

I U C L I D

D a t a s e t

Existing Chemical	Substance ID: 58-08-2
CAS No.	58-08-2
EINECS Name	caffeine
EINECS No.	200-362-1
Molecular Formula	C ₈ H ₁₀ N ₄ O ₂

Dataset created by: EUROPEAN COMMISSION - European Chemicals Bureau

This dossier is a compilation based on data reported by the European Chemicals Industry following 'Council Regulation (EEC) No. 793/93 on the Evaluation and Control of the Risks of Existing Substances'. All (non-confidential) information from the single datasets, submitted in the IUCLID/HEDSET format by individual companies, was integrated to create this document.

The data have not undergone any evaluation by the European Commission.

Creation date: 18-FEB-2000

Number of Pages: 17

Chapters: all

Edition: Year 2000 CD-ROM edition

Flags: non-confidential

1.0.1 OECD and Company Information

Name: Arzneimittelwerk Dresden GmbH
Street: Meißner Straße 35
Town: 01445 Radebeul
Country: Germany
Phone: 0351/8341389
Telefax: 0351/8341703

Name: Boehringer Ingelheim KG
Town: 55218 Ingelheim/Rhein
Country: Germany

Name: Deutsche Sinochem GmbH
Street: Freidrich-Ebert-Damm 160 a
Town: 22047 Hamburg
Country: Germany
Phone: +49(40)694203-0
Telefax: +49(40)694203-90
Telex: 2161129

Name: Helm AG
Street: Nordkanalstrasse 28
Town: 20097 Hamburg
Country: Germany
Phone: +49402375-0
Telefax: +49402375-90
Telex: 2170150

Name: Knoll AG
Town: 67063 Ludwigshafen
Country: Germany

Name: Schweizerhall Pharma GmbH
Street: Winterhuder Weg 27
Town: 22085 Hamburg
Country: Germany
Phone: 040 / 227026/62
Telefax: 040 / 2273220

Name: STABILIMENTO FARMACEUTICO CAV.G.TESTA SpA
Street: DEI MILLE 138
Town: 17031 ALBENGA
Country: Italy
Phone: 003918255811
Telefax: 0039182543813
Telex: 271561 TESTA I

1.0.2 Location of Production Site

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1.0.3 Identity of Recipients

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1.1 General Substance Information**Substance type:** natural substance**Physical status:** solid**Substance type:** organic**Physical status:** solid**1.1.1 Spectra**

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1.2 Synonyms

1,3,7-trimethyl-2,6-dioxopurine

Source: Knoll AG Ludwigshafen

(1)

1,3,7-trimethylxanthine

Source: Knoll AG Ludwigshafen

(1)

3,7-Dihydro-1,3,7-trimethyl-1H-purine-2,6-dione

Remark: CAS name**Source:** Knoll AG Ludwigshafen

(1)

a: Coffein

Source: Arzneimittelwerk Dresden GmbH Radebeul

Anhydrous caffeine

Source: Knoll AG Ludwigshafen

(1)

b: 3,7-Dihydro-1,3,7-trimethyl-1H-purine-2,6-dione

Source: Arzneimittelwerk Dresden GmbH Radebeul

c: 1,3,7-Trimethylxanthin

Source: Arzneimittelwerk Dresden GmbH Radebeul

CAFFEINA ANIDRA

Source: STABILIMENTO FARMACEUTICO CAV.G.TESTA SpA ALBENGA

Caffeine

Source: Schweizerhall Pharma GmbH HamburgCoffein, Caffeine, 1,3,7- Trimethylxanthin,
1H-Purin-2,6-dioxo-3,7-dihydro-1,3,7-trimethyl, 1,3,7-Trimethyl-2,6-dioxopurin,
Methyltheobromin, Thein, Guaranin.**Source:** Boehringer Ingelheim KG Ingelheim/Rhein

Coffein, wasserfrei

Source: Knoll AG Ludwigshafen

(2) (3)

