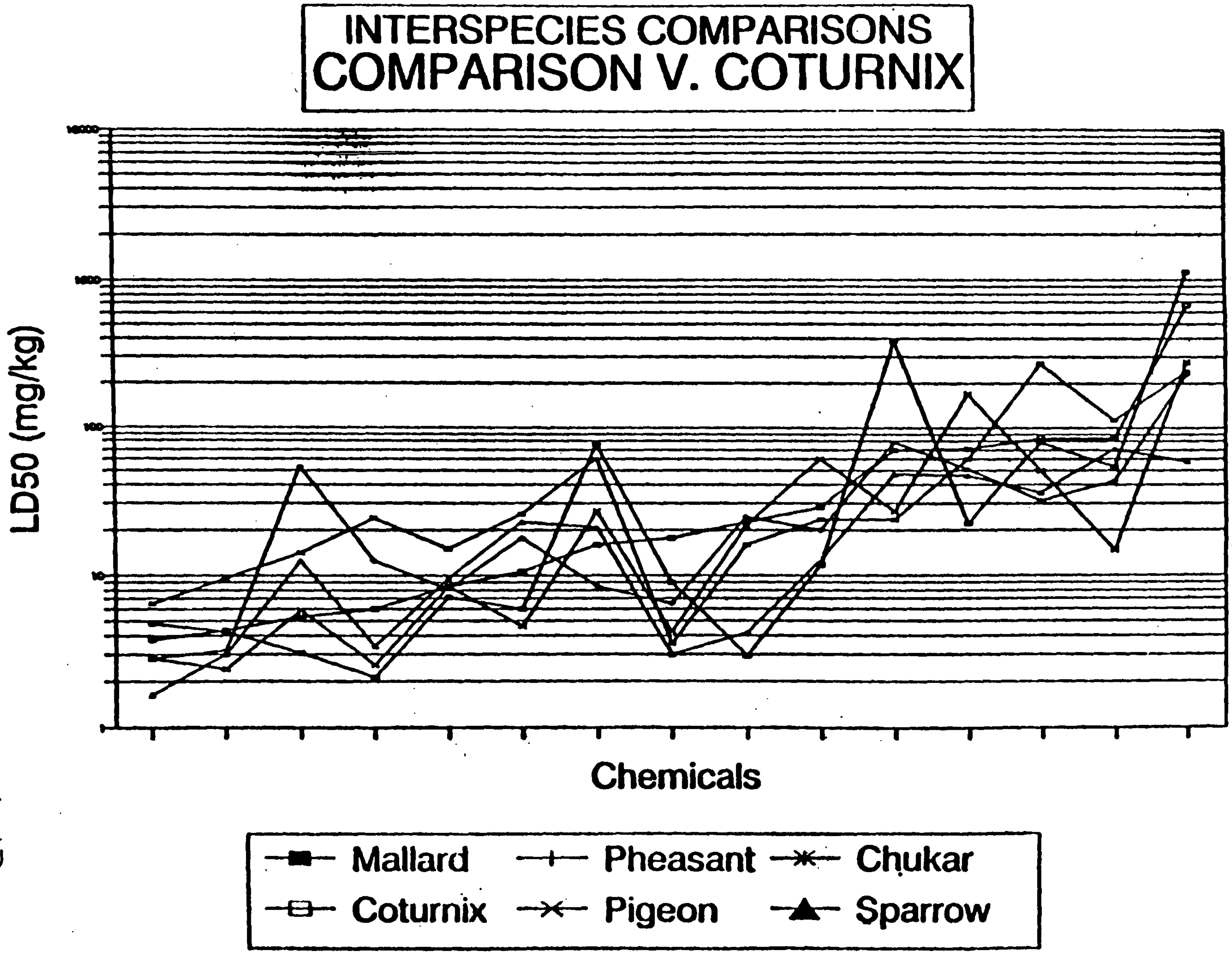



INTERSPECIES COMPARISONS
COMPARISON V. MALLARD
LC50 (ppm)
Chemicals
Bobwhite
Mallard
Pheasant
Coturnix

