Wood E&IS GmbH
Meander 251
6825 MC Arnhem
The Netherlands
+31 (0)88 2174100
www.woodplc.com

Sitech IAZI bv

January 2021
Project No.: 57966013NL

Derivation of the Drinking Water Target Value for Polymaleic acid

TECHNICAL REPORT

Report for

Sitech IAZI bv
t.a.v. dhr. J. Vanholzaets
Koestraat 1
6167 RA Geleen

Issued by

G.J. Stam

Approved by

G.J. Stam

Wood

Copyright and non-disclosure notice

Third-party disclaimer

Management systems

This document has been produced by Wood E&IS GmbH in full compliance with the management systems, which have been certified to ISO 9001:2015 and ISO 14001:2015 (Milan office) by LRQA.

Document revisions

No.	Details	Date
R01-1	Internal draft	2021-01-07
R01-2	First draft report	2021-01-27

Executive Summary

Wood was retained by Sitech IAZI bv to derive substance specific drinking water target value for Polymaleic acid (PMA, CAS# 26099-09-2) using the formal guidance documents. Before mentioned polymer is an important ingredient in conditioning agents used to protect the proper functioning of industrial cooling systems.

Sitech IAZI bv requests the Wetenschappelijke Klankbordgroep normstelling water en lucht to evaluate and approve the proposed value for the drinking water target values for PMA as summarized in below table.

Proposed drinking water target values

Substance	Proposed DTV in mg/L
Polymaleic acid (PMA, CAS# 26099-09-2)	4,4
Copolymer of Maleic acid and Acrylic acid and their Sodium salts (PMAAA)	22

Please note that in this report a comma is used as decimal separator as defined in the methodology to derive (indicative) environmental quality standards [RIVM, 2015]. A point is used as a thousand separator as appropriate.

Contents

1. Introduction

Sitech IAZI bv, hereafter Sitech, operates a wastewater treatment plant at the Industrial Park Chemelot, hereafter referred to as IAZI. The IAZI receives and treats most of the wastewater generated at the site, including the purges from cooling water systems. Before mentioned purges contain cooling water conditioning chemicals, like biocides, dispersants and anti-fouling agents.

Present wastewater discharge permit holds an obligation to minimize the use of the dispersant ATMP (CAS# 6419-19-8) in order to prevent the generation of AMPA (CAS# 74341-63-2) in the IAZI due to biodegradation of ATMP. As AMPA is a persistent chemical, one of the adverse effects of the discharge with the effluent is potential exceedance of the limit value for the intake of surface water for the preparation of drinking water.

Over the past years, Sitech has investigated potential alternatives to replace ATMP as a cooling water dispersant. Products comprising polymers such as polymaleic acid (PMA, CAS# 26099-09-2) are listed as potential alternatives for ATMP.

The potential impact of the discharge of PMA with the effluent of the IAZI on the functions of the receiving water body, like any other discharge of chemical contaminants, needs to be assessed according to the so-called immissietoets (discharge test). In the underlying situation the potential adverse effects of the discharge in regard to aquatic ecology and the drinking water preparation functions are relevant.

The Dutch National Institute for Public health and the Environment compiled a formal guidance on the derivation of substance specific drinking water parameters [RIVM, 2017] which aligns with the procedures of the European Commission. The European Commission published an update of the Guidance Document in 2018 [EC, 2018].

Wood was asked by Sitech to derive substance specific water quality standards for PMA using the formal guidance documents. This report describes results of literature research and proposes values for water quality standards for this substance.

Please note that in this report a comma is used as decimal separator as defined in the methodology to derive (indicative) environmental quality standards [RIVM, 2015]. A point is used as a thousand separator as appropriate.

