Health Canada Santé Canada

Evaluation Report for Category B, Subcategory 1.2 Application

Application Number: 2019-2538
Application: New Technical Grade Active Ingredient (Product Chemistry) – New Source (Site) New Registrant
Product: Dry Fiesta TGAI
Registration Number: 34622
Active ingredient (a.i.): Iron (present as ferric sodium EDTA trihydrate)
PMRA Document Number: 3383727

Purpose of Application

The purpose of this application was to register a new source of the active ingredient iron (present as ferric sodium EDTA trihydrate) by a new registrant.

Chemistry Assessment

Common Name: Ferric sodium EDTA
IUPAC* Chemical Name: Ferric sodium ethylenediaminetetraacetic acid
CAS† Chemical Name: [[N,N'-1,2-ethanediylbis[N-(carboxymethyl)glycinato]](4-)-N,N',O,O',ON,ON'ferrate(1-)sodium,

* International Union of Pure and Applied Chemistry
† Chemical Abstracts Service

Dry Fiesta TGAI has the following properties:

Property	Result
Colour and physical state	Yellow-brown powder
Nominal concentration	13.43% as iron
Odour	Odourless
Density at 20°C	1.01 g/mL
Vapour pressure	No measurable vapour pressure since the product's melting point is > 400°C
pH	4.90 ± 0.01
Solubility in water	90 g/L

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Property	Result
n-Octanol/water partition coefficient	log $K_{ow} < 0$

The required chemistry data for Dry Fiesta TGAI have been provided, reviewed and found to be acceptable.

Health Assessment

The data package in support of Dry Fiesta TGAI consisted of acute toxicity studies (acute oral, dermal and inhalation toxicity) and irritation testing (dermal and eye). Dry Fiesta TGAI is of low toxicity by the oral, dermal and inhalation routes, is minimally irritating to eyes and non-irritating to the skin.

The submitted sensitization study with ferric sodium EDTA (FeNaEDTA) was unacceptable but the potential for dermal sensitization from Dry Fiesta TGAI was addressed with a surrogate study containing FeHEDTA as well as publicly available information on FeNaEDTA and related compounds. Based on this information, Dry Fiesta TGAI is considered to be a dermal sensitizer.

Waivers were accepted for short-term dermal toxicity, prenatal development toxicity, and genotoxicity and mutagenicity testing based on toxicological information in publicly available scientific reports for FeNaEDTA and similar EDTA compounds.

Dietary and occupational exposure assessments were not required with this application.

Environmental Assessment

The environmental risks associated with the use of Dry Fiesta TGAI are acceptable when used according to label directions. Environmental concerns have been mitigated through adequate statements on the product label.

Value Assessment

A value assessment was not required with this application.

Conclusion

The Pest Management Regulatory Agency has completed an assessment of the information provided, and has found the information sufficient to support the registration of Dry Fiesta TGAI.

