2-Propenoic Acid, Isooctyl Ester

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I. IDENTIFICATION

Chemical Name: 2-propenoic acid. isooctyl ester
Synonyms: Isooctyl acrylate; IOA
CAS Number: 29590-42-9
Molecular Formula: $C_{11}H_{20}0_{2}$
Structural Formula:

$$H_2.C = CH\text{-}C(=O)\text{-}O\text{-}C_{2}H_{17}$$

II. CHEMICAL AND PHYSICAL PROPERTIES[1]

Physical State and Appearance: Colorless liquid
Odor Description and Threshold: Acrylate type, < 1 ppm (estimated)
Molecular Weight: 184
Conversion Factors: 1 ppm = 7.5 mg/m^3
1 mg/ m^3: = 0.13 ppm
Melting Point: No data available
Boiling Point: No data available
Specific Gravity: 0.88 at 20°C(68°F)
Vapor Density (Air = 1): > 1
Vapor Pressure: 1mmHg at 50°C (122°F)
Saturated Vapor Concentration: 1316 ppm at 50°C (122°F)
Flammability Limits: No data available
Flash Point: 185°C (365°F) closed cup)
Solubility in Water: 0.0116 g/L at 20°C (68°F)
Stability: Stable
Reactivity and incompatibilities: May polymerize on exposure to heat.

III. USES

IOA is an industrial intermediate used in the synthesis of acrylic copolymers.

IV. ANIMAL TOXICITY DATA

A. Acute Toxicity and Irritancy (1–5 days)

1. *Oral Toxicity*

Rats: LD_{50} = > 5000 mg/kg[2]

2. *Eye Irritation*

Rabbits: Slightly irritating

3. *Skin Absorption*

Rabbits: LD_{50} = > 2000 mg/kg[3]

4. *Skin Irritation*

Rabbits: Slightly irritating

5. *Skin Sensitization*

Sixteen of 20 guinea pigs exhibited scores of +/– (equivocal) response upon challenge at a non-irritating concentration (25% w/w in acetone).[4]

IOA has been copolymerized with polar functional monomers to make medical grade pressure-sensitive adhesives for skin contact applications where hypoallergenicitv is required[5]

B. Subacute Toxicity[2]

Mice received 10 daily 25 µL skin applications of 1%. 5%, 10% and 50% v/v IOA monomer in acetone. These concentrations would result in daily skin doses of approximately 8.8, 44, 88, and 440 mg/kg/day. Mice showed no signs of skin irritation or weight loss in the 1% group. The 5% group showed slight skin irritation but no weight loss, and the 10% and 50% dosage groups showed both skin irritation and weight loss. Mice similarly treated with a 19% w/v IOA (approximately 490 mg/kg/day) polymer in a 70:30 acetone/heptane blend showed no skin irritation or weight loss.

IOA was administered repeatedly to the skin of 20 rabbits for a total of 10 applications (5 week) over

a 2-week period. Each animal received 500 mg/kg/day IOA (2 g/kg/day of 25% w/w IOA in corn oil) Body weight gains in control and treated animals were considered comparable. Irritation was mild and consisted primarily of slight erythema. There were no differences between control and treated groups considered to be related to IOA.[8]

C. Subchronic Toxicity

No data available.

D. Chronic Toxicity/Carcinogenicity[2]

Male mice were randomly assigned to 3 groups of 40 mice per group. Dosages of 25 mL of IOA monomer (5% v/v in acetone) or IOA polymer (19% w/v in 70:30 acetone/heptane) or cetone (solvent control) were applied to the skin of the mice in each group for the lifetime of the animals. Applications with a pipet were made to the shaved backs of the animals 3 days/week.

No significant difference in mean survival times were noted between either treatment group, and controls. Animals treated with IOA monomer exhibited surface f nuclear or cytologic pleomorphism or atypia was noted. A non-treatment- related squamous cell tumor was also identified in the IOA monomer group. In the IOA polymer group, 2 non-treatment-related tumors were noted. No dermal neoplasms were noted i n the acetone control group.