2. Generic approach to derive water quality standards

2.1 Drinkwater target value

The procedure to calculate a substance specific drinking water target is described in RIVM report 2017-0091 [RIVM, 2017] in concordance with Guidance Document No. 27 [EC, 2018]. The drinking water target value is calculated from the Derived No Effect Level, DNEL, or the Tolerable Daily Intake (TDI) using below formula:

$$DTV = \frac{BW * DNEL * \max\_fraction}{DI}$$

with

DTV =	drinking water target value (mg/L)
BW =	average body weight (= 70 kg)
DNEL =	Derived No Effect Level, like the Tolerable Daily Intake in mg per kg body weight per day or the Acceptable Daily Intake in mg per kg body weight per day
max_fraction =	Maximum uptake as a percentage of the DNEL (20%)
DI =	Average daily water consumption (= 2 L / day)

Resulting in

$$DTV = \frac{70 * DNEL * 20\%}{2} = 7 * DNEL$$

Appendix D presents flow diagrams to derive drinking water target values as set by RIVM guidance [RIVM, 2017].

3. Stepped derivation of the drinking water target value for PMA

Carboxylated polymers are, amongst others, used as a water treatment agent to control the fouling of industrial cooling systems. Products comprising polymaleic acid can be suitable to replace agents based on organic phosphates which are traditionally used for this purpose.

To derive a drinking water target value, a literature search was executed regarding polymaleic acid using CAS# 26099-09-2. This substance is an active component of cooling water conditioning products which are anticipated to be used at the Industrial Site Chemelot at Geleen, the Netherlands.

As the literature search did not result in any relevant toxicological information, the drinking water target value is to be derived using an alternative methodology. The generic fallback scenario is to use the so-called Cramer classification as starting point for the drinking water target value. The scenario is not appropriate in the case of polymers. Consequently, the drinking water target value for PMA is to be derived based on a read-across of comparable polymers. As PMA basically is a carboxylic acid polymer, toxicological information regarding the copolymer of maleic acid and acrylic acid (PMAAA) and polyacrylic acid (PAA) is used for this purpose.

Appendix A presents available base information for PMA. Appendix B and Appendix C present the results of a literature search for PMAAA and PAA respectively. Based on these data, a specific drinking water target value is derived. A summary of the relevant properties of both substances is presented in table 3.1.

Table 3.1 Summary of relevant toxicological data for PMAAA and PAA-Na

Parameter	PMAAA	PAA-Na
LD50 oral Rat	12.000 mg/kg-bw	>5.000 mg/kg-bw
Skin irritation	Not irritant under test conditions	Not irritant under test conditions
Eye irritation	No references found	No references found
Skin sensitization	Not irritant under test conditions	No references found
Repeated dose toxicity oral (NOAEL)	1.871 mg/kg-bw/day	1.136 mg/kg-bw/day
Genetic toxicity (in vitro)	No mutagenic activity observed	No mutagenic activity observed
Genetic toxicity (in vivo)	No increase in micronucleus induction observed	No increase in micronucleus induction observed
Reproductive toxicity (NOEL)	6.670 mg/kg-bw/day	375 mg/kg-bw/day

Based on the data in table 3.1 the DNEL for PMAAA and PAA-Na are derived from the NOAEL for repeated dose toxicity oral and reproductive toxicity respectively. The results are presented in table 3.2.

Table 3.2 Derivation of the DNEL for PMAAA and PAA-Na

Parameter	PMAAA	PAA-Na
NOAEL	1.871 mg/kg-bw/day	375 mg/kg-bw/day
Assessment factors		
Subacute to chronic duration	6	6
Rat to human	10	10
Intraspecies variability	10	10
DNEL	3,12 mg/kg-bw/day	0,625 mg/kg-bw/day

The drinking water target value is derived from the calculated DNEL using below formula. The derived values are presented in table 3.3.

$$DTV = \frac{BW * DNEL * \max\_fraction}{DI} = 7 * DNEL$$

Table 3.3 Derivation of the drinking water target value for PMAAA and PAA-Na

Parameter	PMAAA	PAA-Na
DNEL	3,12 mg/kg-bw/day	0,625 mg/kg-bw/day
DTV	21,8 mg/L	4,38 mg/L

Using the results presented in table 3.3 as a read-across assessment of the adverse effects of PMA, the value for the drinking water target value is conservatively based on PAA-Na. Hence the value for the drinking water target value for PMA is set at 4,4 mg/L (rounded to two digits).

