Australian Government
Department of Health and Ageing
NICNAS

INVENTORY MULTI-TIERED ASSESSMENT AND PRIORITISATION (IMAP)

HUMAN HEALTH TIER II ASSESSMENT FOR

Formic acid, sodium salt

CAS Registry Number: 141-53-7

PREFACE

As part of the reform regarding assessment of Existing Chemicals, the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is implementing a new framework to address the human health and environmental impacts of industrial chemicals, not yet assessed, on the Australian Inventory of Chemical Substances (AICS).

The framework provides a more rapid, flexible and transparent approach for the assessment of existing chemicals.

The Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework was developed, with significant input from stakeholders, and will be applied in stages.

Stage One of this program, which will take three years, started 1 July 2012 and is examining 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This includes chemicals for which NICNAS already holds exposure information, chemicals identified as a concern or for which regulatory action has been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

This chemical/group of chemicals is/are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

For more detail on the new program please visit: www.nicnas.gov.au

ACRONYMS & ABBREVIATIONS

ACToR	Aggregated Computational Toxicology Resource (US)
AICS	Australian Inventory of Chemical Substances
ASTDR	Agency for Toxic Substances and Disease Registry (US)
bw	bodyweight
CAS	Chemical Abstracts Service
CFR	Code of Federal Regulations (US)
CHO	Chinese hamster ovary
CosIng	Cosmetic Ingredients and Substances database (EU)
d	day
DNA	Deoxyribonucleic acid
EC	European Commission
EC3	Estimated concentration three
ECHA	European Chemicals Agency
ESIS	European Chemical Substances Information System
EU	European Union
EU RAR	European Union Risk Assessment Report
FDA	Food and Drug Administration (US)
FSANZ	Food Standards Australia and New Zealand
g	gram
g/mol	grams per mole
GHS	Globally Harmonized System of Classification and Labelling of Chemicals*
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
GPMT	Guinea Pig Maximisation Test
h	hour
HGPRT	hypoxanthine guanine phosphoribosyltransferase
HPV	high production volume
HSDB	Hazardous Substances Data Bank
HSIS	Hazardous Substances Information System
HVICL	High Volume Industrial Chemicals List
IARC	International Agency for Research on Cancer
INCHEM	International Programme on Chemical Safety (also known as IPCS)
INCI	International Nomenclature of Cosmetic Ingredients
ip	intraperitoneal
IRIS	Integrated Risk Information System (US)
IUCLID	International Uniform Chemical Information Database
iv	intravenous
kg	kilogram
L	litre
LC50	median lethal concentration
LD50	median lethal dose
LCLo	lowest published lethal concentration
LLNA	local lymph node assay
LOAEL	lowest observed adverse effect level
LOEL	lowest observed effect level
m^3	cubic metre
mg	milligram
mg/cm^3	milligrams per cubic centimetre
mg/kg bw/d	milligrams per kilogram bodyweight per day
min	minute
mL	millilitre
µg	microgram
µL	microlitre
(m)SDS	(material) Safety Data Sheet

NIOSH	National Institute for Occupational Safety and Health (US)
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NOHSC	National Occupational Health and Safety Commission
NTP	National Toxicology Program (US)
OECD	Organisation for Economic Cooperation and Development
OEL	occupational exposure limit
PCBU	person conducting a business or undertaking
PEL	permissible exposure limit
PND	postnatal day
ppb	parts per billion
PPE	personal protective equipment
ppm	parts per million
REACH	Registration Evaluation Authorisation of Chemicals (ECHA)
SD	Sprague Dawley
SIAP	SIDS Initial Assessment Profile (OECD)
SIAR	SIDS Initial Assessment Report (OECD)
SIDS	Screening Information Data Set (OECD)
SMILES	simplified molecular-input line-entry system
SPIN	Substances in Preparations In the Nordic countries
STEL	short-term exposure limits
STV	short-term value
SUSMP	Standard for the Uniform Scheduling of Medicines and Poisons (The Poisons Standard**)
TCLo	lowest published toxic concentration
TEEL	temporary emergency exposure limits
TSCA	Toxic Substances Control Act (US EPA)
TG	test guideline
TGA	Therapeutic Goods Administration
TLV	threshold limit values
TWA	time weighted average
UN	United Nations
US	United States of America
US EPA	United States Environmental Protection Agency
WHS	Work, Health and Safety
wt	weight
w/w	weight per weight

Glossary

NICNAS uses the IPCS Risk Assessment Terminology (IPCS, 2004) glossary, which includes:
Part 1: IPCS/OECD Key Generic Terms used in Chemical Hazard/Risk Assessment; and
Part 2: IPCS Glossary of Key Exposure Assessment Terminology.
The IPCS Risk Assessment Terminology can be accessed at:
http://www.who.int/ipcs/methods/harmonization/areas/ipcsterminologyparts1and2.pdf

