Safety Data Sheet

Capecitabine

according to Regulation (EU) nr. 1907/2006

SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1. Product identifier

Product name	Capecitabine
Product code	04 4111 2

1.2. Relevant identified uses of the substance or mixture and uses advised against

Use	-	pharmaceutical active substance (cytostatic)

1.3. Details of the supplier of the safety data sheet

Company information	Enquiries: F. Hoffmann-La Roche AG Postfach CH-4070 Basel Switzerland Phone +41-61/688 54 80 Fax +41-61/681 72 76 E-Mail info.sds@roche.com	Local representation:

1.4. Emergency telephone number

Emergency telephone number	Phone	+41-61/688 54 80

SECTION 2: Hazards identification

2.1. / 2.2. Classification of the substance or mixture / Label elements

GHS Classification

Health Hazards:

3.5Germ cell mutagenicity (Category 2)
H341 Suspected of causing genetic defects.
3.6 Carcinogenicity (Category 1B)
H350 May cause cancer.
3.7 Reproductive toxicity (Category 1B)
H360D May damage the unborn child.
3.7 Reproductive toxicity (Category 1B)
H360F May damage fertility.

Signalword: Danger

Label:

Precautionary statements:
- P201 Obtain special instructions before use.
- P260 Do not breathe dust
- P281 Use personal protective equipment as required.
- P308 + P313 IF exposed or concerned: Get medical advice/attention.

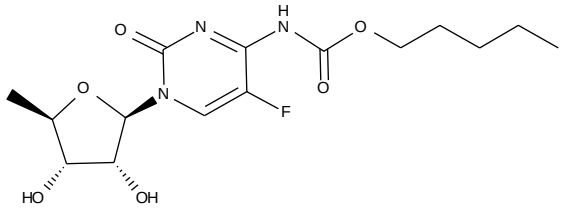
2.3. Other hazards

Note
- Cytostatics in general have to be classified as potentially carcinogenic, teratogenic and mutagenic. During handling any occupational exposure as well as environmental contamination have to be avoided.
- HAZARDOUS SUBSTANCE. NON-DANGEROUS GOODS.
- may form explosible dust-air mixture if dispersed

SECTION 3: Composition/information on ingredients

Characterization	pharmaceutical active substance in the group of fluorinated cytosines
Chemical name	- 5'-Deoxy-5-fluoro-N4-pentyloxycarbonyl-cytidine
Synonyms	- XELODA - NeoFurtulon successor - N-[1-(5-Deoxy-β-D-ribofuranosyl)-5-fluoro-1,2-dihydro-2-oxo-4-pyrimidinyl]-n-pentyl carbamate
CAS number	154361-50-9
Roche number	RO0091978-000
Empirical formula	$C_{15}H_{22}FN_3O_6$

Molecular mass	359.34 g/mol



SECTION 4: First aid measures

4.1. Description of first aid measures

Eye contact	- rinse immediately with tap water for at least 20 minutes - open eyelids forcibly - consult a physician if irritation persists
Skin contact	- remove immediately contaminated clothes, wash affected skin with water and soap - do not use any solvents - consult a physician if skin irritation persists
Inhalation	- remove the casualty to fresh air and keep him/her calm - get medical treatment
Ingestion	- summon a physician immediately - let drink repeatedly plenty of water and induce vomiting (only if conscious), repeat several times

4.2. Most important symptoms and effects, both acute and delayed

Note	- no information available

4.3. Indication of any immediate medical attention and special treatment needed

Note to physician	- treat symptomatically - in case of accidental exposure, keep a sample of urine in order to determine the content of fluoro-β-alanine

SECTION 5: Firefighting measures

5.1. Extinguishing media

Suitable extinguishing media	- water spray jet, dry powder, foam, carbon dioxide

5.2. Special hazards arising from the substance or mixture

Specific hazards	- very high probability of ignition of dust whirled up - formation of toxic and corrosive combustion gases (hydrogen fluoride, nitrogen oxides) possible

5.3. Advice for firefighters

Protection of fire-fighters	- precipitate gases/vapours/mists with water spray - use self-contained breathing apparatus - avoid skin contact

SECTION 6: Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

Personal precautions	- avoid exposure

6.2. Environmental precautions

Environmental protection	- avoid release to the environment - if the substance reaches waters or the sewer system, inform the competent authority

6.3. Methods and material for containment and cleaning up

Methods for cleaning up	- collect spilled material (avoid dust formation) and hand over to waste removal in sealed containers - clean floors and contaminated objects with plenty of water - collect spilled solutions with inert adsorbent and hand over to waste removal

SECTION 7: Handling and storage

7.1. Precautions for safe handling

Technical measures	- connect conductive pieces of equipment, products and packaging to earth - avoid electric charging of dust clouds - handling under inert conditions - avoid dust formation; very high dust explosion hazard

7.2. Conditions for safe storage, including any incompatibilities

Storage conditions	- below 30 °C - with a desiccant
Validity	- see expiry date on the label - 24 months, < 30 °C, with a desiccant
Packaging materials	- tightly closing; material: stainless steel, aluminium

SECTION 8: Exposure controls/personal protection

8.1. Control parameters

Threshold value (Roche) air	- IOEL (Internal Occupational Exposure Limit): 0.01 mg/m3 (defined as 8-hour time-weighted average)

