REACH

Esterification product of sunflower-oil fatty acids, with 1,4:3,6-dianhydro-D-glucitol

EC number: 816-845-0 | CAS number: 1818326-42-9

Toxicological information

Endpoint summary

Administrative data

Description of key information

The oral LD50 is > 2000 mg/kg bw (with no mortality at this dose level).

Key value for chemical safety assessment

Acute toxicity: via oral route

Link to relevant study records

Reference

Reference 1

Endpoint:	acute toxicity: oral
Type of information:	experimental study
Adequacy of study:	key study
Study period:	from 03 April 2009 to 06 June 2009
Reliability:	1 (reliable without restriction)
Rationale for reliability incl. deficiencies:	other: study performed according to OECD testing guideline and GLP.
Qualifier:	according to guideline
Guideline:	OECD Guideline 423 (Acute Oral toxicity - Acute Toxic Class Method)
Deviations:	no
GLP compliance:	yes (incl. QA statement)
Test type:	acute toxic class method
Limit test:	yes
Species:	rat
Strain:	Wistar
Sex:	female
Details on test animals or test system and	TEST ANIMALS - Source: Charles River USA

environmental conditions:	- Age at study initiation: 8-12 weeks - Weight at study initiation: ca. 175 grams - Fasting period before study: yes (feed only) - Housing: standard polypropylene rat cages with stainless steel top grill - Diet: standard gamma irradiated pellet feed supplied by M/s. Tetragon Chemie Pvt. Ltd., Bangalore, ad libidum - Water: ad libitum - Acclimation period: yes (5 days) ENVIRONMENTAL CONDITIONS - Temperature: 19.4°C to 22.4°C - Humidity: 56% to 64% - Air changes: - - Photoperiod: 12 hrs dark / 12 hrs light IN-LIFE DATES: From: 18 April 2009 To: 04 May 2009
Route of administration:	oral: gavage
Vehicle:	corn oil
Details on oral exposure:	VEHICLE - Concentration in vehicle: - - Justification for choice of vehicle: - - Lot/batch no. (if required): - - Purity: - MAXIMUM DOSE VOLUME APPLIED: 10 mL/kg bw CLASS METHOD - Rationale for the selection of the starting dose: -
Doses:	2000 mg/kg bw
No. of animals per sex per dose:	6 females (3 females per step)
Control animals:	no
Details on study design:	- Duration of observation period following administration: 14 days - Frequency of observations and weighing: > body weight: days 0, 7 and 14 > morbidity/mortality: once daily > clinical signs: at 0.5, 1, 2 and 4 hours after dosing, and once daily thereafter - Necropsy of survivors performed: yes
Sex:	female
Dose descriptor:	LD50
Effect level:	> 2 000 mg/kg bw
Based on:	test mat.
Mortality:	No mortality/morbidity was observed in animals throughout the observation period.
Clinical signs:	No clinical signs were observed in animals throughout the observation period.
Body weight:	All the animals showed normal body weight during the experiment period.
Gross pathology:	Animals did not reveal any macroscopic lesions.
Interpretation of results:	not classified
Remarks:	Migrated information Criteria used for interpretation of results: EU
Conclusions:	The oral LD50 of DOI is > 2000 mg/kg bw (with no mortality at this dose level).
Executive summary:	In an acute oral toxicity study according to OECD 423, and GLP, scored as validity 1 according to Klimisch criteria, groups of fasted female Wistar rats were given a single oral dose of DOI in corn oil at the dose of 2000 mg/kg bw (2x3 females) and observed for 14 days. Clinical signs and mortality were checked frequently during the hours following administration of the test substance, and once a day thereafter. Body weight was measured just before administration of the test substance on day 0 and then on days 7 and 14.

No clinical signs of toxicity and no mortality were observed during the study.

At necropsy, no apparent abnormalities were observed in any animal.

Under the experimental conditions, the oral LD50 of the test item DOI was higher than 2000 mg/kg in rats.

No classification for acute oral toxicity is warranted based on the absence of mortality up to 2000 mg/kg bw, according to the criteria of Annex VI Directive 67/548/EEC or UN/EU GHS.

This study is classified as acceptable, as it is performed according to OECD guideline and GLP.