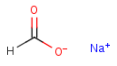
*****Globally Harmonised System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third edition. Can be accessed at: http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html

******The Poisons Standard (the SUSMP) can be accessed at: http://www.tga.gov.au/industry/scheduling-poisons-standard.htm

Formic acid, sodium salt

CAS No: 141-53-7

Chemical Identity

Synonyms	Sodium formate Salachlor Sodium methanoate
Structural Formula	
Molecular Formula	CH2O2.Na
Molecular Weight (g/mol)	68.02
Appearance and Odour (where available)	Colourless/white solid
SMILES	C(=O)O{-}.[Na]{+}

Import, Manufacture and Use

Australian

No specific Australian use, import, or manufacture information has been identified.

International

The following international uses have been identified through the Organisation for Economic Cooperation and Development Screening information data set, International Assessment Report (OECD SIAR), Galleria Chemica, Substances and Preparations in the Nordic countries (SPIN) database, the European Commission Cosmetic Substances and Ingredients (CosIng) database and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

The chemical has reported cosmetic use as:

- a buffering agent; and
- a preservative.

The chemical has reported domestic use including:

- paints, lacquers and varnishes;
- surface treatment;
- corrosion inhibitors;
- cleaning agents including laundry detergents;
- colouring agents;
- adhesives; and
- binding agents.

The chemical has reported commercial use including:

- photographic chemicals;
- process regulators;
- tanning agents;
- anti-freezing agents; and

- viscosity adjustors.

The chemical has reported site limited use including:

- complex and flocculating agents;
- laboratory chemicals; and
- electroplating agents.

Restrictions

Australian

No known restrictions have been identified.

International

European Union: The use of the chemical in cosmetics in the European Union is subject to the restrictions described in EU Regulation ((EC) No 1223/2009) Annex V (Ref 14). This preservative may be used in cosmetics and personal care products at a maximum concentration of 0.5% (as acid).

New Zealand: New Zealand Cosmetic Products Group Standard - Schedule 7: Preservatives Cosmetic Products May Contain With Restrictions; maximum authorised concentration, 0.5 % (expressed as the acid).

Existing Worker Health And Safety Controls

Hazard classification

The chemical is not listed on the Hazardous Substances Information System (HSIS) (Safe Work Australia).

Exposure standards

Australian

There are no specific exposure standards for this chemical. However, the permissible exposure limits (as the time weighted average (TWA)) for dusts apply (10 mg/m³ measured as inspirable dust).

International

The following exposure standards are identified (Galleria Chemica):
An exposure limit (TWA) of 5 – 10 mg/m³ in different countries such as USA (California), Canada (Quebec), Ireland and Spain. The exposure standards are general values for dusts and particles which otherwise do not have an exposure standard.

Health Hazard Information

Health hazard information for formic acid (64-18-6) and potassium hydrogen diformate (20642-05-1) has been included in this report. Similar to the chemical, these chemicals are expected to exist almost entirely as the formate ion in biological solutions and therefore are considered to be suitable analogues for the chemical. However, due to differences in pH the corrosive effects observed with formic acid are not expected.

Toxicokinetics

The chemical is absorbed from the gastrointestinal tract (US EPA, 2001).
The chemical will dissociate in biological fluids to the formate and sodium ions (OECD, 2008).

Acute Toxicity

Oral

The chemical exhibits low acute toxicity in animal tests as evidenced by reported LD50 in rats of > 3,000 mg/kg and in mice of 11,200 mg/kg (OECD, 2008; US EPA, 2001).

Dermal

The chemical exhibits low acute toxicity in animal tests as evidenced by reported LD50 for the chemical in rats following a 24 hour semi-occlusive exposure of > 2000 mg/kg with no adverse effects observed (OECD, 2008).

Inhalation

The chemical exhibits low acute toxicity in animal tests following inhalation exposure. The LC50 for the chemical was > 0.67 mg/L (maximum obtainable concentration) in a study where it was aerosolised (OECD, 2008). Symptoms seen in the study included decreased activity and eye closing, lacrimation and nasal discharge, and a slight and transient reduction in body weight gain.

Corrosion / Irritation

Skin irritation

No signs of skin irritation were seen rats with a 24 hour semi-occlusive exposure to the chemical during an acute dermal toxicity study (OECD, 2008).

Eye irritation

The chemical is reported to be a slight eye irritant in animal studies. Effects were not sufficient to warrant a hazard classification.