8.2. Exposure controls

General protective and hygiene measures	- instruction of employees mandatory - shower after work recommended
Respiratory protection	- in case of open handling or accidental release: particle mask or respirator with independent air supply - Respiratory protection is recommended for dusty operations.
Hand protection	- protective gloves (eg made of neoprene, nitrile or butyl rubber)
Eye protection	- safety glasses
Body protection	- protective clothing - connect persons to earth by means of conductive shoes and conductive floor

SECTION 9: Physical and chemical properties

9.1. Information on basic physical and chemical properties

Colour	white to light yellow
Form	powder
Odour	odourless
Solubility	26’000 mg/l, water (20 °C) 207’000 mg/l, ethanol (20 °C) > 40 %, methanol 11.8 %, acetonitrile > 59 %, dimethyl formamide 2.5 %, ethyl acetate
Partition coefficient	log P_{ow} ~ 4.5 (n-octanol/water) pH 7.4
Melting temperature	116 to 117 °C

9.2. Other information

Bulk density	~ 450 kg/m3
Dissociation constant	pK_1 8.8 (acidic group(s))

SECTION 10: Stability and reactivity

10.1. Reactivity

Note - no information available

10.2. Chemical stability

Stability - stable under the conditions mentioned in chapter 7

10.3. Possibility of hazardous reactions

Note - no information available

10.4. Conditions to avoid

Conditions to avoid - temperatures above 100 °C (decomposition)

10.5. Incompatible materials

Materials to avoid - strong acids (hydrolysis)

10.6. Hazardous decomposition products

Note - no information available

SECTION 11: Toxicological information

11.1. Information on toxicological effects

Acute toxicity	- LD_{50} > 2'000 mg/kg (oral, rat)
Subchronic toxicity	- high doses may damage proliferating cells (e.g., bone marrow, leukocytes)
Local effects	- no information available
Sensitization	- slightly sensitizing (several species)
Mutagenicity	- may cause mutations in vitro (clastogenic effect in lymphocytes) - lymphocyte test; evidence of clastogenicity
Carcinogenicity	- no information available
Reproductive toxicity	- suspected to be teratogenic and to lower parental fertility - decreased weight of testis and epididymis, decrease and degeneration of spermatocytes and spermatids (760 mg/kg/d; oral, mouse, male) - reduced mating ability and fertility rate (760 mg/kg/d; oral, mouse, female)

STOT-single exposure	- no information available
STOT-repeated exposure	- no information available
Aspiration hazard	- no information available
Note	- may cause diarrhoea, nausea, vomiting, loss of appetite, irritation of mucous membranes and alteration of the haemopoietic system (leukopenia) in dependance of the dose - cytostatics are potentially carcinogenic

SECTION 12: Ecological information

12.1. Toxicity

Ecotoxicity

- barely toxic for algae (Selenastrum capricornutum)
  EbC_{50} (72 h) 58 mg/l
  ErC_{50} (72 h) 200 mg/l
  NOEC (72 h) 14 mg/l
  (OECD No. 201)
- barely toxic for planktonic crustaceans (Daphnia magna)
  EC_{50} (48 h) > 850 mg/l
  NOEC (48 h) 500 mg/l
- barely toxic for fish (rainbow trout)
  LC_{50} (96 h) > 867 mg/l
  NOEC (96 h) 867 mg/l
- barely inhibitory on aerobic bacterial respiration
  EC_{50} > 1000 mg/l
  (Activated Sludge Respir. Inhib. Test, OECD No. 209)

12.2. Persistence and degradability

Inherent biodegradability

- inherently biodegradable
  evidence for prior abiotic primary degradation as a rate-limiting process
  29 %, 28 d
  44 %, 56 d
  55 %, 84 d
  (MITI Test II, OECD No. 302 C)

Abiotic degradation

- slow degradation, probably ester hydrolysis 30 mg/l; HPLC
  $t_{1/2}$ ~ 21 d, ~ 22 °C, pH ~ 7
- rapid degradation only at very acidic pH 1000 mg/l, water; HPLC
  $t_{1/2} \geq$ 60 h, ~ 22 °C, pH 2
  $t_{1/2}$ ~ 6 h, ~ 22 °C, pH 1
  $t_{1/2}$ < 2 h, ~ 22 °C, pH 0.5
  $t_{1/2}$ ~ 1 h, 30 °C, pH 0.5

12.3. Bioaccumulative potential

Note

- no information available

12.4. Mobility in soil

Mobility	- medium adsorption to activated sludge, medium mobility (water-activated sludge, 3 h) K_d = 272 l/kg (activated sludge) (Adsorption to activated sludge in biodegradability test)

12.5. Results of PBT and vPvB assessment

Note	- no information available

12.6. Other adverse effects

Note	- strictly avoid contamination of the environment

SECTION 13: Disposal considerations

13.1. Waste treatment methods

Waste from residues	- observe local/national regulations regarding waste disposal - incinerate in qualified installation with flue gas scrubbing

SECTION 14: Transport information

Note	- not classified as Dangerous Good according to the Dangerous Goods Regulations

SECTION 15: Regulatory information

15.1. Safety, health and environmental regulations/legislation specific for the substance or mixture

Water hazard class (Germany)	3: strongly hazardous for water (own classification according to directive VwVwS of 27.07.2005)

SECTION 16: Other information

Safety-lab number	- BS-6606 - BS-8569
Edition documentation	- changes from previous version in sections 2

The information in this safety data sheet is based on current scientific knowledge. It should not be taken as expressing or implying any warranty concerning product characteristics.