

SCREENING-LEVEL HAZARD CHARACTERIZATION

3-Ethoxypropionic acid ethyl ester (CASRN 763-69-9)

The High Production Volume (HPV) Challenge Program¹ was conceived as a voluntary initiative aimed at developing and making publicly available screening-level health and environmental effects information on chemicals manufactured in or imported into the United States in quantities greater than one million pounds per year. In the Challenge Program, producers and importers of HPV chemicals voluntarily sponsored chemicals; sponsorship entailed the identification and initial assessment of the adequacy of existing toxicity data/information, conducting new testing if adequate data did not exist, and making both new and existing data and information available to the public. Each complete data submission contains data on 18 internationally agreed to “SIDS” (Screening Information Data Set^{1,2}) endpoints that are screening-level indicators of potential hazards (toxicity) for humans or the environment.

The Environmental Protection Agency’s Office of Pollution Prevention and Toxics (OPPT) is evaluating the data submitted in the HPV Challenge Program on approximately 1400 sponsored chemicals by developing hazard characterizations (HCs). These HCs consist of an evaluation of the quality and completeness of the data set provided in the Challenge Program submissions. They are not intended to be definitive statements regarding the possibility of unreasonable risk of injury to health or the environment.

The evaluation is performed according to established EPA guidance^{2,3} and is based primarily on hazard data provided by sponsors; however, in preparing the hazard characterization, EPA considered its own comments and public comments on the original submission as well as the sponsor’s responses to comments and revisions made to the submission. In order to determine whether any new hazard information was developed since the time of the HPV submission, a search of the following databases was made from one year prior to the date of the HPV Challenge submission to the present: (ChemID to locate available data sources including Medline/PubMed, Toxline, HSDB, IRIS, NTP, ATSDR, IARC, EXTOXNET, EPA SRS, etc.), STN/CAS online databases (Registry file for locators, ChemAbs for toxicology data, RTECS, Merck, etc.) and Science Direct. OPPT’s focus on these specific sources is based on their being of high quality, highly relevant to hazard characterization, and publicly available.

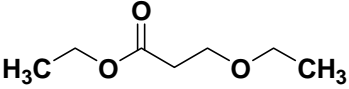
OPPT does not develop HCs for those HPV chemicals which have already been assessed internationally through the HPV program of the Organization for Economic Cooperation and Development (OECD) and for which Screening Initial Data Set (SIDS) Initial Assessment Reports (SIAR) and SIDS Initial Assessment Profiles (SIAP) are available. These documents are presented in an international forum that involves review and endorsement by governmental authorities around the world. OPPT is an active participant in these meetings and accepts these documents as reliable screening-level hazard assessments.

¹ U.S. EPA. High Production Volume (HPV) Challenge Program; <http://www.epa.gov/chemrtk/index.htm>.

² U.S. EPA. HPV Challenge Program – Information Sources; <http://www.epa.gov/chemrtk/pubs/general/guidocs.htm>.

³ U.S. EPA. Risk Assessment Guidelines; <http://cfpub.epa.gov/ncea/raf/rafguid.cfm>.

These hazard characterizations are technical documents intended to inform subsequent decisions and actions by OPPT. Accordingly, the documents are not written with the goal of informing the general public. However, they do provide a vehicle for public access to a concise assessment of the raw technical data on HPV chemicals and provide information previously not readily available to the public.