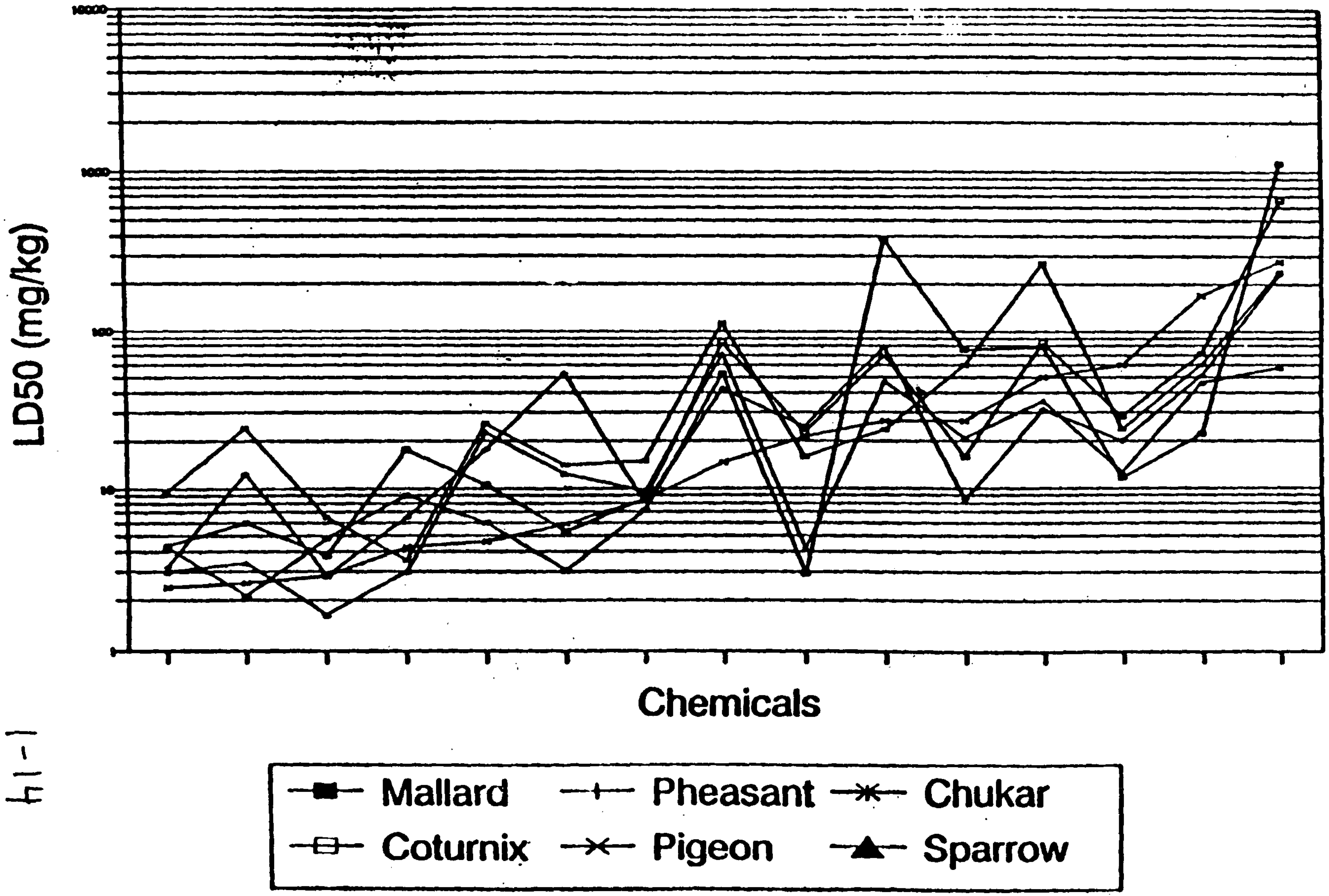

INTERSPECIES COMPARISONS
COMPARISON V. MALLARD
LD50 (mg/kg)
Chemicals
Mallard
Pheasant
Chukar
Coturnix
Pigeon
Sparrow