The chemical caused transient irritation in the eye-conjunctivae in a study in rabbits (OECD, 2008). The mean score (24, 48 and 72 hours) for redness of the conjunctivae was 1.89 and for chemosis was 1.5 in a study in rabbits (Galleria Chemica). It was also noted that the chemical caused eye closure and lacrimation during an acute inhalation toxicity study, where it was aerosolised at the maximum achievable concentration (0.67 mg/L) (OECD, 2008).

Respiratory irritation

Nasal discharge was seen during an acute inhalation toxicity test on rats at the highest achievable concentration; no effects were noted at gross necropsy (US EPA, 2001).

Sensitisation

Skin sensitisation

There are no skin sensitisation data available for the chemical. Two analagous chemicals, formic acid (CAS number 64-18-6) and potassium hydrogen diformate (CAS number 20642-05-1) were not sensitising to skin when tested in the Buehler and the guinea pig maximisation tests respectively (OECD, 2008).

Repeat Dose Toxicity

Oral

No toxicity was detected in a 1.5 year drinking water study in rats exposed to the chemical at concentrations up to 1 % (US EPA, 2001). In a 90 day feeding study in pigs the chemical was administered in the presence of other formates at concentrations of up to 0.6 % without any adverse effects being noted (US EPA, 2001).

The effects of repeated exposure to the analogous chemical potassium hydrogen diformate (CAS number 20642-05-1) has been looked at in 13, 80 and 104 week repeated dose toxicity studies (OECD, 2008). These three dietary studies showed a range for NOAELs of 50 (rat) to 400 (mice) mg/kg-bw/day with main effects on body weights and the stomach, often due to the irritating properties of this analogue.

Dermal

No data are available.

Inhalation

No data are available. The effects of repeated exposure to the analogue chemical formic acid (CAS number 64-18-6) were primarily limited to irritant effects of the respiratory tract. These effects are not expected for the sodium salt.

Genotoxicity

In a bacterial reverse mutation assay with *Salmonella typhimurium* the chemical was negative, both with

and without metabolic activation (US EPA, 2001; US EPA, 2013).

The chemical was not clastogenic to Chinese hamster ovary K1 cells in a well documented study (US EPA, 2001). However, the chemical was reported to be positive in a mouse lymphoma assay in both the presence and absence of metabolic activation in a 1982 study, where no further details were reported (US EPA, 2001).

The chemical produced by neutralisation of 0.1% formic acid with a glycine-NaOH buffer, was tested on *Drosophila melanogaster* in a Drosophila (SLRL test) using feeding for the entire larval stage of development. No increase in mutation rate was observed; however, feeding the acid form without neutralisation produced a statistically significant positive result (US EPA, 2001; US EPA, 2013).

The analogue potassium hydrogen diformate (CAS number 20642-05-1) was negative in *in vitro* chromosomal aberration and gene mutation assays and in an *in vivo* rat bone marrow micronucleus test.

Based on the weight of evidence and the lack of genotoxicity seen in the analogue potassium hydrogen diformate (CAS number 20642-05-1) the chemical is not considered to be genotoxic.

Carcinogenicity

No carcinogenicity tests on the chemical are available. However, in an 80 week feeding study in mice and a 104 week study in rats with doses up to 2,000 mg/kg bw/d with the analogue potassium hydrogen diformate (CAS number 20642-05-1) no evidence of increased carcinogenicity was observed (OECD, 2008).

Reproductive and developmental toxicity

There are no reproductive studies available on the chemical.

The chemical was administered to rats in a developmental study at doses up to 945 mg/kg bw/d during gestation days 6 to 19. No maternal toxicity or developmental effects were seen at any concentration tested (OECD, 2008). In a similar test in rabbits at concentrations up to 1000 mg/kg bw/d via oral gavage during gestation days 6 to 28, the NOAEL was also determined to be the highest dose tested (OECD, 2008).

Risk Characterisation

Critical Health Effects

The main critical effect to human health is slight eye irritancy.

Public Risk Characterisation

Provided that normal precautions are taken to avoid prolonged eye contact, the public health risk posed by cosmetic or domestic products containing the chemical is is not considered to be unreasonable.

Occupational Risk Characterisation

Given the critical health effects the risk to workers from this chemical is not considered to be unreasonable. The chemical currently has no hazard classification for worker health and safety; this is considered appropriate based on available data.

NICNAS Recommendation

The risk to workers and public from this chemical is not considered to be unreasonable. The chemical is not recommended for classification and labelling under the current approved criteria and adopted GHS. This does not consider classification of physical hazards and environmental hazards. No recommendations or further assessment is required.

References

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