<p>Chemical Abstract Service Registry Number (CASRN)</p>	<p>763-69-9</p>
<p>Chemical Abstract Index Name</p>	<p>Propanoic acid, 3-ethoxy, ethyl ester</p>
<p>Structural Formula</p>	
<p style="text-align: center;">Summary</p> <p>CASRN 763-69-9 is a liquid with high water solubility and moderate to high vapor pressure at room temperature. It is expected to have high mobility in soil. Volatilization is considered moderate based on its Henry's Law constant. The rate of hydrolysis is considered negligible. The rate of atmospheric photooxidation is considered moderate. CASRN 763-69-9 is expected to have low persistence (P1) and low bioaccumulation potential (B1).</p> <p>The acute toxicity of CASRN 763-69-9 is low in rats by the oral and inhalation routes and low in rabbits by the dermal route. There were no adverse treatment-related effects in a 28-day oral gavage repeated-dose toxicity study in rats; the NOAEL is 1000 mg/kg-day (highest dose tested). A 90-day inhalation repeated-dose toxicity study in rats showed decreases in body weights at the two highest concentrations; the NOAEC for systemic toxicity is 1.49 mg/L/day. No reproductive toxicity studies were available. However, the 90-day inhalation study in rats showed no adverse treatment-related effects on reproductive organs. In a prenatal inhalation developmental toxicity study of CASRN 763-69-9 in rats, maternal weight gain was decreased at 1.46 mg/L/day and above; the NOAEC for maternal toxicity is 0.73 mg/L/day. Slight increases in the incidence of some minor internal soft tissue alterations and skeletal variants, and the appearance of rudimentary 14th ribs were seen at 5.82 mg/L/day (highest concentration tested); the NOAEC for developmental toxicity is 2.98 mg/L/day. In a prenatal inhalation developmental toxicity study with CASRN 763-69-9 in rabbits, decreased body weight gain was seen in dams at 5.97 mg/L/day (highest concentration tested); the NOAEC for maternal toxicity is 2.98 mg/L/day. No effects were noted on developmental parameters; the NOAEC for developmental toxicity is 5.97 mg/L/day (highest concentration tested). CASRN 763-69-9 was not mutagenic in bacteria and did not induce chromosomal aberrations in mammalian cells <i>in vitro</i>.</p> <p>For CASRN 763-69-9, the 96-hour LC₅₀ for fish is 50 mg/L. The 48-hour EC₅₀ for aquatic invertebrates is 785 mg/L. The 72-hour EC₅₀ for aquatic plants is > 115 mg/L (biomass and growth rate).</p> <p>There are no data gaps identified under the HPV Challenge Program.</p>	

The sponsor, the Eastman Chemical Company/ the Dow Chemical Company, submitted a Test Plan and Robust Summaries to EPA for 3-ethoxypropionic acid ethyl ester (CASRN 763-69-9; CA Index name: propanoic acid, 3-ethoxy, ethyl ester) on October 4, 2001. EPA posted the submission on the ChemRTK HPV Challenge website on October 16, 2001 (<http://www.epa.gov/chemrtk/pubs/summaries/3ethox/c13220tc.htm>). EPA comments on the original submission were posted to the website on April 12, 2002. Public comments were also received and posted to the website. The sponsor submitted updated/revised documents on May 22, 2002, which were posted to the ChemRTK website on June 19, 2002.

1. Chemical Identity

1.1 Identification and Purity

The following description is taken from the 2002 Test Plan and Robust Summary. 3-Ethoxypropionic acid ethyl ester is a simple alkyl ester. Test substance purity, when noted in the Robust Summaries, was given as $\geq 99\%$.

1.2 Physical-Chemical Properties

The physical-chemical properties of CASRN 763-69-9 are summarized in Table 1.

Property	Value
CASRN	763-69-9
Molecular Weight	146.19
Physical State	Liquid
Melting Point	-50°C (measured) ²
Boiling Point	165–172°C (measured) ²
Vapor Pressure	0.9 mm Hg at 20°C (measured) ³ ; 1.5 mm Hg at 25°C (estimated)
Water Solubility	55,000 mg/L at 25°C (measured) ^{4,6}
Dissociation Constant (pK _a)	Not applicable
Henry's Law Constant	3.1×10^{-6} atm·m ³ /mole (estimated) ⁵
Log K _{ow}	1.08 (estimated)

¹ Eastman Chemical Company/The Dow Chemical Company. May 22, 2002. Final Revised Test Plan and Robust Summary for 3-ethoxypropionic acid ethyl ester. Available from:

<http://www.epa.gov/chemrtk/pubs/summaries/3ethox/c13220tc.htm> as of June 19, 2002.

² Tau, K.D.; Elango, V.; McDonough, J.A. 1994. Esters, Organic. In: Kirk-Othmer's Encyclopedia of Chemical Technology, 4th Edition, Kroschwitz JI (ed.), New York, NY: John Wiley & Sons, Inc., Volume 9, p. 78.

³ Lewis, R.J., Sr. 1997. Hawley's Condensed Chemical Dictionary, 13th Edition, New York, NY: John Wiley & Sons, Inc., p. 472.