4. Discussion

The objective of this report is to derive a drinking water target value for Polymaleic acid (PMA, CAS# 26099-09-2). The value for this parameter is set at 4,4 mg/L based on the toxicity of the comparable polymer PAA. As the derived drinking water target value for PMAAA, basically PAA diluted with Maleic acid monomers, is significant higher in comparison with the value for PAA, setting the drinking water target value for PMA at 4,4 mg/L can be considered as a very conservative approach.

In order to monitor the ultimate discharge of the PMA to surface water, Sitech IAZI BV, the operator of the IAZI, together with the suppliers of the corresponding products, will start the development of a protocol for the analysis of the polymer in the effluent of the wastewater treatment plant from scratch once it is decided that PMA comprising products will be used onsite.

The main functionality of the evaluated polymer is to bind and disperse bivalent cations, like Calcium and Magnesium, in order to prevent scaling in industrial cooling water systems. These properties result in a high removal in a wastewater treatment plant, predominantly because of adsorption to sludge.

Discharged amounts of the polymer will behave in a similar manner in surface water and the water treatment facilities drinking water companies apply in the production of drinking water. Treatment systems used for the production of drinking water from surface water typically comprise sand filtration and activated carbon adsorption. This implies that PMA present in surface water used for the preparation of drinking water will be removed with a high efficiency as well, thus further reducing potential risk for public health.

5. Proposed substance specific drinking water target value

Below table presents an overview of the proposed drinking water target values.

Table 5.1 Proposed drinking water target values

Substance	DTV in mg/L
Copolymer of Maleic acid and Acrylic acid and their Sodium salts (PMAAA)	22
PMA (CAS# 26099-09-2)	4,4

6. References

EC, 2018. "Technical Guidance for Deriving Environmental Quality Standards"; Guidance Document No. 27, updated version 2018.

Min IenW, 2019. "Handboek immissietoets, versie 2019"; Ministerie van Infrastructuur en Milieu, Rijkswaterstaat; concept document versie oktober 2019.

RIVM, 2015. "Handleiding voor de afleiding van indicatieve milieurisicogrenzen"; RIVM Rapport 2015-0057, L.R.M. de Poorter et al, RIVM Centrum voor Veiligheid van Stoffen en Producten.

RIVM, 2017. "Evaluatie signaleringsparameter nieuwe stoffen drinkwaterbeleid"; RIVM Rapport 2017-0091, N.G.F.M. van der Aa et al, RIVM Centrum voor Veiligheid van Stoffen en Producten.

Appendix A
Base information PMA (CAS# 26099-09-2)

PMA (CAS# 26099-09-2)

Identification and classification

Name	Polymaleic acid
IUPAC-name	
Synonyms	PMA z-(2)butenedioic acid homopolymer (2R, 3R)-2,3-dimethylbutanedioic acid
CAS-number	26099-09-2 30915-61-8 (Sodium salt of PMA)
Chemical group according to EPIwin	Polymers
Cramer class	Not applicable
Know uses	Dispersant to control fouling in industrial cooling water systems
Toxicity mechanism	-
Harmonized classification	TBD
Molecule formula	$[C_4H_4O_4]_n$
Smiles	$[C(C(O)O)\ C(C(O)O)]_n$
Molecule structure ¤	-

Fysico-chemical properties and dispersion

Property	Value	Additional information	Reference
Molecular weight (g/mol)	No data		
Melting point (°C)	No data		
Boiling point (°C)	No data		
Vapour pressure (Pa)	No data		
Solubility in water (mg/L)	Complete		
Log K_{ow}	<0		Expert judgement
Henry-coëfficiënt (Pa m^3/mol)	No data		
pKa	4,7		ECHA

Appendix B
Derivation of the drinking water target value for copolymers of Maleic Acid and Acrylic Acid (PMAAA)