Coffeinum

Source: Knoll AG Ludwigshafen

(1)

d: 1,3,7-Trimethyl-2,6-dioxopurine

Source: Arzneimittelwerk Dresden GmbH Radebeul

e: Coffeine

Source: Arzneimittelwerk Dresden GmbH Radebeul

f: Caffeine

Source: Arzneimittelwerk Dresden GmbH Radebeul

g: Thein

Source: Arzneimittelwerk Dresden GmbH Radebeul

guaranine

Source: Knoll AG Ludwigshafen

(1)

h: Guaranine

Source: Arzneimittelwerk Dresden GmbH Radebeul

i: Methyltheobromine

Source: Arzneimittelwerk Dresden GmbH Radebeul

Methyltheobromine

Source: Knoll AG Ludwigshafen

(1)

Methyltheothylline

Source: Knoll AG Ludwigshafen

(1)

1.3 Impurities

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1.4 Additives

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1.5 Quantity**Quantity**

500 000 - 1 000 000 tonnes

1.6.1 Labelling

Labelling: as in Directive 67/548/EEC
Symbols: Xn
E
Specific limits: no data
R-Phrases: (22) Harmful if swallowed
S-Phrases: (2) Keep out of reach of children

1.6.2 Classification

Classification: as in Directive 67/548/EEC
Class of danger: corrosive
R-Phrases: (22) Harmful if swallowed

1.7 Use Pattern

Type: type
Category: Non dispersive use

Type: type
Category: Wide dispersive use

Type: industrial
Category: other: Getränkeindustrie

Type: industrial
Category: other: Pharmaindustrie

Type: industrial
Category: other

Type: use
Category: Food/foodstuff additives

Type: use
Category: Pharmaceuticals

1.7.1 Technology Production/Use

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1.8 Occupational Exposure Limit Values

Type of limit: other
Limit value: .5 mg/m³
Country: Soviet Union (USSR)
Remark: Maximum acceptable concentration (MAC) in air; occupational environment exposure
Source: Knoll AG Ludwigshafen

Type of limit:**Limit value:****Remark:**

LD 50 orale , ratto : 355 mg/Kg
LD 50 cutaneo , ratto : >2000 mg/Kg
LC 50 inalatoria, ratto : 4,1 - 4,9 mg/l/4h

Source:

STABILIMENTO FARMACEUTICO CAV.G.TESTA SpA ALBENGA

Type of limit:**Limit value:****Source:**

Arzneimittelwerk Dresden GmbH Radebeul

1.9 Source of Exposure**Remark:**

Sources of exposure depend on the production procedures and the usage. Caffeine is produced by extraction (direct decaffeination, extraction from tea wastes and dusts and from fragments of tea leaves) and by synthetic processes (methylation of various xanthines). Exposure results from its use as drug or as drug ingredient as well as of caffeine containing food or beverages with a varying content.

Source:

Knoll AG Ludwigshafen

(1)

1.10.1 Recommendations/Precautionary Measures

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1.10.2 Emergency Measures

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1.11 Packaging

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1.12 Possib. of Rendering Subst. Harmless

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1.13 Statements Concerning Waste

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1.14.1 Water Pollution**Classified by:**

other: Knoll AG

Labelled by:

other: Knoll AG

Class of danger:

1 (weakly water polluting)

Source:

Knoll AG Ludwigshafen

(5)

1.14.2 Major Accident Hazards

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1.14.3 Air Pollution

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1.15 Additional Remarks

Remark: Die Reinheit von Coffein entspricht als Pharmasubstanz den Forderungen der europäischen Pharmakopoe (EP). Angaben zu Verunreinigungen sind Grenzwerte der Pharmakopöen und werden in der Praxis weit unterschritten.