⁴ SRC. The Physical Properties Database (PHYSPROP). SRC: Syracuse, NY. Available online from <http://www.syrres.com/what-we-do/free-demos.aspx> as of March 30, 2010.

⁵ U.S. EPA. 2010. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.00. U.S. Environmental Protection Agency, Washington, DC, USA. Available online from:

<http://www.epa.gov/opptintr/exposure/pubs/episuitedl.htm> as of March 30, 2010.

⁶ Beilstein, E3, Volume 3, part 1, page 528.

2. General Information on Exposure

2.1 Production Volume and Use Pattern

According to the 2006 IUR submissions, CASRN 763-69-9 had an aggregated production and/or import volume(s) in the United States between 10 and 50 million pounds.

Non-confidential industrial processing and uses reported in the 2006 IUR submissions for this chemical include other basic organic chemical manufacturing as solvents (which become part of product formulations or mixtures). Non-confidential commercial and consumer uses of this chemical include paints and coatings.

2.2 Environmental Exposure and Fate

CASRN 763-69-9 is expected to have high mobility in soil. CASRN 763-69-9 achieved 60 and 66% degradation as measured by CO₂ evolution using a modified Sturm test (OECD 301B). The results did not meet the technical criteria for ready biodegradability; however, the loss of the test substance measured by dissolved organic carbon (DOC) analysis indicated that primary biodegradation was 99.9% and the conclusion was that CASRN 763-69-9 is not persistent. A second modified Sturm test indicated that CASRN 763-69-9 was completely degraded after 18 days. CASRN 763-69-9 degraded over 90% within 23 days using a Zahn-Wellens test (OECD 302B) for inherent biodegradability. Volatilization of CASRN 763-69-9 is considered moderate based on the Henry's Law constant. The rate of hydrolysis is considered negligible under environmental conditions; however, under highly alkaline conditions chemical hydrolysis may be important. CASRN 763-69-9 is expected to have low persistence (P1) and low bioaccumulation (B1).

Table 2 lists the environmental fate properties of CASRN 763-69-9.

Property	Value
Photodegradation Half-life	8.1 hours (estimated)
Hydrolysis Half-life	102.8 days at 25°C and pH 8 (estimated); 2.8 years at 25°C and pH 7 (estimated)
Biodegradation	60–66% after 28 days (not readily biodegradable); 100% after 18 days (readily biodegradable); 98% after 23 days (inherently biodegradable); 43% after 28 days (moderately biodegradable)
Bioaccumulation Factor	BAF = 1.4 (estimated) ²
Log K _{oc}	1.0 (estimated) ²
Fugacity (Level III Model) ²	
Air (%)	1.3
Water (%)	39.7
Soil (%)	58.8
Sediment (%)	0.1
Persistence ³	P1 (low)
Bioaccumulation ³	B1 (low)

¹ Eastman Chemical Company. May 19, 2002. Revised Robust Summary for Propanoic Acid, 3-Ethoxy-, Ethyl Ester. Available online from: <http://www.epa.gov/chemrtk/pubs/summaries/3ethox/c13220tc.htm> as of March 30, 2010.

² U.S. EPA. 2010. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.00. U.S. Environmental Protection Agency, Washington, DC, USA. Available online from: <http://www.epa.gov/opptintr/exposure/pubs/episuitedi.htm> as of March 30, 2010.

³ Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

3. Human Health Hazard

The human health data are summarized in Table 3.

Acute Oral Toxicity

Sprague-Dawley rats (5/sex) were administered a single dose of the test substance via gavage at 5000 mg/kg-bw and observed for 14 days. No males died, but three females died within two days of exposure. In the robust summary, the sponsor indicated that the LD₅₀ range for females is from 3200 – 5000 mg/kg based on results from another study in which no females died following an acute oral exposure of 3200 mg/kg. No additional information was provided.

LD₅₀ > 5000 mg/kg (males)

LD₅₀ = 3200 - 5000 mg/kg (females)

Acute Dermal Toxicity

Male New Zealand albino rabbits (4/dose) were administered the test substance via the dermal route at unspecified doses, to intact skin for 24 hours with occlusion and observed for 14 days. Mortality results were not reported (Smyth *et al.*, 1951; Smyth *et al.*, 1962).