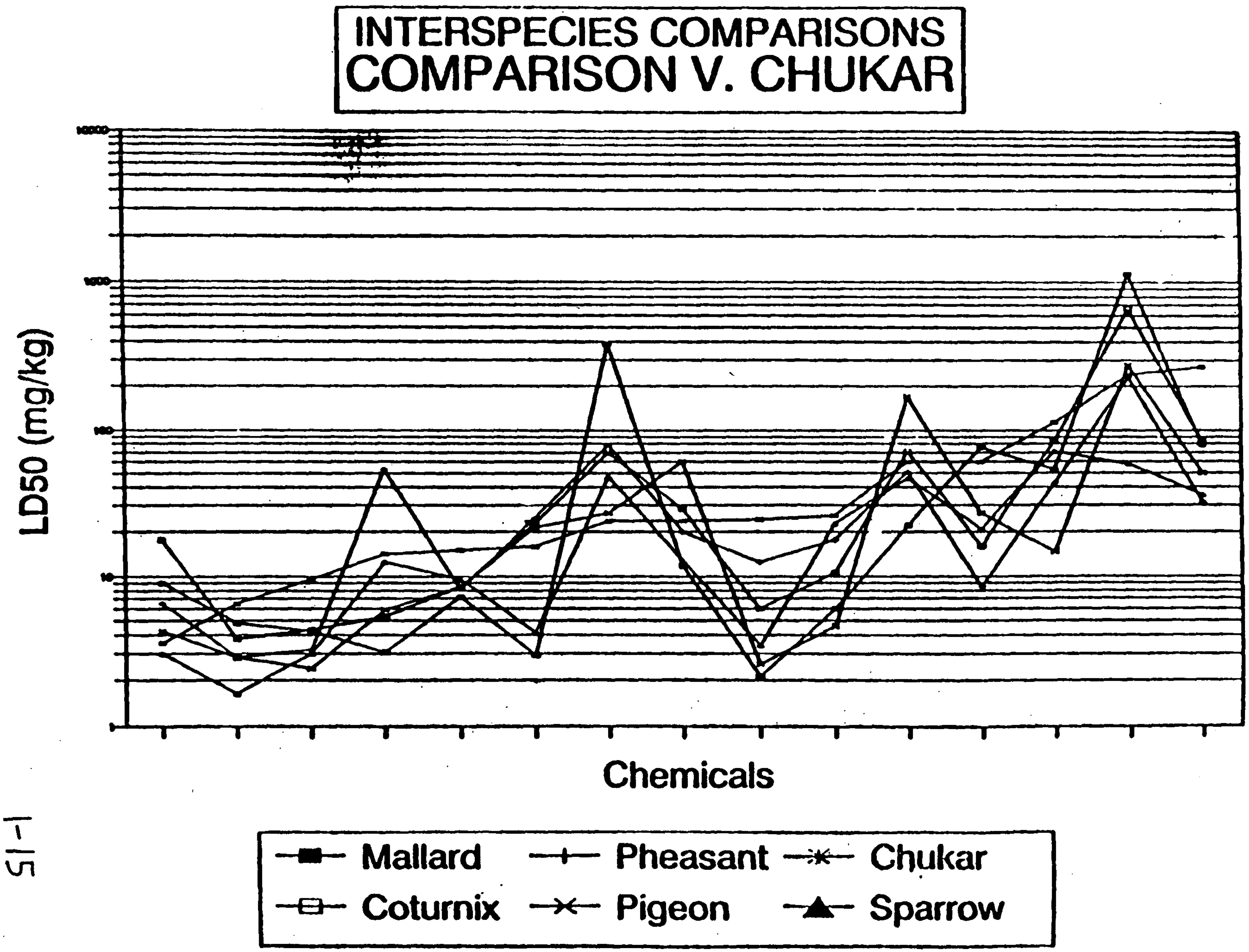
INTERSPECIES COMPARISONS
COMPARISON V. PHEASANT




INTERSPECIES COMPARISONS
COMPARISON V. COTURNIX
LD50 (mg/kg)
Chemicals
Mallard
Pheasant
Chukar
Coturnix
Pigeon
Sparrow