Summary

As there is no specific toxicological profile for available for PMA, the toxicological profile of polycarboxylates acid drafted by HERA [2014] has been used as the basic document for toxicity information. The HERA report describes the toxicology of copolymers of maleic acid and acrylic acid, hereafter PMAAA.
The lowest NOAEL was selected from a range of toxicological endpoints in studies with rodents. The lowest NOAEL was found to be 1.871 mg/kg-bw/day related to the oral feed study for a period of 90 days in rats. This NOAEL was taken as starting point for deriving a maximum concentration in drinking water.
For deriving a DNEL (Derived No Effect Level) of copolymers of maleic acid and acrylic acid for the general population, the following assessment factors were considered:

- subacute to chronic duration (6)
- interspecies variability (10)
- intraspecies variability (10)

Applying above assessment factors to the lowest NOAEL results into a DNEL for the general population of (1.871/(6*10*10) =) 3,12 mg/kg-bw/day. In addition, the daily dose via drinking water uptake (2 litres at 70 kg bodyweight per day) may not exceed 20% of the DNEL of the general population.
This results in a drinking water limit of (20%*70*3,12/2 =) 21,8 mg PMAAA per litre.

1. Introduction

Polymaleic acid (PMA) belongs to the category of polymers. PMA is a water-soluble polycarboxylate produced from maleic acid monomer. As the polymer is not readily biodegradable and is not affected by chlorine or other biocides, PMA is widely used as a corrosion inhibitor in industrial water systems as well as in household detergents, like laundry products and dishwashing detergents.

The backbone of PMA is shown in figure 1.

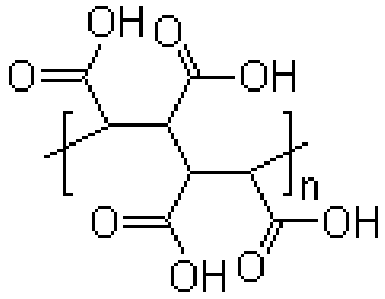

Fig. 1 Backbone of PMA

PMA is a weak acid (pK_a=4,7), comparable with Acetic acid. If the carboxylic groups are occupied by an H^+-ion, the aqueous solution has a low pH and is irritant to the eyes and the skin. If all carboxylic groups contain a Na^+-ion, the pH is about neutral. This is shown in figure 2.

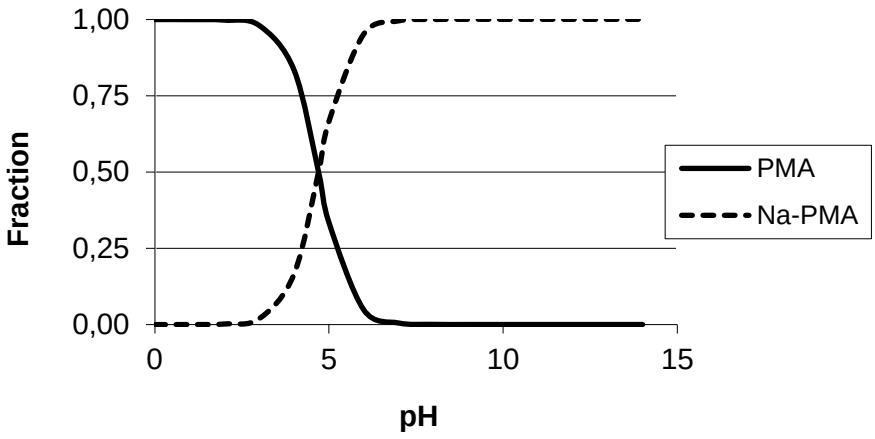

Fig. 2 Distribution of PMA / PMA-Na in relation to the pH

As result of using PMA containing products in industrial processes, discharges of wastewater into surface water may contain the substance. Surface water can be the raw material for drinking water. The technical processes for the preparation of drinking water are not always able to remove PMA completely from the drinking water.

This note reviews the existing toxicological information of PMAAA with the aim to derive a limit for this component in drinking water.

2. Toxicological information regarding copolymers of maleic acid and acrylic acid

The objective of this report is to derive a drinking water target value for PMA. As no reliable PMA specific information is available the derivation of before mentioned will be executed based on a read across of similar substances.
The toxicology of polycarboxylates has been studied and reported by the HERA (Human and Environmental Risk Assessment) project participants, a European voluntary initiative launched in 1999 by the following organisations:

- A.I.S.E. representing the formulators and manufacturers of household and maintenance cleaning products.
- CEFIC representing the suppliers and manufacturers of the raw materials.