LD₅₀ > 9500 mg/kg

Acute Inhalation Toxicity

Male Sprague-Dawley rats (4/dose) were exposed to the test substance as a vapor at 0, 500 or 1000 ppm (actual levels 481 and 998 ppm, or approximately 2.87 and 5.96 mg/L) for 6 hours and were observed for 14 days. There were no deaths reported.

LC₅₀ > 5.96 mg/L

Repeated-Dose Toxicity

Oral

In a 28-day study, Sprague-Dawley rats (5/sex/dose) were administered the test substance via gavage at 0, 100 or 1000 mg/kg-day, 5 days/week. There were two deaths in the high-dose group due to gavage errors, and these animals were replaced with animals of comparable age and weight on Day 3. There were no deaths or clinical signs, no abnormal body weight changes and no treatment-related histopathological findings at necropsy. The only effect seen was an increase in serum enzymes (AST and SDH) and creatinine levels in high-dose animals.

NOAEL = 1000 mg/kg/day (highest dose tested)

Inhalation

In a 90-day study, Sprague-Dawley rats (15/exposure concentration; males and females) were exposed to the test substance as a vapor at 0, 250, 500 or 1000 ppm (actual exposure concentrations were 251, 510 and 996 ppm, or approximately 1.49, 2.98 and 5.97 mg/L/day), 6 hours/day, 5 days/week. One female at 1000 ppm died. Statistically significant decreases in body weights were seen in males and females at 500 and 1000 ppm. The major clinical sign of toxicity in both sexes was irritation manifesting as lacrimation, discoloration of facial hair and unkempt appearance (concentrations not specified). Lethargy was seen in animals at 1000 ppm only during the first few exposures. Clinical chemistry changes at 1000 ppm included a slight increase in lymphocyte percentage (females), a statistically significant decrease in serum glucose (males), and an increase in creatinine (both sexes). A significant increase in alkaline phosphatase levels was also observed in females at 500 and 1000 ppm. There were no treatment-related histopathological findings at necropsy.

LOAEC ~2.98 mg/L/day (based on decreased body weights)

NOAEC ~1.49 mg/L/day

Reproductive Toxicity

No reproductive toxicity studies are available. In the 90-day repeated-dose inhalation toxicity study in rats described above, there were no treatment-related histopathological or weight changes in reproductive organs examined (testes and ovaries were weighed; testes, epididymides, male accessory gland, ovaries, vagina, uterus and fallopian tubes were microscopically examined).

Developmental Toxicity

(1) In a prenatal developmental toxicity study, pregnant Sprague-Dawley rats (25/exposure concentration) were exposed to the test substance as a vapor (whole-body) at concentrations of 0, 125, 250, 500 or 1000 ppm for 6 hours/day on days 6 through 15 of gestation. Actual exposure concentrations were 123, 245, 500 and 975 ppm (approximately 0.73, 1.46, 2.98 and 5.82 mg/L/day). During days 6 through 16 of gestation, absolute body weights in dams were decreased at 500 and 1000 ppm and dam food consumption and weight gain was decreased at 250 ppm and higher. Clinical signs of toxicity (lethargy, salivation) were noted at 1000 ppm. In pups, slight increases in the incidence of some minor internal soft tissue alterations and skeletal variants were seen at 1000 ppm. The appearance of rudimentary 14th ribs was also increased at 1000 ppm.

LOAEC (maternal toxicity) ~ 1.46 mg/L/day (based on decreased body weight gain)

NOAEC (maternal toxicity) ~ 0.73 mg/L/day

LOAEC (developmental toxicity) ~ 5.82 mg/L/day (based on increases in the incidence of internal soft tissue alterations and skeletal variants)

NOAEC (developmental toxicity) ~ 2.98 mg/L/day

(2) In a prenatal developmental toxicity study, pregnant New Zealand White rabbits (18/exposure concentration) were exposed to the test substance as a vapor at concentrations of 0, 125, 250, 500 or 1000 ppm. Actual exposure concentrations were 124, 247, 498 and 997 ppm (approximately 0.75, 1.49, 2.98 and 5.97 mg/L/day) for 6 hours/day on days 6 through 18 of gestation. Reduced food consumption in maternal animals was seen on days 6 and 7 at 250 ppm and above and decreased body weight gain was seen in animals at 1000 ppm. No treatment related findings were observed following gross or microscopic examination of the liver, kidneys, spleen or thymus. No effects were noted on developmental parameters.