Source: Boehringer Ingelheim KG Ingelheim/Rhein

(6)

Remark: provisionally classified in water hazard class 1 (Wassergefährdungsklasse) by the producer and according the VCI recommendation of Oct. 10, 1987

Source: Knoll AG Ludwigshafen

(2) (3)

1.16 Last Literature Search

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1.17 Reviews

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1.18 Listings e.g. Chemical Inventories

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2.1 Melting Point

Value: > 234 - 236.5 degree C
Source: Schweizerhall Pharma GmbH Hamburg

Value: 234 - 238 degree C
Decomposition: ambiguous
Sublimation: yes
Method: other
GLP: no data
Source: Arzneimittelwerk Dresden GmbH Radebeul

(7)

Value: = 238 degree C
Decomposition: ambiguous
Sublimation: yes
Method: other
GLP: no data
Source: Arzneimittelwerk Dresden GmbH Radebeul

(8)

2.2 Boiling Point

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2.3 Density

Type: density
Value: = 1.23 at 18 degree C
Method: other
GLP: no data
Source: Arzneimittelwerk Dresden GmbH Radebeul

(8)

Type: bulk density
Value: ca. 300 - 600 kg/m³
Method: other
GLP: no data
Remark: Firmeninterne Angabe ohne Methodennachweis.
Source: Arzneimittelwerk Dresden GmbH Radebeul

2.3.1 Granulometry

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2.4 Vapour Pressure

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2.5 Partition Coefficient

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2.6.1 Water Solubility

Value: ca. 20 g/l at 20 degree C
pH: 5.5 - 6.5
Method: other
GLP: no data
Remark: Firmeninterne Angabe ohne Methodennachweis.
Source: Arzneimittelwerk Dresden GmbH Radebeul

Value: = 25.872 g/l at 30 degree C
Method: other
GLP: no data
Source: Arzneimittelwerk Dresden GmbH Radebeul

(9)

pH: = 6.9 at 1 vol%
Method: other
GLP: no data
Source: Arzneimittelwerk Dresden GmbH Radebeul

(8)

Qualitative: of low solubility
Result: leicht löslich in siedendem Wasser
Source: Arzneimittelwerk Dresden GmbH Radebeul

(10)

2.6.2 Surface Tension

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2.7 Flash Point

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2.8 Auto Flammability

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2.9 Flammability

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2.10 Explosive Properties

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2.11 Oxidizing Properties

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2.12 Additional Remarks

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3.1.1 Photodegradation

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3.1.2 Stability in Water

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3.1.3 Stability in Soil

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3.2 Monitoring Data (Environment)

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3.3.1 Transport between Environmental Compartments

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3.3.2 Distribution

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3.4 Mode of Degradation in Actual Use

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3.5 Biodegradation

Type:

Inoculum:

Result: other

Method: other

Year: GLP: no data

Test substance: as prescribed by 1.1 - 1.4

Method: BSB

Result: schwer abbaubar (<20%)

Source: Arzneimittelwerk Dresden GmbH Radebeul

(11)

3.6 BOD5, COD or BOD5/COD Ratio

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3.7 Bioaccumulation

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3.8 Additional Remarks

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AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: other
Species: other
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC0: = 50
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: Daten betreffen "Goldorfe", Typ unbekannt, veröffentlicht imEG-Sicherheitsdatenblatt der Knoll AG vom 21.07.1993.
Source: Arzneimittelwerk Dresden GmbH Radebeul

Type: other
Species: other
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC50: = 87
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: Daten betreffen "Goldorfe", Typ unbekannt, veröffentlicht imEG-Sicherheitsdatenblatt der Knoll AG vom 21.07.93, in Bezug auf Quelle BASF.
Source: Arzneimittelwerk Dresden GmbH Radebeul

4.2 Acute Toxicity to Aquatic Invertebrates

Species: Daphnia sp. (Crustacea)
Exposure period: 4 hour(s)
Unit: mg/l **Analytical monitoring:** no data
EC50: = 182.12
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: Daten veröffentlicht im EG-Sicherheitsdatenblatt der Knoll AG vom 21.07.1993, in Bezug auf Quelle BASF.
Source: Arzneimittelwerk Dresden GmbH Radebeul

4.3 Toxicity to Aquatic Plants e.g. Algae

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4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species: other bacteria
Exposure period: 17 hour(s)
Unit: mg/l **Analytical monitoring:** no data
EC10: = 1530
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: Daten veröffentlicht im EG-Sicherheitsdatenblatt der Knoll
AG vom 21.07.1993, in Bezug auf Quelle BASF.
Source: Arzneimittelwerk Dresden GmbH Radebeul