HERA has issued the 3rd version of the report on the Human and Environmental Risk Assessment in 2014 [HERA, 2014]. The report shows that PMAAA, copolymers of PMA with polyacrylic acid, has such a low toxicity, that there is no obligation to classify this substance as a hazardous substance according to the REACH-CLP requirements (CLP= Classification, Labelling and Packaging).

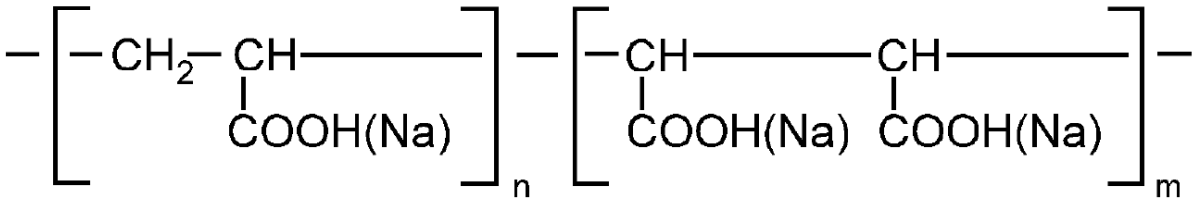

Fig. 3 Backbone of PMAAA copolymers

The HERA report refers to below PMAAA copolymers

CAS#	Name
29132-58-9	2-butenediocic acid (Z), polymer with 2-propenoate
51025-75-3	2-butenediocic acid (Z), monosodium salt, polymer with sodium-2-propenoate
51344-35-5	2-butenediocic acid (Z), sodium salt, polymer with sodium-2-propenoate
60449-78-7	2-butenediocic acid (Z), disodium salt, polymer with sodium-2-propenoate
60472-42-6	2-butenediocic acid (Z), polymer with sodium-2-propenoate, sodium salt
61842-61-3	2-butenediocic acid (Z), disodium salt, polymer with sodium-2-propenoic acid
61842-65-7	2-butenediocic acid (Z), monosodium salt, polymer with 2-propenoic acid
63519-67-5	2-butenediocic acid (Z), sodium salt, polymer with 2-propenoic acid
112909-09-8	2-butenediocic acid (Z), disodium salt, polymer with sodium-2-propenoate
52255-49-9	2-butenediocic acid (Z), polymer with sodium-2-propenoate
51025-75-3	2-propenoic acid, polymer with 2,5-furandione, sodium salt

The toxicological findings form the HERA report have been summarized in the following paragraphs:

2.1 Acute oral toxicity (rat)

The acute oral toxicity was studied in rats for PMAAA with different average molecular weight (50.000 through 70.000). The LD50 appeared to be larger than 5 g/kg-bw.
In several MSDS for PMA present an LD50 of 12 g/kg-bw.

2.2 Acute dermal toxicity(rabbit)

No references found to this type of study.

2.3 Acute inhalation toxicity (LC50 4 hours)

No references found to this type of study.

2.4 Skin Irritation

Two studies with PMAAA (molecular weights of 50.000 and 70.000), both performed according to OECD Guideline 404, showed no skin irritation. The test substances have been applied to the skin as a 45% aqueous solution. No erythema or oedema have been reported.
None of the copolymers tested at very high concentrations has been reported to be irritating to the skin.

