UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, DC 20460

JUN 1 1989

OFFICE OF
PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: REVISION OF EXPOSURE ASSESSMENT FOR CHILDREN PLAYING
ON RESIDENTIAL TURF TREATED WITH ISOXABEN

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Please find below the NDEB review of ....

HED Project #: _____ 9-1469A _____

RD of SRRD Record #: _____ 245254, 245255 _____

Registration #: _____

Caswell #: _____ 419F _____

Company Name: Elanco Products _____

Date Received: 5/17/89   Action Code: 116

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_____ Science Coordination and Analysis Branch

_____ TB - Insecticide/Rodenticide Support Branch

_____ TB - Herbicide/Fungicide/Antimicrobial
Support Section

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Elanco Products has submitted a rebuttal to an estimate of the
exposure of children to their fungicide isoxaben, used on
residential turf. The original submission did not contain any
data specific to isoxaben but rather provided an exposure and risk
assessment using surrogate dislodgeable residue data for another
chemical used on turf. In response to this submission, NDEB provided
an estimate for exposures of children on residential turf treated
with isoxaben in a memorandum dated 14 March 1989 (1). Two methods,
one estimating exposure from a correlation found in the scientific
literature between dislodgeable residues and dermal exposure of
fruit harvesters and the other derived using certain arbitrary
assumptions were used for the assessment. Neither of these techniques
has been substantiated. These two methods yielded similar dermal
exposures, differing by only about 20 percent. The fruit harvester
correlation, while adequate for some situations, was judged by the
registrant not to be representative of a scenario where children
might be playing on treated lawns. Estimates based on other
assumptions were considered to be more appropriate for this scenario.

Most of the assumptions used by NDEB and the registrant were similar.
The few assumptions that were different resulted in unequal estimates
of exposure. Detailed explanations of the effects of changes for
each of the assumptions are presented in the following sections.

EFFECT OF INITIAL DISLODGEABLE RESIDUE LEVELS OF ISOXABEN ON TREATED
TURF

The registrant estimated the initial amount of dislodgeable isoxaben
residue on a treated lawn to be 1.69 ug/cm^2 using a ratio of total
to dislodgeable residues of 4.4. This factor was derived from
data obtained in a field dissipation study measuring dislodgeable
residues of the growth regulator flurprimidol (Cutless 50W) on
turf. No data were submitted to support the use of this compound
as a surrogate for isoxaben. The registrant cited similarities in
usage pattern, application rate,and formulation type in defense of
the use of this information to estimate isoxaben residues.
Flurprimidol is not structurally similar to isoxaben. It is not
certain whether isoxaben and flurprimidol exhibit the same properties
with regard to dislodgeable residues and environmental fate. NDEB
used the conservative assumption that the surface residue level
was 11.2 ug per cm^2, approximately 6.6 times that estimated by
the registrant using surrogate data from a different compound, and
that all of this material was available for transfer to the child.
It is NDEB's opinion that surrogate data, while useful for worker
exposure estimation in some situations, are not applicable for any
exposure estimate that can be appreciably affected by the nature
of residues, environmental fate, other specific properties of the
compound in question.