References

A. List of Studies/Information Submitted by Registrant

PMRA Document Number	Reference
3000478	2019, Binder 1 Product Chemistry, DACO: 2.0,2.1,2.11,2.11.1,2.11.2,2.11.3,2.11.4,2.12,2.12.1,2.13,2.13.1,2.13.2,2.13.3,2.13.4, 2.14,2.14.1,2.14.10,2.14.11,2.14.12,2.14.13,2.14.14,2.14.2,2.14.3,2.14.4,2.14.5,2.14. 6,2.14.7,2.14.8,2.14.9 CBI
3000486	2009, Accelerated (2 week 54) storage stability of Slugkil TGAI, DACO: 2.14.14 CBI
3101409	2020, Final Report - Preliminary Analysis Source #1, DACO: 2.13 CBI
3193797	2019, Annex1_internal specs_EFE13, DACO: 2.11.2 CBI
3193803	2020, Preliminary (5-Batch) Analysis Testing of Sodium Ferric EDTA, DACO: 2.13.1 CBI
3193804	2020, EDTA chromatograms all samples, DACO: 2.13.1 CBI
3193805	2020, [CBI Removed] chromatograms all samples, DACO: 2.13.1 CBI
3193806	2019, COA for Sodium Ferric EDTA samples, DACO: 2.13.3 CBI
3193807	2021, Preliminary (5-Batch) Analysis Testing of Sodium Ferric EDTA AM #01, DACO: 2.13.3 CBI
3193809	2020, Preliminary (5-Batch) Determination of Water Content by Loss on Drying in Sodium Ferric EDTA, DACO: 2.13.3 CBI
3197073	2020, [Privacy removed] Memorandum, DACO: 2.11.3 CBI
3197075	2020, Fe-EDTA Manufacturing Process, DACO: 2.11.3 CBI
3211349	2021, [Privacy removed] Memorandum, DACO: 2.11.3 CBI
3211351	2021, Colour of Dry Fiesta TGAI, DACO: 2.14.1 CBI
3211352	2021, Physical State of Dry Fiesta TGAI, DACO: 2.14.2 CBI
3211353	2021, Odor of Dry Fiesta TGAI, DACO: 2.14.3 CBI
3211354	2021, Density of Dry Fiesta TGAI, DACO: 2.14.6 CBI
3211355	2021, pH of Dry Fiesta TGAI, DACO: 2.14.15,830.7000 CBI
3355271	US EPA, 2000, [CBI Removed] Compounds Hazard Summary, DACO: 2.13.4
3355274	2022, Certificate of Analysis, DACO: 2.13.4 CBI
3355282	2022, Dry Sieve Analysis of Dry Fiesta TGAI and RTU, DACO: 2.13.4 CBI
3355284	National Institutes of Health, 2021, [CBI Removed] Fact Sheet for Consumers, DACO: 2.13.4
1753358	Candela, E. et.al., 1984, Iron Absorption by Humans and Swine from Fe(III)-EDTA. Further Studies, Candela, E., et al, Iron Absorption by Humans and Swine from FE(111)-EDTA. Further Studies, J. Nutr. 114:2204-2211, 1984., DACO: 4.8
1753359	Dunkel, V.C. et. al., 1998, Genotoxicity of Iron Compounds in Salmonella typhimurium and L5178Y Mouse Lymphoma Cells, Dunkel, V.C, et al, Genotoxicity of Iron Compounds in Salmonella typhimurium and L5178Y Mouse Lymphoma Cells, Environmental and Molecular Mutagenesis 33:28-41 (1999), DACO: 4.8