E. Reproductive/Developmental Toxicity

IOA was administered by gavage at a dose of 1000 mg/kg of body weight to a group of 22 pregnant rats from Days 6–15 of gestation. There was an increased incidence of skeletal variants and lagging ossification noted in the fetuses. Maternal toxicity-related effects consisted of effects on body weight gain, clinical signs, and gross pathology. The types of skeletal anomalies noted were believed to be due to maternal toxicity.[6]

In another study, rats (10/sex/group) received 0% (control), %, 7.5%, 15%, and 25% IOA in acetone, applied to the skin for at least 6 hr/day at a dose volume of 100 µL per day. These concentrations would result in dermal doses of approximately 0, 3.5, 26.4, 52.8, and 88 mg/kg/day. Both male and female rats received this dosing for 2 weeks prior to mating and throughout mating until sacrifice

Dosing at 25% was reduced to 20% (approximately 70.4 mg/kg/day) after 1 week due to excessive skin irritation. The no observable effect level (NOEL) for effects on reproductive performance was 20%. No overt toxicity or reproductive effects were noted at the 20% concentration. Clinical pathology and anatomical pathology revealed no compound-related effects. Minimal increases in aspartate aminotransferase and alanine aminotransferase were associated with the 20% IOA concentration.[7]

F. Genotoxicity[2]

IOA was not mutagenic when tested in 5 strains of *Salmonella typhimurium* bacteria (Ames Assay), with and without metabolic activation.

In the Saccharomyces cerevisiae D3 recombinogenicity Assay, IOA was not recombinogenic at any concentration tested both with and without metabolic activation.

IOA was not mutagenic in the Mouse Lymphoma Cell Assay.

In the C3HJ1OT1/2 Mouse Embryo Cell Transformation Assay, IOA did not cause morphological transformation of test cells.

G. Metabolism/Pharmacokinetics

No data available.

V. HUMAN USE AND EXPERIENCE[9]

Skin irritation has been reported following accidental dermal exposure.

VI. RATIONALE

IOA was found to be mildly irritating to the eyes and slightly irritating to the skin in primary eye and skin irritation studies. However, IOA monomer is significantly irritating to skin on repeated dermal application. IOA was found to have a low order of toxicity orally and was also found to be non-genotoxic based on in vitro mutagenicity assays.

IOA was found to be non-carcinogenic at concentrations that did cause excessive skin irritation in the dermal lifetime bioassay. The high incidence of epidermal hyperplasia observed among IOA monomer-treated animals does show that IOA monomer can induce cell proliferation. It cannot be concluded as to whether chronic, severely irritating doses of IOA in contact with the skin would be carcinogenic, but such doses would not be realistic in terms of known human exposures. It should be noted that in a 2-year skin application carcinogenicity study on mice (predetermined to be more resistant to irritation) involving 2-Ethylhexyl acrylate, none of the mice developed skin tumors at the application sites[10]

Based on the irritation of IOA, and in comparison with similar acrylates such as Ethyl acrylate and n-Butyl acrylate, an OEL of 5 ppm is recommended.

VII. RECOMMENDED OEL

8-hr time-weighted average: 5 ppm (37.5 mg/m^3).

VIII. REFERENCES

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2. **Gordon, S.C., D.D. Zimmerman, and F.D. Griffith:** Acute Toxicity, Genotoxicity, and Dermal Carcinogenicity Assessment of Isooctyl Acrylate. *J. Toxicol. Environ. Health 34*:279–296 (1991).
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6. **Hazleton Laboratories America, Inc.:** "Teratology Screen in Rats" (Project No. 299–534). [Unpublished data; submitted to Celanese Corporation, New York, NY]. Vienna, VA: Hazleton Laboratories America, Inc., 1983.
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NOTE: The following databases were searched for this 2010 WEEL Revision:

MEDLINE (1989 – 2008)
IPA (1970 – 2008)
CURRENT CONTENTS (1990 – 2008)
CAB (Global Health)(1973 – 2008)
CINAHL (1982 – 2008)