LOAEC (maternal toxicity) ~5.97 mg/L/day (based on decreased body weight gain)

NOAEC (maternal toxicity) ~2.98 mg/L/day

NOAEC (developmental toxicity) ~5.97 mg/L/day (highest concentration tested)

Genetic Toxicity -- Gene Mutation

In vitro

In a reverse-mutation assay, *S. typhimurium* strains (TA98, TA100, TA1535, TA1537 and TA1538) were exposed to CASRN 763-69-9 at concentrations up to 15,000 µg/plate, in the presence and absence of metabolic activation. Both positive and negative controls were used in the study; responses were not reported. Cytotoxicity was evident at ≥3164 µg/plate. No precipitate was observed. No positive responses of the test substance were observed in any tester strain.

CASRN 763-69-9 was not mutagenic in this assay.

Genetic Toxicity -- Chromosomal Aberrations

In vitro

A cytogenetic assay was performed with CHO cells using test concentrations up to 1500 µg/mL in the presence and absence of metabolic activation. Positive controls were used but responses to controls were not reported. No cytotoxicity or precipitation was observed at concentrations up to 1500 µg/mL; the maximum tested concentration. No significant increase in cells with chromosomal aberrations was observed.

CASRN 763-69-9 did not induce chromosomal aberrations in this assay.

Conclusion: The acute toxicity of CASRN 763-69-9 is low in rats by the oral and inhalation routes and low in rabbits by the dermal route. There were no adverse treatment-related effects in a 28-day oral gavage repeated-dose toxicity study in rats; the NOAEL is 1000 mg/kg-day (highest dose tested). A 90-day inhalation repeated-dose toxicity study in rats showed decreases in body weights at the two highest concentrations; the NOAEC for systemic toxicity is 1.49 mg/L/day. No reproductive toxicity studies were available. However, the 90-day inhalation study in rats showed no adverse treatment-related effects on reproductive organs. In a prenatal inhalation developmental toxicity study of CASRN 763-69-9 in rats, maternal weight gain was decreased at 1.46 mg/L/day and above; the NOAEC for maternal toxicity is 0.73 mg/L/day. Slight increases in the incidence of some minor internal soft tissue alterations and skeletal variants, and the appearance of rudimentary 14th ribs were seen at 5.82 mg/L/day (highest concentration tested); the NOAEC for developmental toxicity is 2.98 mg/L/day. In a prenatal inhalation developmental toxicity study with CASRN 763-69-9 in rabbits, decreased body weight gain was seen in dams at 5.97 mg/L/day (highest concentration tested); the NOAEC for maternal toxicity is 2.98 mg/L/day. No effects were noted on developmental parameters; the NOAEC for developmental toxicity is 5.97 mg/L/day (highest concentration tested). CASRN 763-69-9 was not mutagenic in bacteria and did not induce chromosomal aberrations in mammalian cells *in vitro*.

Table 3. Summary of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program – Human Health Data	
Endpoints	SPONSORED CHEMICAL 3-Ethoxypropionic acid ethyl ester (CASRN 763-69-9)
Acute Oral Toxicity LD₅₀ (mg/kg)	> 5000 (males) 3200 – 5000 (females)
Acute Dermal Toxicity LD₅₀ (mg/kg)	> 9500
Acute Inhalation Toxicity LC₅₀ (mg/L)	> 5.96
Repeated-Dose Toxicity NOAEL/LOAEL Oral gavage (mg/kg/day)	NOAEL = 1000 (hdt)
Repeated-Dose Toxicity NOAEC/LOAEC Inhalation (mg/L/day)	NOAEC ~ 1.49 LOAEC ~ 2.98
Reproductive Toxicity Inhalation	No effects were seen following evaluation of reproductive organs in a 90-day repeated-dose inhalation toxicity study in rats.
Developmental Toxicity NOAEC/LOAEC Inhalation (mg/L)	rat
Maternal Toxicity	NOAEC ~ 0.73 LOAEC ~ 1.46
Developmental Toxicity	NOAEC ~ 5.82 LOAEC ~ 2.98
Developmental Toxicity NOAEC/LOAEC Inhalation (mg/L)	rabbit
Maternal Toxicity	NOAEC ~ 5.97 (hct) LOAEC ~ 2.98
Developmental Toxicity	NOAEC ~ 5.97 (hct)
Genetic Toxicity – Gene Mutations <i>in vitro</i>	Negative

