THIS DOCUMENT HAS BEEN PREPARED ACCORDING TO THE PROVISIONS OF ARTICLE 136(3) “TRANSITIONAL MEASURES REGARDING EXISTING SUBSTANCES” OF REACH (REGULATION (EC) 1907/2006). IT IS NOT A PROPOSAL FOR A RESTRICTION ALTHOUGH THE FORMAT IS THE SAME

Annex XV dossier

Transitional Dossier

Substance Name: **Trisodium nitrilotriacetate**

EC Number: **225-768-6**

CAS Number: **5064-31-3**

CONTENTS

TABLES

RESTRICTION PROPOSAL

Substance Name: Trisodium nitrilotriacetate

EC Number: 225-768-6

CAS number: 5064-31-3

Restriction proposal: None

Other Risk reduction measures see attached Risk Reduction Strategy.

INFORMATION ON HAZARD AND RISKS

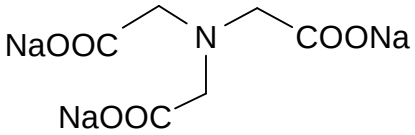
1 IDENTITY OF THE SUBSTANCE AND PHYSICAL AND CHEMICAL PROPERTIES

1.1 Name and other identifiers of the substance

Chemical Name:	Trisodium nitrilotriacetate (NTA)
EC Name:	Glycine, N,N-bis(carboxymethyl)-, trisodium salt
CAS Number:	5064-31-3
IUPAC Name:	Trisodium nitrilotriacetate

1.2 Composition of the substance

For each constituent/ impurity/ additive, fill in the following table (which should be repeated in case of more than one constituent). The information is particularly important for the main constituent(s) and for the constituents (or impurity) which influence the outcome of the dossier.

Chemical Name:	Trisodium nitrilotriacetate (NTA)
EC Number:	225-768-6
CAS Number:	5064-31-3
IUPAC Name:	Trisodium nitrilotriacetate
Molecular Formula:	$C_6H_6NNa_3O_6$
Structural Formula:	
Molecular Weight:	257.1 g/mol
Typical concentration (% w/w):	≥ 92 % w/w

1.3 Physico-chemical properties

Table 1: Summary of physico- chemical properties

REACH ref Annex, §	Property	IUCLID section	Value	[enter comment/reference or delete column]
VII, 7.1	Physical state at 20°C and 101.3 KPa	3.1	colourless crystalline powder	
VII, 7.2	Melting/freezing point	3.2	410 °C with decomposition above 200 °C	BASF, 1996
VII, 7.3	Boiling point	3.3	not applicable	
VII, 7.4	Relative density	3.4 density	1.77 at 20 °C [1)]	
VII, 7.5	Vapour pressure	3.6	not determined	
VII, 7.6	Surface tension	3.10	not determined	
VII, 7.7	Water solubility	3.8	about 640 g/l at 20 °C	
VII, 7.8	Partition coefficient n-octanol/water (log value)	3.7 partition coefficient	-2.62 (calculated) [2)]	
VII, 7.9	Flash point	3.11	not determined	
VII, 7.10	Flammability	3.13	not highly flammable [3)]	
VII, 7.11	Explosive properties	3.14	not explosive	
VII, 7.12	Self-ignition temperature		no selfignition up to decomposition (200 °C)	
VII, 7.13	Oxidising properties	3.15	no oxidising properties	
VII, 7.14	Granulometry	3.5		
XI, 7.15	Stability in organic solvents and identity of relevant degradation products	3.17		
XI, 7.16	Dissociation constant	3.21		
XI, 7.17,	Viscosity	3.22		
	Auto flammability	3.12		
	Reactivity towards container material	3.18		
	Thermal stability	3.19		

[1)] Relative density: pycnometer method

[2)] Partition coefficient: The logPow was calculated according to the Rekker method with the computer program Pro-logP (version 2.0).

[3)] Flammability: According to guideline 92/69/EEC test method A.10 (determination of the flammability for solids), the substance did not propagate combustion. The tests according to A.12 (determination of the flammability in contact with water) and A.13 (determination of pyrophoric properties) were not conducted. Due to the properties and the handling of the substance it has not to be assumed that flammable gases formate in contact with water or that the substance has pyrophoric properties.

2 MANUFACTURE AND USES

See Risk Assessment Report - draft from 20th of August 2008.

3 CLASSIFICATION AND LABELLING

3.1 Classification in Annex I of Directive 67/548/EEC

Environment

Proposal of the rapporteur

For the classification of biodegradation, the available laboratory tests with uncomplexed NTA should not be used, because biodegradation of this chelator is strongly dependent on the metal speciation. Studies on the degradation in biological treatment plants as well as degradation tests conducted in river water reveal that the degradation properties of NTA (resp. of its metal complexes) are comparable with a readily degradable substance. In addition the substance has no bioaccumulation potential.

In tests on the acute toxicity on fish and daphnia effects were only observed when NTA was present in over-stoichiometric concentrations compared to the content of metal ions. The lowest LC50 values were 98 mg/l for both trophic levels.

Results of algae growth inhibition tests have to be interpreted carefully, because the observed effects are mainly cause by nutrient deficiency, which is an artefact and not relevant for the environment. Tests with increased concentrations of nutrient metals (where nutrient deficiency is suppressed) reveal that intrinsic toxicity of NTA is expected only at concentrations far above 10 mg/l.

Considering all results, a classification of Na_3NTA is not recommended with respect to the environment.

