

## Lactofen; CASRN 77501-63-4

Human health assessment information on a chemical substance is included in the IRIS database only after a comprehensive review of toxicity data, as outlined in the [IRIS assessment development process](#). Sections I (Health Hazard Assessments for Noncarcinogenic Effects) and II (Carcinogenicity Assessment for Lifetime Exposure) present the conclusions that were reached during the assessment development process. Supporting information and explanations of the methods used to derive the values given in IRIS are provided in the [guidance documents located on the IRIS website](#).

### STATUS OF DATA FOR Lactofen

**File First On-Line 06/30/1988**

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	06/30/1988
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	not evaluated	

## I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

### I.A. Reference Dose for Chronic Oral Exposure (RfD)

Substance Name — Lactofen  
CASRN — 77501-63-4  
Primary Synonym — Cobra  
Last Revised — 06/30/1988

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of

substances that are also carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

### I.A.1. Oral RfD Summary

Critical Effect	Experimental Doses*	UF	MF	RfD
Increased absolute and relative liver weight; hepatocytomegaly in males	NOEL: none  LEL: 10 ppm (1.5 mg/kg/day)	1000	1	2E-3 mg/kg/day
78-Week Oncogenic Study in Mice				
PPG Industries, 1985a				

\*Conversion Factors -- 1 ppm = 0.15 mg/kg/day (assumed mouse food consumption)

### I.A.2. Principal and Supporting Studies (Oral RfD)

PPG Industries. 1985a. MRID No. 00150343, 00150366. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Albino mice (240/sex/dose) were randomly assigned to groups of 60/sex/dose and administered dose levels of 0, 10, 50, or 250 ppm in the diet for 78 weeks. An increase in the incidence of hepatocellular carcinoma and/or adenoma was observed at 250 ppm in both sexes. At the high dose, adenomas were significantly increased in males only. An increase in absolute and relative liver weight and incidence of hepatocytomegaly were observed in males at 10 ppm and above, and in females at 50 ppm and above. At the highest dose increased incidence of cataracts and kidney pigmentation were observed in both sexes.

Based on the increase in absolute and relative liver weight and incidence of hepatocytomegaly at 10 ppm (LDT) and above in males, a NOEL for systemic toxicity has not been demonstrated in this study.

### **I.A.3. Uncertainty and Modifying Factors (Oral RfD)**

UF — An uncertainty factor of 100 was used to account for the inter- and intraspecies differences. An additional UF of 10 was used to account for the lack of an established NOEL.

MF — None

### **I.A.4. Additional Studies/Comments (Oral RfD)**

Data Considered for Establishing the RfD:

- 1) 78-Week Oncogenic - mice: Principal study - see previous description; core grade guideline (PPG Industries, 1985a)
- 2) 1-Year Feeding - dog: NOEL=200 ppm (5 mg/kg/day); LEL=1000/3000 ppm (25/75 mg/kg/day) (renal dysfunction; decreased Hgb, HCT, RBC, cholesterol); core grade minimum (PPG Industries, 1982a)
- 3) 2-Year Feeding (oncogenic) - rat: NOEL=500 ppm (25 mg/kg/day); LEL=1000 ppm (50 mg/kg/day) (increased kidney and liver pigmentation, increased incidence of proliferative nodules and foci of cellular alteration); core grade guideline (PPG Industries, 1985b)
- 4) 2-Generation Reproduction - rat: Reproductive NOEL=50 ppm (2.5 mg/kg/day); Reproductive LEL=500 ppm (25 mg/kg/day) (reduced mean pup weight, increased relative and absolute weight of brain, heart, liver, spleen and testes; brown pigment in liver; extramedullary hematopoiesis, hyperplasia of spleen); core grade minimum (PPG Industries, 1983a)
- 5) Teratology - rat: Fetotoxic NOEL=50 mg/kg/day; Fetotoxic LEL=150 mg/kg (bent ribs); Teratogenic NOEL=150 mg/kg/day; Maternal NOEL=50 mg/kg/day; Maternal LEL=150 mg/kg/day (post implantation loss; reduced body weight); core grade minimum (PPG Industries, 1982b)
- 6) Teratology - rabbit: Maternal NOEL=4 mg/kg/day; Maternal LEL=20 mg/kg/day (decreased food consumption); Fetotoxic NOEL=20 mg/kg/day; core grade minimum (PPG Industries, 1985c)

Other Data Reviewed:

- 1) 90-Day Feeding - mouse: LEL=200 ppm (increased leucocytes, decreased Hct, Hgb, WBC); increased alkaline phosphatase, SGOT, SGPT, cholesterol; increased liver weight and enlarged

spleen, liver and heart; liver vacuolation necrosis of individual hepatocytes, biliary hyperplasia, extramedullary hematopoiesis, kidney nephrosis and fibrosis; follicular atresia, abnormal sperm forms); core grade minimum (PPG Industries, 1983b)

2) 90-Day Feeding - rat: NOEL=200 ppm (10 mg/kg/day); LEL=1000 ppm (50 mg/kg/day) (brown pigment in liver and kidney; decreased Hgb, HCT and RBC); core grade guideline (PPG Industries, 1982c)

3) 12-Month Feeding - rat: LEL=40 ppm (2 mg/kg/day); Significant trend for bile duct hyperplasia in all dose groups); core grade supplementary (PPG Industries, 1982d)

Data Gap(s): none

### **I.A.5. Confidence in the Oral RfD**

Study — High

Database — High

RfD — High

The critical study is of good quality and is given a high confidence rating. Additional studies are also of good quality; therefore, the database is given a high confidence rating. High confidence in the RfD follows.

### **I.A.6. EPA Documentation and Review of the Oral RfD**

Source Document — This assessment is not presented in any existing U.S. EPA document.

Other EPA Documentation — Pesticide Registration Files

Agency Work Group Review — 07/15/1987

Verification Date — 07/15/1987

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfD for Lactofen conducted in November 2001 did not identify any critical new studies. IRIS users who know of important new studies may provide that information to the IRIS Hotline at [hotline.iris@epa.gov](mailto:hotline.iris@epa.gov) or (202)566-1676.

### **I.A.7. EPA Contacts (Oral RfD)**

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or [hotline.iris@epa.gov](mailto:hotline.iris@epa.gov) (internet address).

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### **I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)**

Substance Name — Lactofen

CASRN — 77501-63-4

Primary Synonym — Cobra

Not available at this time.

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## **II. Carcinogenicity Assessment for Lifetime Exposure**

Substance Name — Lactofen

CASRN — 77501-63-4

Primary Synonym — Cobra

This substance/agent has not undergone a complete evaluation and determination under US EPA's IRIS program for evidence of human carcinogenic potential.

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### **III. [reserved]**

### **IV. [reserved]**

### **V. [reserved]**

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## **VI. Bibliography**

Substance Name — Lactofen

CASRN — 77501-63-4

Primary Synonym — Cobra

### **VI.A. Oral RfD References**

PPG Industries. 1982a. MRID No. 00128446, 00150367. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

PPG Industries. 1982b. MRID No. 00117566. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

PPG Industries. 1982c. MRID No. 00117564. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

PPG Industries. 1982d. MRID No. 00133308. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

PPG Industries. 1983a. MRID No. 00132885. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

PPG Industries. 1983b. MRID No. 00132882. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

PPG Industries. 1985a. MRID No. 00150343, 00150366. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

PPG Industries. 1985b. MRID No. 00132883, 00150329. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

PPG Industries. 1985c. MRID No. 00150367, 00163307. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

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## **VI.B. Inhalation RfD References**

None

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## **VI.C. Carcinogenicity Assessment References**

None

## **VII. Revision History**

Substance Name — Lactofen

CASRN — 77501-63-4

Primary Synonym — Cobra

Date	Section	Description
12/03/2002	I.A.6.	Screening-Level Literature Review Findings message has been added.

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## VIII. Synonyms

Substance Name — Lactofen

CASRN — 77501-63-4

Primary Synonym — Cobra

Last Revised — 06/30/1988

- 77501-63-4
- Benzoic acid, 5-(2-chloro-4-(trifluoromethyl)phenoxy)-2-nitro-,2-ethoxy-1-methyl-2-oxoethyl ester
- Benzoic acid, 5-(2-chloro-4-(trifluoromethyl)phenoxy)-2-nitro-,2-ethoxy-1-methyl-2-oxoethyl ester, (+-)- (9CI)
- Cobra
- Cobra [herbicide]
- (+-)-2-Ethoxy-1-methyl-2-oxoethyl 5-(2-chloro-4-(trifluoromethyl)phenoxy)-2-nitrobenzoate
- Lactofen
- Lactofen [ANSI]
- PPG 844