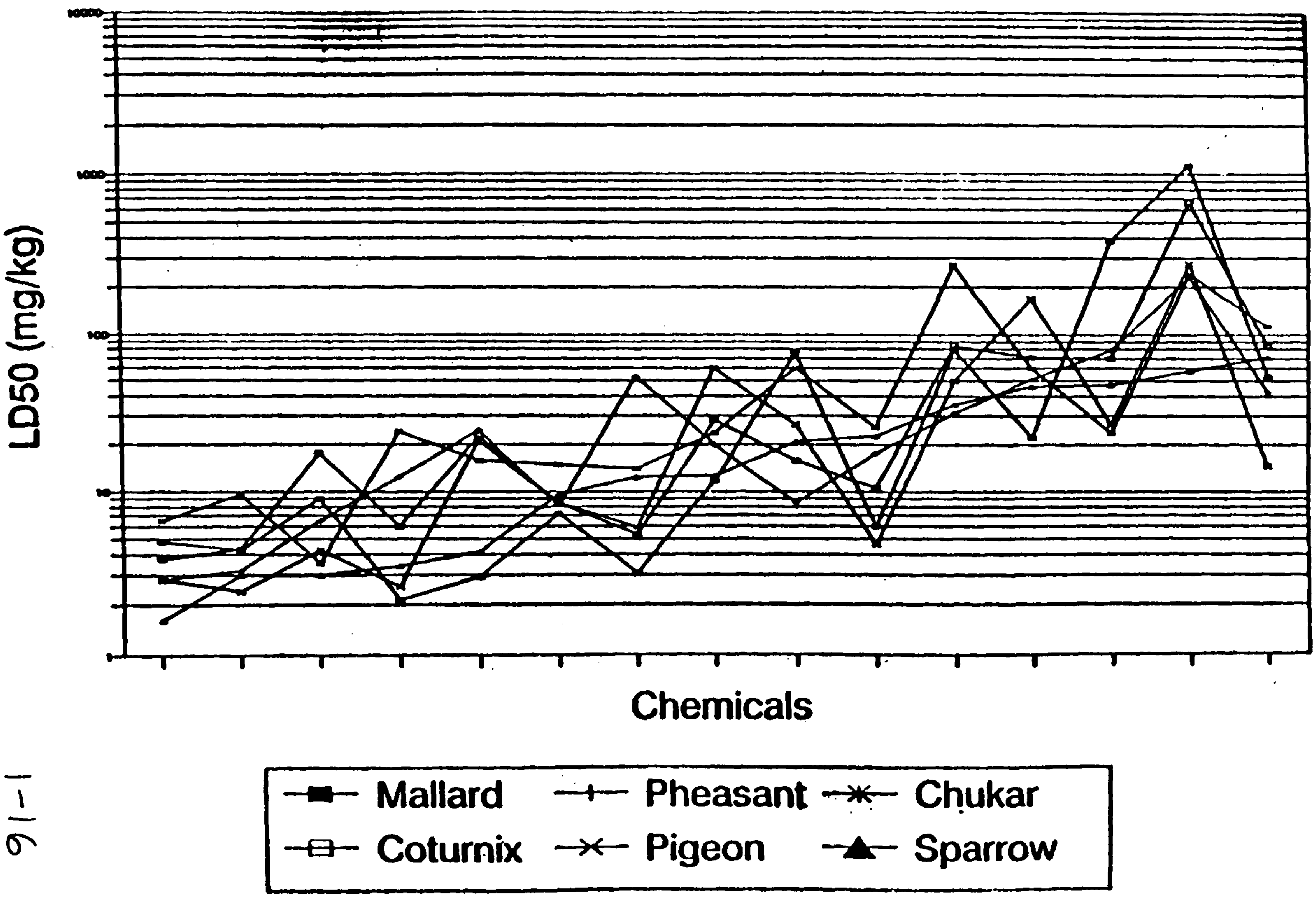
INTERSPECIES COMPARISONS
COMPARISON V. PIGEON




INTERSPECIES COMPARISONS
COMPARISON V. CHUKAR
LD50 (mg/kg)
Chemicals
Mallard
Pheasant
Chukar
Coturnix
Pigeon
Sparrow

1-15

INTERSPECIES COMPARISONS
COMPARISON V. SPARROW



Most Sensitive Species for Fish and Avian Toxicity Data

Fish Toxicity Data

Comparison of 42 LC_{50} values for four fish species (Mayer and Ellersieck, 1986) yielded the following frequencies for most sensitive species:

Rainbow trout	48%
Bluegill sunfish	33%
Channel catfish	14%
Fathead minnow	5%

The OECD species include common carp, zebrafish, Japanese medaka and guppy. These species are more closely related taxonomically to the fathead minnow than to the other three species.

Avian Toxicity Data

Comparison of 49 LC_{50} values for four avian species (Hill *et al.*, 1975) yielded the following frequencies for most sensitive species:

Bobwhite quail	59%
Japanese quail	22%
Pheasant	12%
Mallard duck	6%

Comparison of 16 LD_{50} values for six avian species (Tucker and Haegele, 1979) yielded the following frequencies for most sensitive species:

Mallard duck	44%