1753363	Kimmel, C.A., 1976, Effect of Route of Administration on the Toxicity and Teratogenicity of EDTA in the Rat, Kimmel, C.A., Effect of Route of Administration on the Toxicity and Teratogenicity of EDTA in the Rat, Toxicology and Applied Pharmacology 40, 299-306 (1977)., DACO: 4.8
1753364	McGregor, D.B. et. al., 1988, Responses of the L5178Y tk+/tk- Mouse lymphoma Cell Forward Mutation Assay: III. 72 Coded Chemicals, McGregor, D.B. et al., Responses of the L5178Y tk+/tk- Mouse lymphoma Cell Forward Mutation Assay: III. 72 Coded Chemicals, Environmental and Molecular Mutagenesis 12:85-154 (1988)., DACO: 4.8
1753366	Oser, B.L. et al, 1962, Safety Evaluation Studies of Calcium EDTA, Osler, B.L. et al, Safety Evaluation Studies of Calcium EDTA, Toxicology and Applied Pharmacology 5, 142-162 (1963), DACO: 4.8
1753367	PMRA, 2007, Proposed Registration Decision Ferric Sodium EDTA, Pest Management Regulatory Agency, Proposed Registration Decision Ferric Sodium EDTA, PRD2007-13, DACO: 4.8
1753368	Swenerton, H. and L.S. Hurley, 1971, Teratogenic Effects of a Chelating Agent and their Prevention by Zinc, DACO: 4.8
1753369	Munro, I.C., 2005, Sodium Iron EDTA (WHO Food Additives Series 32), Munro, I.C., Sodium Iron EDTA, WHO Food Additives Series 32), DACO: 4.8
1753370	Yang, S.S. and M.S. Chan, 1964, Summaries of Toxicological Data: Toxicology of EDTA, Yang, S.S. and M.S. Chan, Summaries of Toxicological Data: Toxicology of EDTA, Fd Cosmet, Toxicol. Vol. 2, pp. 763-767. Pergamon Press 1964, Printed in GB, DACO: 4.8
3000488	2019, Binder 2 TGAI Toxicology, DACO: 4.2,4.2.1,4.2.2,4.2.3,4.2.4,4.2.5,4.2.6,4.3,4.5.4,4.5.5,4.8
3000489	2007, Acute Oral Toxicity study of FeNaEDTA in Rats, DACO: 4.2.1
3000490	2007, Acute Dermal Toxicity study of FeNaEDTA in CD Rats, DACO: 4.2.2
3000491	2008, Acute Inhalation study of FeNaEDTA in Rats, DACO: 4.2.3
3000492	2007, Acute Eye Irritation/Corrosion of FeNaEDTA in Rabbits, DACO: 4.2.4
3000493	2007, Acute Dermal Irritation/Corrosion Test of FeNaEDTA in Rabbits, DACO: 4.2.5
3000494	2007, FeNaEDTA Skin Sensitisation: Local Lymph Node Assay in Mice, DACO: 4.2.6
3000495	2019, Data Evaluation Record, DACO: 4.8
3000499	EPA, 2006, 58th Report of the TSCA, DACO: 4.8
3000500	EPA, 2008, Biopesticides Registration Notice: Iron HEDTA, DACO: 4.8
3000501	PMRA, 2018, Final Screening Assessment: EDTA and its Salts, DACO: 4.8
3000502	J. Heimbach et. al., 2000, Safety Assessment of Iron EDTA [Sodium Iron (Fe3+) ethylenediaminetetracetic acid]: Summary of Toxicological, Fortification and Exposure Data, DACO: 4.8
3264085	2021, Binder 2 Addendum Toxicology, DACO: 4.1,4.3,4.5.4,4.5.5
3264089	JECFA, 1999, Sodium Iron (III) Ethylenediaminetetraacetate, Trihydrate, DACO: 4.1,8.1,9.1
3264090	Takeda, M., 1986, Iron-57 Mossbauer Spectroscopic Study of Six-Coordinate and Seven-Coordinate Iron(III)-EDTA Complexes, DACO: 4.1,8.1,9.1
3264093	2021, Nouryon Letter to Neudorff - Revised, DACO: 4.1,8.1,9.1 CBI

3264095	C.T.J. Wreesman, 2014, Reasons for raising the maximum acceptable daily intake of EDTA and the benefits for iron fortification of foods for children 6-24 months of age, DACO: 4.1,8.1,9.1

B. Additional Information Considered

i) Published Information

PMRA Document Number	Reference
3367916	Whittaker, P., H. E. Seifried, R. H. C. San, J.J. Clarke and V.C. Dunkel. 2001, Genotoxicity of iron chelators in L5178Y Mouse Lymphoma Cells, Environ. Mol. Mutagen. 38: 347-356., doi: 10.1002/em.10033, DACO: 4.5.5
3367925	J McCann, E Choi, E Yamasaki, B N Ames, 1975, Detection of carcinogens as mutagens in Salmonella/microsome test: assay of 300 chemicals, Proc Natl Acad Sci USA. 72(12):5135-9., DACO: 4.5.5
3367927	European Chemicals Bureau, 2004, EU Risk Assessment Report edetic acid (EDTA). 1st Priority List,, DACO: 4.5.5
3367928	EFSA, 2010, EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS); Scientific Opinion on the use of ferric sodium EDTA as a source of iron added for nutritional purposes to foods for the general population (including food supplements) and to foods for particular nutritional uses, EFSA Journal 2010; 8(1):1414, doi: 10.2903/j.efsa.2010.1414, DACO: 4.3
3367940	Lanigan and Yamarik, 2002, Final report on the safety assessment of EDTA, calcium disodium EDTA, diammonium EDTA, dipotassium EDTA, disodium EDTA, TEA-EDTA, tetrasodium EDTA, tripotassium EDTA, trisodium EDTA, HEDTA, and trisodium HEDTA., J. Tox 21(2):95-142, doi: 10.1080/1091581029009652 2, DACO: 4.6.6
3367943	P. Sanchez-Pedreno, P, B. Garcia-Bravo and J. Frias-Iniesta., 2009, Contact allergy to tetrasodium EDTA in a sunscreen, Contact Dermatitis 2009: 61: 125-126, DACO: 4.6.6