Table 3. Summary of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program – Human Health Data	
Endpoints	SPONSORED CHEMICAL 3-Ethoxypropionic acid ethyl ester (CASRN 763-69-9)
Genetic Toxicity – Chromosomal Aberrations <i>in vitro</i>	Negative

hdt = highest dose tested; hct = highest concentration tested

4. Hazard to the Environment

A summary of aquatic toxicity data submitted for SIDS endpoints is provided in Table 4. The sponsor reported the results for both replicates of the acute fish and aquatic invertebrate tests, and these results are given below. For fish, the geometric mean average of the test replicates is reported in Table 4. For aquatic invertebrates, the more conservative of the replicate test results is reported.

Acute Toxicity to Fish

Fathead minnows (*Pimephales promelas*) were exposed to CASRN 763-69-9 at nominal concentrations of 0, 10.5, 19, 34.5, 61.5, 111 or 200 mg/L for 96 hours under static conditions. Measured concentrations were 0, 9.5, 13.2, 25.4, 46.4, 100.1 and 174 mg/L in test replicate A and 0, 9.4, 13.4, 23.8, 44.2, 83.2 or 174.4 mg/L in test replicated B. Mortality and decreased activity were observed in fish at concentrations \geq 61.5 mg/L. The 96-hour LC₅₀ for test replicate A is 55 mg/L, and for test replicate B is 45 mg/L.

96-h LC₅₀ = 50 mg/L (geometric mean average of the test replicates)

Acute Toxicity to Aquatic Invertebrates

Daphnia magna were exposed to CASRN 763-69-9 at nominal concentrations of 0, 95.0, 171.5, 308.5, 555.5 or 1000 mg/L for 48 hours under static conditions. Measured concentrations were 0, 70.2, 133.1, 245.7, 479.7 or 911.1 mg/L for test replicate A and 0, 67.2, 136.1, 260.9, 461.4 or 918.7 mg/L for test replicate B. Depressed activity and immobilization were observed only at the highest test concentration. The 48-hour EC₅₀ for test replicate A is > 480 mg/L, and for test replicate B is 785 mg/L.

48-h EC₅₀ = 785 mg/L

Toxicity to Aquatic Plants

Green algae (*Pseudokirchneriella subcapitata*) were exposed to CASRN 763-69-9 at nominal test concentrations of 0 or 120 mg/L for 72 hours under static conditions. Measured test

concentrations were 0 and 114.9 mg/L (geometric mean over 3 days). There were no effects on algal growth.

72-h EC₅₀ (Growth rate) > 115 mg/L

72-h EC₅₀ (Biomass) > 115 mg/L

Conclusion: For CASRN 763-69-9, the 96-hour LC₅₀ for fish is 50 mg/L. The 48-hour EC₅₀ for aquatic invertebrates is 785 mg/L. The 72-hour EC₅₀ for aquatic plants is > 115 mg/L (biomass and growth rate).

Table 4. Summary of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program – Aquatic Toxicity Data	
Endpoints	SPONSORED CHEMICAL 3-Ethoxypropionic acid ethyl ester (CASRN 763-69-9)
Fish 96-h LC₅₀ (mg/L)	50
Aquatic Invertebrates 48-h EC₅₀ (mg/L)	785
Aquatic Plants 72-h EC₅₀ (mg/L) Growth rate Biomass	> 115 > 115

Bold = measured data

5. References

Smyth, H. F., Jr., Carpenter, C. P., and Weil, C. S. (1951). Range-finding toxicity data: List IV. *A M A Arch Ind Hyg Occup Med* **4**, 119-122.

Smyth, H. F., Jr., Carpenter, C. P., Weil, C. S., Pozzani, U. C., and Striegel, J. A. (1962). Range-finding toxicity data: List VI. *Am Ind Hyg Assoc J* **23**, 95-107.