EFFECT OF DISSIPATION PATTERN OF ISOXABEN ON TURF

The proposed label requires that the treated turf be watered within
21 days of application to activate the fungicide. The assessment
conducted by NDEB assumed that, since the effects of watering the
treated area on residue levels are not known, the quantity of isoxaben
residue on treated turf remained constant over a 21 day period.
It was further assumed that all of the material deposited on a
treated surface was available for transport to the skin. After
this time all material was assumed to be dissipated and no further
exposure would occur. The registrant assumed that residues
dissipation followed first order kinetics and that this decay began
immediately after application. The registrant referenced a soil
dissipation study which included measurements of isoxaben in turf
and in the first 6 inches of soil. The half life of isoxaben residues
on treated turf was estimated to be 87 days. A soil dissipation
study was reviewed in the Isoxaben Addendum to the Registration
Standard. This study measured soil residues after application of
isoxaben at 1.0 lb ai per acre. The initial total residues on the
turf or in first six inches of soil were 0.96 lb per acre. The
relative contribution of residues on the turf foliage to this total
was not reported (2). The registrant then reduced this half life
estimate to 21 days based on the behavior of other lawn treatment
chemicals and on the assumption that the watering of the turf would
decrease the surface residues within a 21 day period. After 21
days the residues were assumed to remain constant at 10 percent of
those estimated for day 21. No supporting data for either of these
assumptions are available. The two dissipation patterns assumed
by NDEB and the registrant are presented in Figure 1. The soil
dissipation study cited above found that, after 211 days and after
receipt of 28 inches of water by the treated plot, the residues in
the surface/six inch samples were still at a level of 0.17 lb ai
per acre (1.9 ug per cm^2 if all material is assumed to be located
on the surface). If the unsubstantiated assumption that dislodgeable
residues are decreased by a factor of 4.4 is accepted, the dislodgeable
residues would then be 0.43 ug/cm^2. The effect of dissipation
pattern on exposure varies with the spacing of the exposure events.
The overall exposure is more dependent on other assumptions rather
than any specific dissipation pattern. If other assumptions are
kept constant, the dissipation pattern changes the exposure by a
factor of about 1.1-1.4

EFFECT OF CLOTHING

Both NDEB and the registrant assumed that the entire surface area
of the body would be uniformly exposed to the surface residues of
isoxaben and that transfer from the treated surface to the skin
was 100 percent efficient. The surface areas of a 2-6 year old
and a child at ages 7-12 were assumed to be 0.7 and 0.9 m^2,
respectively. No adjustments were made for the wearing of clothing
in NDEB's previous assessment. The trunk of the body of a child
has been estimated to contribute approximately 34 percent to the

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total surface area (3). If it is assumed that the trunk is covered
by clothing (ie, wearing a tee shirt and shorts) and that the clothing
completely protects covered areas, the dermal component of exposure
would be reduced by that percentage. NDEB notes that clothing is
unlikely to provide complete protection, particularly if it is wet
or torn. Uniform exposure of each area of the body is not likely
to occur and this factor contributes to the uncertainty associated
with these estimates.

EFFECT OF ACTIVITY PATTERN

Both NDEB and the registrant assumed a total of 42 exposure days
per year for 10 years (ages 2-12). NDEB assumed daily exposure
for 21 consecutive days immediately after treatment with 2
applications per year. The registrant assumed the 42 exposure
days were spread out over a 183 day period between two treatments.
Children may be exposed to treated turf for more than 42 days,
depending on climate. The average residues, assuming the registrant's
dissipation pattern, were 0.22 ug per cm^2 as opposed to the 11.2
ug per cm2 under NDEB's scenario. Both parties assumed 100 percent
transfer between turf residues and the skin and that the entire
surface of a child is exposed only one time per day. The differences
in the spacing of the exposure periods result in a 1.7-9 fold
difference between the exposure estimates provided by NDEB and the
registrant, depending on the other assumptions for a given scenario.

CONCLUSIONS

NDEB has calculated exposures for various combinations of initial
residue level, dissipation order, and activity pattern. The
calculations are explained in detail in Appendix A. The dermal
component greatly exceeded exposure by the oral route. The
registrant and NDEB used some different assumptions to estimate
exposures. Data to support the assumptions used in any of these
calculations are currently lacking. It is reasonable to assume
that the watering of a treated lawn would affect the available
residues in some way. However, since the soil dissipation study
neglected to determine the fraction that remained in or on the
treated turf, it is not possible to determine the magnitude of
this effect. Appreciable residues were present in the turf/six
inch fraction after considerable time and after extensive watering
of the treated area. NDEB believes that, in lieu of additional
information, any assumption of a decay pattern, such as the 21-day
half life with 90 percent reduction after day 21, is unsupported
and that the conservative assumption of no decay for 21 days is
both prudent and appropriate. The registrant's assumption of a
dislodgeable residue level of 1.69 ug per cm^2 is based on surrogate
data for chemicals whose environmental fate and dislodgeable fraction
may, or may not, adequately represent those of isoxaben. The
assumption of complete dissipation after 21 days, which was used
by NDEB, is not so conservative and may underestimate actual