Pigeon and sparrow	19%
Pheasant	12%
Chukar	6%
Japanese quail	0%

Comparison of 17 LD_{50} values for bobwhite quail and mallard ducks (Hudson *et al.*, 1984) yielded the following frequencies for most sensitive species:

Bobwhite quail	65%
Mallard duck	35%

Appendix 2:

Case Studies

2

Corn Cluster Chemicals:
Freshwater Fish 96-hr LC_{50}s (ppb)

Chemical	Species	No. Tests	Range	Median
TERBUFOS	Rainbow Trout	10	8-15	10
	Fathead Minnow	2	150-390	270
	Channel Catfish	1	---	1800
	Bluegill sunfish	10	1.1-2.4	2
CHLORPYRIFOS	Cutthroat Trout	4	5-26	16
	Rainbow Trout	4	1-51	11
	Lake Trout	6	73-244	170
	Channel Catfish	1	---	280
	Bluegill sunfish	5	1.7-4.2	2
FONOFOS	Rainbow Trout	1	---	20
	Bluegill sunfish	1	---	7
PHORATE	Cutthroat Trout	2	44-66	55
	Rainbow Trout	2	13-21	17
	Northern Pike	1	---	110
	Channel Catfish	1	---	280
	Bluegill sunfish	6	1.0-4.0	2
	Largemouth Bass	1	---	5
	Walleye	2	57-340	200
TEFLUTHRIN	Rainbow Trout	1	---	0.06
	Bluegill sunfish	1	---	0.13
CHLORETOXYPHOS	Bluegill sunfish	1	---	2.30
ETHOPROP	Rainbow Trout	1	---	1150
	Bluegill sunfish	1	---	300

Corn Cluster Chemicals:
Freshwater Fish 96-hr LC_{50}s (ppb) cont'd.