4.5 Chronic Toxicity to Aquatic Organisms**4.5.1 Chronic Toxicity to Fish**

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4.5.2 Chronic Toxicity to Aquatic Invertebrates

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TERRESTRIAL ORGANISMS**4.6.1 Toxicity to Soil Dwelling Organisms**

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4.6.2 Toxicity to Terrestrial Plants

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4.6.3 Toxicity to other Non-Mamm. Terrestrial Species

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4.7 Biological Effects Monitoring

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4.8 Biotransformation and Kinetics

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4.9 Additional Remarks

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5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Sex:
Number of
Animals:
Vehicle:
Value: = 192 mg/kg bw
Method: other
Year: GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Source: Arzneimittelwerk Dresden GmbH Radebeul (12)

Type: LD50
Species: mouse
Sex:
Number of
Animals:
Vehicle:
Value: = 127 mg/kg bw
Method: other
Year: GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Source: Arzneimittelwerk Dresden GmbH Radebeul (13)

Type: LD50
Species: rabbit
Sex:
Number of
Animals:
Vehicle:
Value: = 224 mg/kg bw
Method: other
Year: GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Source: Arzneimittelwerk Dresden GmbH Radebeul (13)

Type: LDLo
Species: cat
Sex:
Number of
Animals:
Vehicle:
Value: = 100 mg/kg bw
Method: other
Year: GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Source: Arzneimittelwerk Dresden GmbH Radebeul (14)

Type: LD50
Species: dog
Sex:
Number of Animals:
Vehicle:
Value: = 140 mg/kg bw
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Source: Arzneimittelwerk Dresden GmbH Radebeul (15)

Type: LD50
Species: guinea pig
Sex:
Number of Animals:
Vehicle:
Value: = 230 mg/kg bw
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Source: Arzneimittelwerk Dresden GmbH Radebeul (16)

Type: LD50
Species: hamster
Sex:
Number of Animals:
Vehicle:
Value: = 230 mg/kg bw
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Source: Arzneimittelwerk Dresden GmbH Radebeul (13)

Type: LDLo
Species: human
Sex:
Number of Animals:
Vehicle:
Value: = 192 mg/kg bw
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Source: Arzneimittelwerk Dresden GmbH Radebeul (12)

Type: LDLo
Species: human
Sex:
Number of Animals:
Vehicle:
Value: = 1000 mg/kg bw
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Source: Arzneimittelwerk Dresden GmbH Radebeul

(17)

5.1.2 Acute Inhalation Toxicity

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5.1.3 Acute Dermal Toxicity

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5.1.4 Acute Toxicity, other Routes

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5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

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5.2.2 Eye Irritation

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5.3 Sensitization

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5.4 Repeated Dose Toxicity

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5.5 Genetic Toxicity 'in Vitro'

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5.6 Genetic Toxicity 'in Vivo'

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5.7 Carcinogenicity

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5.8 Toxicity to Reproduction

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5.9 Developmental Toxicity/Teratogenicity

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5.10 Other Relevant Information

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5.11 Experience with Human Exposure

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- (2) Boehringer Ingelheim KG, DIN Sicherheitsdatenblatt (1994)
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- (7) Monographie Europäische Pharmakopoe 3.
- (8) Merck - Index
- (9) Veröffentlicht im Beilstein Gutman; Higuchi, L.Am.Pharm.Assoc., 46<1957>4,9
- (10) Monographie Europäische Pharmakopoe 3
- (11) EG-Sicherheitsdatenblatt Knoll AG vom 21.07.93
- (12) RTECS-Nr.: EV6475000
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- (13) RTECS-Nr.: EV6475000
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- (14) RTECS-Nr.: EV6475000
Abdernalden's Handbuch der Biologischen Arbeitsmethoden 4, 1335, 35
- (15) RTECS-Nr.: EV6475000
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- (16) RTECS-Nr.: EV6475000
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- (17) RTECS-Nr.: EV6475000
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7.1 Risk Assessment

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