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dislodgeable residues. The differing assumptions and their approximate effects on the total exposures estimated are summarized in Table 1. The actual exposure estimates for each scenario are presented in Table 2 and also depicted in Figure 2.

NDEB notes that a number of other factors could influence the exposures of individuals to materials on residential turf. The number of exposure days could be quite different than the 42 assumed in this assessment. The clothing worn could range from minimal, such as a diaper or shorts to long sleeve shirt and trousers. The activity pattern will change as the individual grows older. Exposure is also likely to continue to some extent through adulthood. The effects of rainfall and the presence of moisture on the turf could affect both the dissipation of the material and the rate of transfer from the treated surface to the skin. The effects of these factors is not known. It is clear that the exposures of individuals to compounds used on residential turf presents a complex matrix of possibilities. Should Toxicology Branch decide that the risks justify a more refined exposure assessment additional data, both compound specific and addressing activity patterns, will be necessary.

POSSIBLE OPTIONS TO MITIGATE EXPOSURE

There are some options available for mitigating exposures of persons contacting treated residential turf that should be considered. Typical actions such as protective clothing, engineering controls and extended reentry intervals are not suitable for a residential turf scenario. One reasonable change that could be incorporated into the isoxaben label would be to limit the number of applications to one time per year. A second possibility would be to require watering the treated lawn before the 21 day interval currently recommended by the label. NDEB notes that the effect of watering on dislodgeable residues is currently unknown and that data addressing these residues would still be necessary in order to conduct a more reliable exposure assessment.

cc: Correspondence file
       Isoxaben file
       Circulation
       TB-HFAS
       SACB

Table 1. Comparison of Assumptions Used by Elanco Products and
NDEB to Estimate the Exposures of Children Playing on
Lawns Treated with Isoxaben (Gallery.

NDEB ASSUMPTIONS:	Difference Factor	ELANCO ASSUMPTIONS:
The surface residue on treated turf is 11.2 ug/cm^2. All of this is considered to be available for transfer to the skin. Isoxaben is applied at the maximum label rate of 1.33 lb product per acre (1.0 lb ai/A). Isoxaben is applied 2 times per year at 183 day intervals.	6.2-6.8	**Initial dislodgeable residue on treated turf is 1.69 ug/cm^2.** This estimate is based ratio of total to dislodgeable residues of 4.4 for a surrogate compound, flurprimidol, which is applied in the same manner. Flurprimidol is **NOT** structurally similar to isoxaben. Isoxaben is applied at rate of 0.75 lb product per acre, less than the maximum label rate. Isoxaben is applied 2 times per year at 183 day intervals.
Residues on the treated surface remain constant for 21 days after application. Following this interval all residues are assumed to have dissipated.	1.1-1.4	**Residues on the treated surface dissipate with a half life of 21 days. After 21 days the surface residues drop to 0.085 ug/cm^2 and remain constant at this level until the next treatment.** The average dislodgeable residue level over this interval is 0.22 ug/cm^2.

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Table 1 (Continued). Comparison of Assumptions Used by Elanco
Products and NDEB to Estimate the Exposures of Children
Playing on Lawns Treated with Isoxaben (Gallery).