Reference 2

Endpoint:	acute toxicity: oral
Type of information:	(Q)SAR
Adequacy of study:	weight of evidence
Study period:	February 2019
Reliability:	2 (reliable with restrictions)
Rationale for reliability incl. deficiencies:	results derived from a valid (Q)SAR model and falling into its applicability domain, with adequate and reliable documentation / justification
Justification for type of information:	For detailed description of the model and its applicability, see below : "QPRF_Acute oral_RAP-006-2019-CHR-ROQ"
Qualifier:	no guideline available
Principles of method if other than guideline:	T.E.S.T. (Toxicity Estimation Software Tool) estimates the acute oral toxicity of organic compounds by taking an average of the predicted toxicities from QSAR methods (Hierarchical method, FDS method and nearest neighbour method) provided the predictions are within the respective applicability domains
GLP compliance:	no
Test type:	other: QSAR
Specific details on test material used for the study:	The 3 main constituents are : - Linoleic diester with 1,4:3,6-dianhydro-D-glucitol (MW 671): CCCCCC=C\C\C=C\CCCCCCCC(=O)OC1COC2C(COC12)OC(=O)CCCCCCC\C=C\C\C=CCCCCC - Oleic diester with 1,4:3,6-dianhydro-D-glucitol (MW 675): CCCCCCCC\C=C\CCCCCCCC(=O)OC1COC2C(COC12)OC(=O)CCCCCCC\C=C\CCCCCCCC - and Linoleic and oleic diester with 1,4:3,6-dianhydro-D-glucitol (MW= 673) CCCCCCCC\C=C/CCCCCCCC(=O)OC1COC2C(COC12)OC(=O)CCCCCCC\C=C/C\C=C/CCCCC
Species:	rat
Strain:	other: not applicable
Sex:	not specified
Details on test animals or test system and environmental conditions:	not applicable
Route of administration:	oral: gavage
Vehicle:	other: not applicable
Details on oral exposure:	not applicable
Doses:	not applicable
No. of animals per sex per dose:	not applicable
Control animals:	other: not applicable
Details on study design:	not applicable
Statistics:	not applicable
	Key result
Sex:	not specified
Dose descriptor:	LD50
Effect level:	3 572 mg/kg bw
Based on:	test mat.
Remarks on result:	other: Acute oral toxicity, LD50 estimation, made on Linoleic diester with 1,4:3,6-dianhydro-D-glucitol using the QSAR "T.E.S.T."

	Key result
Sex:	not specified
Dose descriptor:	LD50
Effect level:	13 246 mg/kg bw
Based on:	test mat.
Remarks on result:	other: Acute oral toxicity, LD50 estimation, made on Oleic diester with 1,4:3,6-dianhydro-D-glucitol using the QSAR "T.E.S.T."
	Key result
Sex:	not specified
Dose descriptor:	LD50
Effect level:	12 650 mg/kg bw
Based on:	test mat.
Remarks on result:	other: Acute oral toxicity, LD50 estimation, made on Linoleic and Oleic diester with 1,4:3,6-dianhydro-D-glucitol using the QSAR "T.E.S.T."
Clinical signs:	not applicable
Body weight:	not applicable
Gross pathology:	not applicable
For detailed description of the results, see the attached document "QPFR_Acute oral_RAP-006-2019-CHR-ROQ"	
Interpretation of results:	GHS criteria not met
Conclusions:	Based on a worse case approach, taking into account the lowest acute oral toxicity estimated with the QSAR "T.E.S.T." for the 3 main constituents of the substance "Esterification products of 1,4:3,6-dianhydro-D-glucitol with sunflower oil fatty acids" , it is considered that a DL50 ≥ 3572 mg/kg is obtained for this substance.
Executive summary:	In conformity with Article 47 of REACH, a QSAR approach was performed to estimate the DL50 of the substance "Esterification products of 1,4:3,6-dianhydro-D-glucitol with sunflower oil fatty acids". The QSAR " T.E.S.T. (Toxicity Estimation Software Tool), version 4.2.1 was used on the 3 main constituents of the registered substance, i.e. the Linoleic diester of isosorbide, the Oleic diester of isosorbide and the Linoleic/oleic diester of isosorbide. The consensus method, which is an average of the predicted toxicities obtained with the hierarchical method, the FDA method and nearest neighbour method (results only used when the domain of applicability is fulfilled) is considered as reliable and the following DL50, 3572 mg/kg bw, 13246 mg/kg bw and 12650 mg/kg bw are obtained for the Linoleic diester of isosorbide, the Oleic diester of isosorbide and the Linoleic/oleic diester of isosorbide, respectively. Based on a worse case approach, taking into account the lowest acute oral toxicity estimated with the QSAR "T.E.S.T." for the 3 main constituents of the substance "Esterification products of 1,4:3,6-dianhydro-D-glucitol with sunflower oil fatty acids" , it is considered that the DL50 is greater than or equal to 3572 mg/kg bw. Hence, according to CLP criteria, no classification for acute oral toxicity was required for the registered substance.

Reference 3

Endpoint:	acute toxicity: oral
Type of information:	read-across from supporting substance (structural analogue or surrogate)
Adequacy of study:	weight of evidence
Study period:	from 03 April 2009 to 06 June 2009
Reliability:	2 (reliable with restrictions)
Rationale for reliability incl. deficiencies:	other: read-across data with original study of reliability 2
Justification for type of information:	ANALOGUE APPROACH JUSTIFICATION and DATA MATRIX see attached document
Reason / purpose for cross-reference:	other: read-across data with original study of reliability 2
Qualifier:	according to guideline
Guideline:	OECD Guideline 423 (Acute Oral toxicity - Acute Toxic Class Method)
Deviations:	no
GLP compliance:	yes (incl. QA statement)
Test type:	acute toxic class method
Limit test:	yes
Species:	rat
Strain:	Wistar
Sex:	female