Chemical	Species	No. Tests	Range	Median
PERMETHRIN	Rainbow Trout	9	2.9-8.2	5.20
	Brook Trout	3	2.3-5.2	3.20
	Fathead Minnow	2	5.7-5.7	5.70
	Channel Catfish	1	---	7.20
	Bluegill sunfish	10	4.5-13.0	7.00
ESFENVALERATE	Rainbow Trout	1	---	1.20
	Bluegill sunfish	1	---	0.30
METHOMYL	Cutthroat Trout	1	---	6800
	Rainbow Trout	21	860-3200	1400
	Atlantic Salmon	9	560-1400	1050
	Brook Trout	3	1220-2200	1500
	Fathead Minnow	3	1500-2800	1800
	Channel Catfish	5	300-1800	530
	Bluegill sunfish	20	870-2800	690
	Largemouth Bass	2	760-1250	1005
PHOSTEBUPIRIM	Bluegill sunfish	1	---	89
CARBARYL	Coho Salmon	5	1150-4340	2400
	Chinook Salmon	1	---	2400
	Cutthroat Trout	10	970-7100	4500
	Rainbow Trout	18	320-3500	1205
	Brown Tout	2	2000-6300	4150
	Brook Trout	9	680-4560	1700
	Lake Trout	5	690-2300	870
	Goldfish	2	12800-13200	13000
	Carp	1	---	5280
	Fathead Minnow	3	7700-14600	14000
	Black Bullhead	1	---	20000

Corn Cluster Chemicals:
Freshwater Fish 96-hr LC_{50}s (ppb) cont'd.

Chemical	Species	No. Tests	Range	Median
CARBARYL (cont'd.)	Channel Catfish	3	7790-17300	15800
	Green Sunfish	2	9460-11200	10550
	Bluegill sunfish	13	1800-3900	6200
	Largemouth Bass	1	---	6400
	Black Crappie	1	---	2600
	Yellow Perch	14	350-13900	3800
METHYL PARATHION	Coho Salmon	1	---	5300
	Cutthroat Trout	2	1850-4800	3365
	Rainbow Trout	2	2750-3700	3225
	Brown Trout	1	---	4700
	Lake Trout	2	3360-3780	3570
	Goldfish	1	---	9000
	Carp	1	---	7130
	Fathead Minnow	3	7200-9960	8900
	Black Bullhead	1	---	6640
	Channel Catfish	1	---	5240
	Green Sunfish	2	6860-6900	6880
	Bluegill sunfish	3	1000-6900	4380
	Largemouth Bass	1	---	5200
	Yellow Perch	1	---	3060
TRIMETHECARB	Rainbow Trout	1	---	1000

Corn Cluster Chemicals:
Trials of Three Random Species

Chemical	Random Trial I	Random Trial II	Random Trial III
TERBUFOS	Rainbow Trout	Fathead Minnow	Channel Catfish
CHLORPYRIFOS	Channel Catfish	Lake Trout	Rainbow Trout
FONOFOS	Rainbow Trout	Bluegill sunfish	Bluegill sunfish
PHORATE	Walleye	Channel Catfish	Bluegill sunfish
TEFLUTHRIN	Bluegill sunfish	Bluegill sunfish	Rainbow Trout
CHLORETHOXYPHOS	Bluegill sunfish	Bluegill sunfish	Bluegill sunfish
ETHOPROP	Rainbow Trout	Bluegill sunfish	Bluegill sunfish
PERMETHRIN	Bluegill sunfish	Rainbow Trout	Fathead Minnow
ESFENVALERATE	Rainbow Trout	Rainbow Trout	Bluegill sunfish
METHOMYL	Rainbow Trout	Fathead Minnow	Bluegill sunfish
PHOSTEBUPIRIM	Bluegill sunfish	Bluegill sunfish	Bluegill sunfish
CARBARYL	Coho Salmon	Yellow Perch	Yellow Perch
METHYL PARATHION	Yellow Perch	Lake Trout	Largemouth Bass
TRIMETHECARB	Rainbow Trout	Rainbow Trout	Rainbow Trout