Human Health

- (Classification according to Annex I)

Xn	Harmful	R 22	Harmful if swallowed
Xi	Irritant	R 36	Irritating to eyes

- (Proposal of the rapporteur)

Classification and Labelling of Na_3NTA has been concluded by the EU C&L Committee in March 2006 (See ANNEX 1 Draft list 31st ATP New entries 16/10/2006 (31B).

Xn	Harmful	R 22	Harmful if swallowed
Xi	Irritant	R 36	Irritating to eyes
Carcinogenic, cat. 3		R 40	Limited evidence of a carcinogenic effect

Oral LD50 values of approximately 750 mg/kg bw were determined for monkeys, of 1300-1470 mg/kg bw for female rats and of 1600-2220 mg/kg bw for male rats. Based on these data the substance has to be classified as "Xn, harmful" and labelled with "R 22 - harmful if swallowed".

There is no valid information on eye irritation testing according to current international test guidelines. On animal welfare reasons, we propose to assess the eye irritating properties of Na_3NTA on the basis of the test carried out for Monsanto (1968) and BASF (1982) and taking also into account the strongly basic nature of a 1% aqueous solution. The Monsanto test reports on conjunctival irritation and corneal effects which were not reversible within 7 days. However, based on the nature of effects, reversibility is to be expected within an observation time of 21 days. Correspondingly, effects of a 38% aqueous solution were moderate (BASF 1982). These results are sufficient to confirm "R 36 irritating to eyes".

Carcinogenicity of NTA was demonstrated for the oral route. NTA is carcinogenic in both sexes of two species, the rat and the mouse. No or sparse data were evident for the other inhalative or dermal routes. NTA is not metabolised and exerts its carcinogenic activities via the urinary excretion route. NTA induced primary tumors at several localisations in the urinary tract. Multiple tumor types were observed. Tumors in the rat kidney originated from the tubular-cell epithelium and from the pelvic transitional cell epithelium. Tumors from the transitional cell type were also found in the ureter and the urinary bladder. For the mice, tumors originated from the renal tubular epithelium and occasionally from the renal pelvis.

Based on the actual knowledge a direct genotoxic mechanism of NTA carcinogenesis could not be demonstrated. At present, it is thought that NTA might be operative at target sites by other actions. It seems to be reasonable that NTA related cytotoxicity plays a crucial role in the development of tumors. The facts that the cytotoxicity and tumors were seen in identical target regions of the kidneys, that cytotoxicity is an early lesion that leads to regenerative hyperplasia and that hyperplasia was often associated to tumor growth provide evidence for this mode of action, which is in line with the criteria for a carcinogen, category 3. .

Beside the sequential cascade of morphological events – cytotoxicity, hyperplasia/dysplasia, neoplasia – other factors might contribute to disregulated cell growth and to the manifestation of neoplastic cell growth either as initial events before obvious cytotoxicity or in parallel to the cascade from cytotoxicity to tumor. Interference with metal cations and forming of metal complexes might be suspected. However, the data presently available were insufficient to give sufficient evidence for their contribution in the NTA carcinogenicity.

Concentration Limits

$C \geq 25$ %: Xn; R22-36-40

$20 \leq$ % $C < 25$ %: Xn; R36-40

$5 \leq$ % $C < 20$ %: Xn; R40

3.2 Self classification(s)

This should include the classification, the labelling and the specific concentrations limits. The reason and justification for no classification should be reported here.

It should be stated whether the classification is made according to Directive 67/548/EEC criteria or according to GHS criteria.

4 ENVIRONMENTAL FATE PROPERTIES

See Risk Assessment Report - draft from 20th of August 2008.

5 HUMAN HEALTH HAZARD ASSESSMENT

See Risk Assessment Report - draft from 20th of August 2008.

6 HUMAN HEALTH HAZARD ASSESSMENT OF PHYSICO-CHEMICAL PROPERTIES

See Risk Assessment Report - draft from 20th of August 2008.

7 ENVIRONMENTAL HAZARD ASSESSMENT

See Risk Assessment Report - draft from 20th of August 2008.

8 PBT AND VPVB ASSESSMENT

9 EXPOSURE ASSESSMENT

See Risk Assessment Report - draft from 20th of August 2008.

10 RISK CHARACTERISATION

See Risk Assessment Report - draft from 20th of August 2008.

INFORMATION ON ALTERNATIVES

11 INFORMATION ON THE RISKS TO HUMAN HEALTH AND THE ENVIRONMENT RELATED TO THE MANUFACTURE OF USE OF THE ALTERNATIVES

12 AVAILABILITY OF ALTERNATIVE, INCLUDING THE TIME SCALE

13 TECHNICAL AND ECONOMICAL FEASIBILITY

JUSTIFICATION FOR RESTRICTION AT COMMUNITY LEVEL

14 JUSTIFICATION THAT ACTION IS REQUIRED ON THE COMMUNITY-WIDE BASIS

None

Other measures see Risk Reduction Strategy from 16th of September 2008.

15 JUSTIFICATION FOR THE PROPOSES RESTRICTION

15.1 Effectiveness

15.2 Practicality

15.3 Monitorability

SOCIO ECONOMIC ASSESSMENT

OTHER INFORMATION

It is suggested to include here information on any consultation which took place during the development of the dossier. This could indicate who was consulted and by what means, what comments (if any) were received and how these were dealt with. The data sources (e.g registration dossiers, other published sources) used for the dossier could also be indicated here.

REFERENCES

See Risk Assessment Report - draft from 20th of August 2008.

ANNEX

See Risk Assessment Report - draft from 20th of August 2008.

Risk Reduction Strategy from 16th of September 2008.