Details on test animals or test system and environmental conditions:	TEST ANIMALS - Source: Charles River USA - Age at study initiation: 8-12 weeks - Weight at study initiation: ca. 175 grams - Fasting period before study: yes (feed only) - Housing: standard polypropylene rat cages with stainless steel top grill - Diet: standard gamma irradiated pellet feed supplied by M/s. Tetragon Chemie Pvt. Ltd., Bangalore, ad libidum - Water: ad libitum - Acclimation period: yes (5 days) ENVIRONMENTAL CONDITIONS - Temperature: 19.4°C to 22.4°C - Humidity: 56% to 64% - Air changes: - - Photoperiod: 12 hrs dark / 12 hrs light IN-LIFE DATES: From: 18 April 2009 To: 04 May 2009
Route of administration:	oral: gavage
Vehicle:	corn oil
Details on oral exposure:	VEHICLE - Concentration in vehicle: - - Justification for choice of vehicle: - - Lot/batch no. (if required): - - Purity: - MAXIMUM DOSE VOLUME APPLIED: 10 mL/kg bw CLASS METHOD - Rationale for the selection of the starting dose: -
Doses:	2000 mg/kg bw
No. of animals per sex per dose:	6 females (3 females per step)
Control animals:	no
Details on study design:	- Duration of observation period following administration: 14 days - Frequency of observations and weighing: > body weight: days 0, 7 and 14 > morbidity/mortality: once daily > clinical signs: at 0.5, 1, 2 and 4 hours after dosing, and once daily thereafter - Necropsy of survivors performed: yes
Sex:	female
Dose descriptor:	LD50
Effect level:	> 2 000 mg/kg bw
Based on:	test mat.
Mortality:	No mortality/morbidity was observed in animals throughout the observation period.
Clinical signs:	No clinical signs were observed in animals throughout the observation period.
Body weight:	All the animals showed normal body weight during the experiment period.
Gross pathology:	Animals did not reveal any macroscopic lesions.
Interpretation of results:	not classified
Remarks:	Migrated information Criteria used for interpretation of results: EU
Conclusions:	The oral LD50 of DOI is > 2000 mg/kg bw (with no mortality at this dose level).
Executive summary:	In an acute oral toxicity study according to OECD 423, and GLP, scored as validity 1 according to Klimisch criteria, groups of fasted female Wistar rats were given a single oral dose of DOI in corn oil at the dose of 2000 mg/kg bw (2x3 females) and observed for 14 days. Clinical signs and mortality were checked frequently during the hours following administration of the test substance, and once a day thereafter. Body weight was measured just before administration of the test substance on day 0 and then on days 7 and 14. No clinical signs of toxicity and no mortality were observed during the study. At necropsy, no apparent abnormalities were observed in any animal. Under the experimental conditions, the oral LD50 of the test item DOI was higher than 2000 mg/kg in rats. No classification for acute oral toxicity is warranted based on the absence of mortality up to 2000 mg/kg bw, according to the criteria of Annex VI Directive 67/548/EEC or UN/EU GHS.

This study is classified as acceptable, as it is performed according to OECD guideline and GLP.

Endpoint conclusion

Endpoint conclusion: no adverse effect observed

Acute toxicity: via inhalation route

Endpoint conclusion

Endpoint conclusion: no study available

Acute toxicity: via dermal route

Endpoint conclusion

Endpoint conclusion: no study available

Additional information

Acute oral toxicity:

- Based on a worse case approach, taking into account the lowest acute oral toxicity estimated with the QSAR "T.E.S.T." for the 3 main constituents of the substance "Esterification products of 1,4:3,6-dianhydro-D-glucitol with sunflower oil fatty acids", the target substance is considered to have an LD50 ≥ 3572 mg/kg bw.

- In an acute oral toxicity study according to OECD 423, and GLP, scored as validity 1 according to Klimisch criteria, groups of fasted female Wistar rats were given a single oral dose of source substance, 1,4:3,6-dianhydro-2,5-di-O-octanoyl-D-glucitol, in corn oil at the dose of 2000 mg/kg bw and observed for 14 days.

Under the experimental conditions, the oral LD50 of the test item was higher than 2000 mg/kg in rats.

No classification for acute oral toxicity is warranted based on the absence of mortality up to 2000 mg/kg bw, according to the criteria of Annex VI Directive 67/548/EEC or UN/EU GHS.

Acute dermal toxicity:

No data available.

Acute inhalation toxicity:

No data is available.

Justification for selection of acute toxicity – oral endpoint

GLP and OECD guideline

Justification for classification or non-classification

Using weight of evidence approach for the target substance with data available on QSAR T.E.S.T. and data available on source substance, we can conclude that the target substance, Esterification products of 1,4:3,6-dianhydro-D-glucitol with sunflower oil fatty acids, is considered to have a LD50 > 2000 mg/kg bw/d and no classification for acute oral toxicity is warranted.