	1.7-9	
Exposure occurs once per day on the 21 days immediately following treatment. Dermal exposure occurs over the entire surface of the child (0.7 and 0.9 m^2 for a 2-6 year old and a 7-12 year old child, respectively). Repeated contact is assumed not to occur. Body weights are assumed to be 17 kg for children 2-6 and 31 kg for ages 7-12.		**Children are exposed to isoxaben for 42 days per year, spread over 183 day intervals after each treatment.** Such exposure occurs once per day. Repeated contact is assumed not to occur. Dermal exposure occurs over the entire surface of the child (0.7 and 0.9 m^2 for a 2-6 year old and a 7-12 year old child, respectively). Body weights are assumed to be 17 kg for children 2-6 and 31 kg for ages 7-12.
	1.03	
Oral exposure occurs from licking a surface equal to that of one hand **AND** from licking the surface of a 3 inch diameter ball.		Oral exposure occurs from licking a surface equal to that of one hand **OR** from licking the surface of a 3 inch diameter ball.
Transfer of isoxaben from the treated surface to the skin is assumed to be 100 percent efficient. Skin surface residues are equal to those on the treated area.		Transfer of isoxaben from the treated surface to the skin is assumed to be 100 percent efficient. Skin surface residues are equal to those on the treated area.
Lifetime exposure of a child will encompass 10 years (ages 2-12). A child is exposed for 42 days per year.		Lifetime exposure of a child will encompass 10 years (ages 2-12). A child is exposed for 42 days per year.

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FIGURE 1.

ESTIMATED ISOXABEN RESIDUES ON RESIDENTIAL TURF

ISOXABEN (ug/sq cm)