Turf Cluster: Avian LD_{50} Data For NTN Alternatives

CHEMICAL	DIAZINON	TRICHLORFON	ISONFENPHOS	BENDIOCARB	ISAZOPHOS	CHLORPYRIFOS	NTN
EEC = mg/ft^2	50	83	21	43	20	47	5.2
ORIGINAL RQ*	BW 56	BW 42	BW 27	BW 25	BW 20	BW 16	BW0.4
SPECIES LD_{50}s							
Canada goose						60	
Mallard duck (M)	2.5	37	32	3.1	61		
Bobwhite quail (BW)	10.0	22	8.7	19	11	32	152
California quail						68	
Japanese quail	4.2					16	
Ring-necked pheasant (Ph)	4.3					13	
Chukar (Ch)						61	
Sandhill crane						38	
Common pigeon	3.2					18	
Common crow						32	
Starling (St.)	85.0	40				43	
Red-winged blackbird (RW)	3.2	43	5.3	6.9		13	
Common grackle (CG)	7.5					10	
House sparrow (HS)	7.5					15	41
RANDOM RQs* I	St.6.6	M 25	M 7.3	BW 26	BW 20	Ph 40	HS 1.4
II	CG 75	RW 22	RW 44	BW 26	M 3.7	Ch 8.6	HS 1.4
III	HS 75	St. 24	M 7.3	RW 71	M 3.7	M 5.6	BW0.4

* Risk Quotients are calculated for the weight of a Bobwhite quail

Appendix 3:

International Requirements for Test Species

International Requirements for Test Species

In response to a request from the SOG, OPP surveyed a number of pesticide regulatory authorities, as well as a key industry representative, about international requirements for ecotoxicological test species. OPP contacted the European Community (EC), Canada and New Zealand. OPP also contacted the chairman of NACA's International Committee, who represents the association in obtaining multi-national registrations.

Based on this survey, it appears that the majority of OECD member nations, including the EC, are generally using the same set of test species that are in use in the United States. Thus, it is likely that if we were to go to the OECD and request that test species be considered, that we could be effective in achieving a significant narrowing of recommendations.

<u>Summary</u>

A survey of other countries' regulatory authorities and multinational industry shows that the ecotoxicological test species in actual use internationally are generally very close to those used in the United States. The attached chart lists the test species used by OPP an those of the EC and compares them with species recommended by OECD.

Other authorities typically use safety factors with ecotoxicological hazard data. The size of the safety factor is generally adjusted to take into account the number of species for which test data are available and any differences in sensitivity between the species tested and those ecologically or commercially important native species potentially at risk. Thus, when high potential risk is indicated, other countries are likely to require an additional round of tests in native species. The OPP approach, in contrast, gives us results directly.

<u>European Community</u>

The EC scientific experts felt it was essential to recommend a concise set of test species as standards for its 12-member national in order to ensure mutual acceptance of test data developed for registration. With one minor exception, the interchangeable use of Japanese quail or bobwhite quail as representative upland game birds, the EC species are identical to United States species. In choosing their standard species, the EC considered three factors:

- existence of a relevant data base;
- availability of guidelines validated for that species; and
- ecological or commercial importance, if possible.

Dr. Mark Lynch of the EC feels that in light of these criteria, the species listed in Figure 7 are the best choice for use by the 12 EC member nations.

<u>Industry</u>

Multinational companies in the United States are comfortable in testing pesticides in United States test species. They find that databases using these species are generally acceptable internationally.

<u>New Zealand and Canada</u>

In polling New Zealand and Canada, OPP had selected representatives of two countries outside of the EC, with relatively minor pesticide markets. In each case, pesticide authorities take a flexible approach to test species. The U.S. test species, with the exception of the bluegill sunfish, are also native to Canada. When pesticides for use in either country pose high potential risks, particular non-target native species will be tested. In addition, each country relies on field testing or monitoring for high risk pesticides.