NDEB assumes that all exposure occurs before day 22

DAYS AFTER TREATMENT

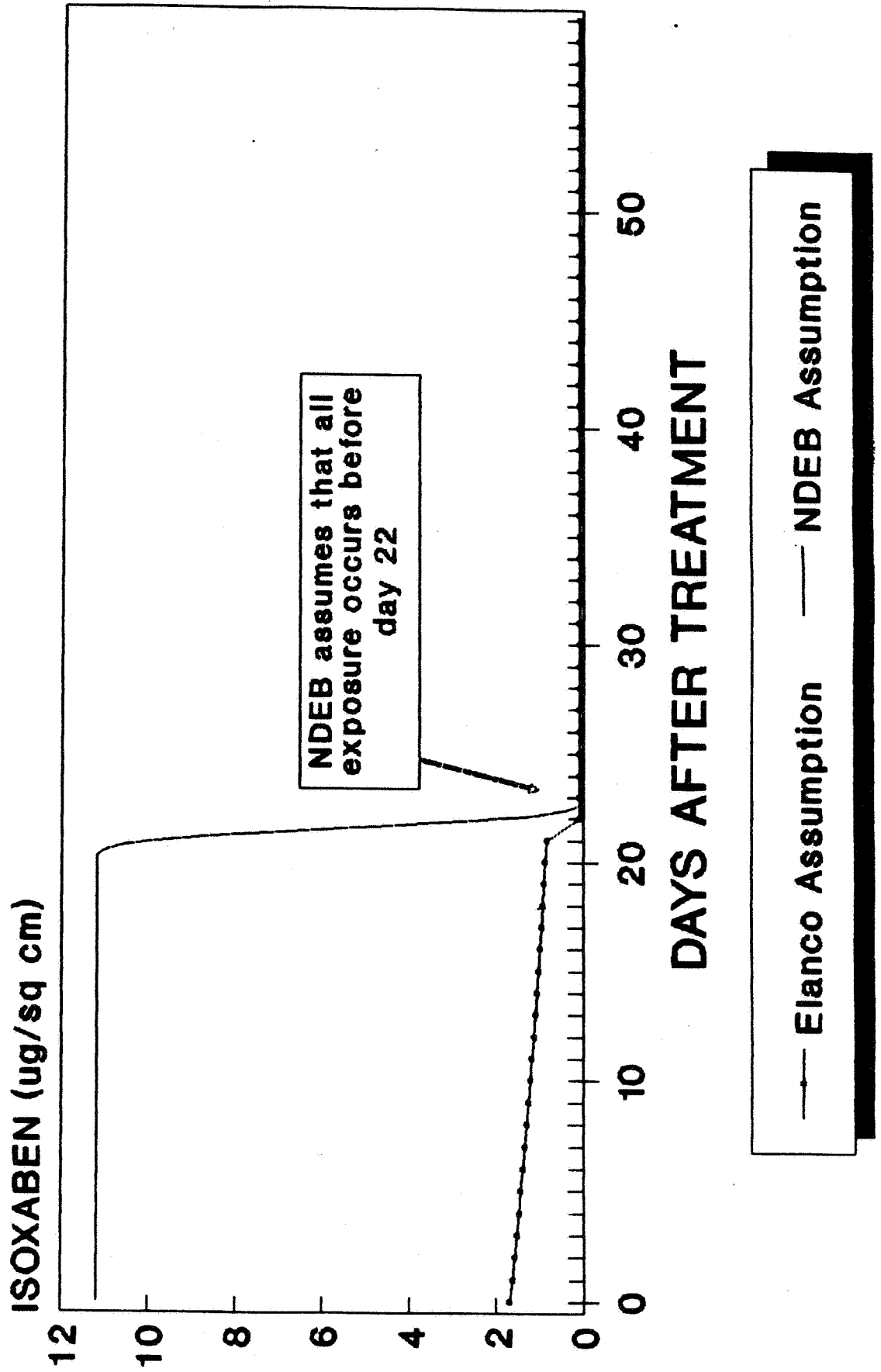Elanco Assumption   NDEB Assumption

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Table 2. Estimated Average Lifetime Exposures of Individuals to Isoxaben Applied to Residential Turf. Exposure is assumed to occur for 42 days per year during ages 2-12 only. Margins of Safety (MOS) are based on a 2 year rat study and were provided by Toxicology Branch.

Initial Residue (ug/cm^2)	Dissipation Pattern	Exposed on First 21 Days After Treatment Only		Exposure Spread Over 183 Days After Treatment	
		Average Residues (ug/sq cm)	Lifetime Exposure mg/kg/yr (MOS)	Average Residues (ug/sq cm)	Lifetime Exposure mg/kg/yr (MOS)
(1) 11.2	None for 21 days, 0 thereafter	11.2	24 (76)	1.29	2.82 (647)
(2) 11.2	First order with 21 day half life	8.1	18 (100)	1.87	4.07 (448)
(3) 11.2	First order with 21 day half life, constant at 0.56 after 21 days.	8.1	18 (100)	1.46	3.23 (565)
(4) 11.2	First order with 87 day half life	10.3	23 (79)	5.9	12.54 (146)
(5) 11.2	First order with 87 day half life, constant at 0.56 after 21 days.	10.3	23 (79)	2.07	4.59 (398)
(6) 1.69	None for 21 days, 0 thereafter	1.69	3.8 (480)	0.19	0.42 (4345)
(7) 1.69	First order with 21 day half life	1.22	2.7 (676)	0.28	0.63 (2897)
(8) 1.69	First order with 21 day half life, constant at 0.085 after 21 days.	1.22	2.7 (676)	0.22	0.52 (3510)
(9) 1.69	First order with 87 day half life	1.56	3.4 (537)	0.89	1.98 (922)
(10) 1.69	First order with 87 day half life, constant at 0.085 after 21 days.	1.56	3.4 (537)	0.31	0.73 (2500)

FIGURE 2.