EC Choice of Test Species

Dr. Lynch, who has written the guidance for testing and risk assessment of pesticides in the EC, has noted that the driving force for selection by the EC of a limited set of test species for development of data for pesticides is the desirability of ensuring production of reliable data, while satisfying Article 10 of Directive 91/414/EC Concerning the Placing of Plant Protection Products on the Market. Article 10 specifies that a member state, in handling an application for a product already authorized by another member state must:

> . . . refrain from requiring the repetition of tests and analyses already carried out in connection with the authorization of the product in that member state, . . . also authorize the placing of that product on the market in its territory, to the extent that agricultural, plant health and environmental (including climatic) conditions relevant to the use of the product are comparable in the regions concerned.

In developing testing guidance for the EC, the scientific experts felt that if mutual recognition of testing and registrations was to work effectively and at the same time minimize testing on vertebrate species, they would have to specify a limited set of test species.

In choosing standard test species for use by registrants applying for registrations in EC member nations, three criteria were used:

- existence of a relevant data base;
- availability of guidelines validated for that species; and
- ecological or commercial importance, if possible.

The test species recommended by the EC are shown in Figure 7. They are very similar to those used in the United States for registration of pesticides. The EC recommends the mallard duck and either the Japanese quail or bobwhite quail. All three species have large data bases. Of the fish recommended, bluegill sunfish is not ecologically relevant, but there is a large body of test data for it. The rainbow trout is commercially important in Europe and known to be sensitive. The EC also specifies Daphnia magna, which recently has been recommended by an OECD expert panel.

Test Species -- U.S. Industry Point of View

Dr. Richard Nielsen chairs NACA's International Committee and participates in OECD meetings as the industry representative to the U.S. delegation. He also has experience at American Cyanamid Co. in multinational registration of pesticides. His company must pick test species that will satisfy the rest of the world, as well as EPA. He feels this can be done readily; in his experience, tests on U.S. species are acceptable worldwide. The only exception to this is for product applications to Japan, which also requires testing on the carp. For those few registrations in Japan, his company performs an extra LC_{50} test on the carp.

Test Species -- Canadian Registrations

Canadian guidelines do not explicitly specify test species. According to Dr. Pierre Mineau, Canadian authorities generally receive test data performed on U.S. species and may also receive studies performed on a wider range of test species as well. For pesticide chemicals that have high potential toxicity, Canada prefers testing in a wide variety of species. When tests are performed only in two avian or aquatic species, safety factors are used. The more species tested, the narrower the safety factor.

Canadian authorities will accept avian testing of the bobwhite quail and mallard duck, both native game species. They also accept test data, when available, from Japanese quail. However, they pointed out that smaller birds, and possibly passerines, are more sensitive to many pesticides.

Canadian authorities require aquatic testing of the rainbow trout and a second species. They accept studies of bluegill sunfish. Rainbow trout is a native species and is more sensitive to pesticides. For pesticides with high exposure or high potential risk, testing will also be required on salmon, which are native to Canada and ecologically and commercially important.

Test Species -- New Zealand

Dr. Adrian Foley in New Zealand said that companies generally register pesticides in that country after they are registered elsewhere. As a result, the data New Zealand uses for ecotoxicological risk assessment are generated for other authorities. They must extrapolate from whatever species are tested, but they prefer to see several species tested.

They generally see data in mallard ducks and bobwhite quail, and are likely to see tests performed on rainbow trout. If a chemical poses a special risk, as was the case for certain aquatic herbicides, they will also require testing in native species for registration. New Zealand pesticide authorities may require monitoring of pesticides in use, such as vertebrate poisons. In those cases, they will receive information on effects in native species.

Germans

German govt doesn't like using the zebrafish but test labs like it. They are "OK" c moving to more relevant species.