LIFETIME EXPOSURES TO ISOXABEN ON TURF
(42 Days of Exposure Per Year)

Average Lifetime Exposure (mg/kg/yr)

Exposure Scenario

☐ During Days 1-21   ■ During Days 1-183
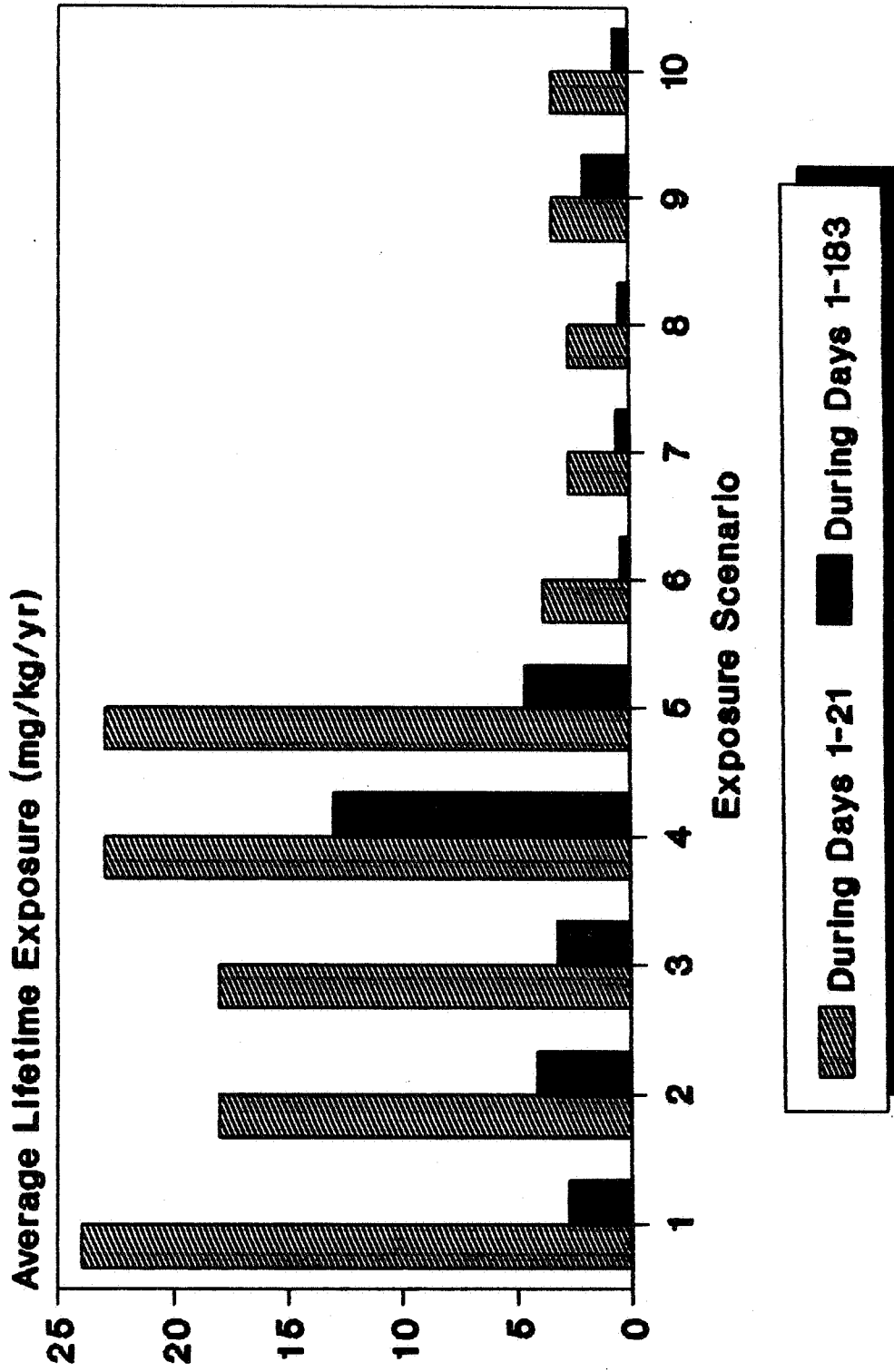
See Table 2 for Scenario Description

Appendix A.
Calculation of Lifetime Exposures of Individuals to
Isoxaben Applied to Residential Turf

Assumptions:

1) Children are exposed to isoxaben 42 days per year for 10 years
(ages 2-12). No further exposure occurs after that time.

2) The body weights for a 2-6 and 7-12 year old child are 17 and
31 kg, respectively. The corresponding surface areas are 7000
and 9000 cm^2.

3) The entire surface area of the child is exposed to the treated
surface. Exposure occurs only one time per day.

4) Transfer of isoxaben from the treated surface is 100 percent
efficient. Residues on the skin are equal to those on the turf.

5) Dermal penetration is assumed to be 11 percent as provided by
the registrant.

6) Oral exposure occurs from licking an area equal to that of one
hand and the surface of a 3 inch diameter ball. The hand surface
area is assumed to be 140 cm^2 for a 2-6 year old and 180 cm^2
for ages 7-12.

Calculation of Exposure:

The daily dermal exposure of a child to isoxaben is calculated by
the following equation:

$$\text{Daily Dermal Exposure (mg/kg)} = \frac{\text{Surface Residues (ug/cm}^2\text{)} \times \text{Surface Area (cm}^2\text{)}}{\text{Body weight (kg)} \times 1000 \text{ ug/mg}}$$

The annual exposure, adjusted for 11 percent dermal absorption
would be:

$$\text{Annual Dermal Exposure (mg/kg/yr)} = \text{Daily Dermal Exposure} \times 42 \text{ days/yr} \times 0.11$$

Appendix A.
Calculation of Lifetime Exposures of Individuals to
Isoxaben Applied to Residential Turf

Combining equations and substituting the appropriate constants
yields the following:

$$\text{Mean Lifetime Exposure (mg/kg/yr)} = \frac{\left[\dfrac{(\text{Residue} \times SA_1)}{BW_1 \times 1000} + \dfrac{(\text{Residue} \times SA_2)}{BW_2 \times 1000}\right] \times \dfrac{42 \text{ day}}{\text{year}} \times 5 \text{ yr} \times PF}{70 \text{ years}}$$

where:

  Residue = Average residue (ug/cm^2) **during the exposure
            period**
  SA_1 = Surface area of a 2-6 year old child = 7000 cm^2
  SA_2 = Surface area of a 7-12 year old child = 9000 2m^2
  BW_1 = Body Weight of a 2-6 year old child = 17 kg
  BW_2 = Body Weight of a 2-6 year old child = 31 kg
  PF   = Penetration factor = 11 % = 0.11

Substituting the constant values:

$$\text{Exposure} = \frac{\left[\dfrac{(7000 \text{ cm}^2)}{17 \text{ kg}} + \dfrac{(9000 \text{ cm}^2)}{31 \text{ kg}}\right] \times \dfrac{42 \text{ days/yr}}{1000 \text{ ug/mg}} \times 5 \text{ yr} \times 0.11}{70 \text{ years}}$$

   or, after combining constant values:

Exposure = Residue x 2.11

For an average residue level of 11.2 ug/cm^2, this lifetime exposure
becomes:

Average lifetime exposure (mg/kg/yr) = 11.2 ug/cm^2 x 2.11

                                     = 24 mg/kg/yr

Each of the scenarios considered yields a different average residue
value. The oral component of exposure can be calculated in the
same manner by substituting the appropriate hand surface areas
and the surface area of a 3 inch diameter ball into the above
equations. The corresponding multiplication factor for estimation
of exposure from surface residues reduces to 0.091.

REFERENCES

1) Memorandum from M. Firestone (NDEB) to R. Mounfort (RD) titled "Isoxaben Exposure Estimate for Children Playing on Treated Lawns", dated 14 March 1989.

2) Rutherford, B.S. and O.D. Decker (1988) Isoxaben Turf Field Dissipation Study - Illinois Site. MRID No. 40532102.

3) U.S. Dept of Commerce (1985) Development of Statistical Distributions of Standard Factors Used in Exposure Assessments. NTIS No. PB85-242667