2.5 Skin sensitisation

PMA-PAA (molecular weight 70.000) was tested in the Magnusson and Kligman Guinea pig maximization assay. The test concentrations in contact with the skin were between 20 and 80%. PMAAA showed no sensitising potential in the GMPT as a low or high molecular weight polymer

2.6 Repeated dose toxicity (oral)

PMA-PAA (average molecular weight 70.000) has been tested according to OECD Guideline 408 under GLP conditions. The test substance was administered to 10 male and 10 female Wistar rats for 90 d in drinking water at dose levels of 1.000, 4.000 and 16.000 ppm, the top dose being equivalent to 1.871 mg/kg-bw/day for male rats and 2.216 mg/kg-bw/day for female rats.
At the beginning of the study the low-dose males consumed about 119 mg/kg-bw/day and the mid-dose males about 445 mg/kg-bw/day. The females with the low dose showed a substance intake of about 126 mg/kg-bw/day and those with the mid dose about 499 mg/kg-bw/day. Ophthalmoscopic investigations were performed on control and high-dose animals prior to and at the end of test substance administration. Clinical chemistry and urinalysis were performed in week 6 of the study and at the end. Furthermore, macroscopic and histopathological examinations were conducted. With the exception of increased water consumption in both sexes (more pronounced in the females) of the high-dose group, no other test substance related findings were reported. Especially, no adverse effects to the gonads were reported.
The NOAEL determined in this study was 16.000 ppm, which is equivalent to 1.871 mg/kg-bw/day for male rats and 2.216 mg/kg-bw/day for female rats.

2.7 Repeated dose toxicity by inhalation

PMAAA (molecular weight 70.000) has been tested in a 91-day inhalation study. The study was conducted in compliance with the guidelines for the EPA's Toxic Substances Control Act and in compliance with the EPA GLP

Regulations (40CR, Part 792). 25 male and 25 female rats were exposed to 0,2, 1,0 and 5,0 mg/m3 for 6h/day, 5 day/wk for 13 weeks.
The substance was administered as a dust aerosol. Ten animals/group were allowed to recover for a period of a further 91 days. Body and organ weights, food and water consumption, clinical observation and blood chemistry were all within the normal range. Histopathology of lung tissues from the animals necropsied after the last exposure revealed signs of mild pulmonary irritation based on at least one of the following local lung effects: increase in polymorphonuclear granulocytes or alveolar macrophages, pneumocyte hyperplasia, alveolar wall thickening and focal alveolitis in the animals exposed to 5 mg/m3 PMAAA. Histopathological examination of the animals in the recovery group showed no lasting or residual microscopic lesions, which could be considered treatment related.
From these studies it was concluded that the NOEC is 1 mg/m3 for respirable dust of PMAAA for local lung effects typical of insoluble respirable polymer dust whereas the NOEC for systemic effects was above 5 mg/m3.

2.8 Repeated dose toxicity by dermal exposure (bath water)

No references found to this type of study.

2.9 Genetic toxicity in vitro

PMAAA (molecular weight 12.000 and 65.000) were tested for mutagenic activity in vitro in the Ames test, HGPRT assay with Chinese hamster ovary, chromosome aberration assay, unscheduled DNA assay etc. These tests are able to detect point and frameshift mutations and chromosome breaks. No mutagenic activity was observed in these in vitro tests.
No references found to this type of study. Genetic toxicity is not indicated by Toxtree.

2.10 Genetic toxicity in vivo

PMAAA, molecular weight 70.000, has been tested for chromosome aberrations in the bone marrow of male and female Chinese hamsters following a single injection of 200; 600 and 1.780 mg/kg-bw. The doses were applied in a volume of 10 ml/kg-bw.
For control purposes, a solvent control group and a positive control group (cyclophosphamide) were used. 20 animals (10 animals of each sex) were used for the solvent control, 10 animals (5 of each sex) for the positive control and the low- and mid-dose groups, respectively, and 30 animals (15 of each sex) for the high dose group. High-dose animals were killed, and bone marrow was examined at 6, 24 and 48 h after dosing (10 animals at each time point). The animals (10 per group, 5 of each sex) from the other two dose groups and the solvent and positive control groups were killed 24 h after dosing.
No increase in aberrant metaphases and no significant differences in the types and frequency of aberrations between the dose groups and the solvent control group were observed. No chromosome-damaging effects were seen under the present study conditions.
The negative test results obtained in-vitro for induction of DNA damage and chromosomal aberrations were corroborated with a test for chromosomal aberrations in-vivo. As no positive

2.11 Carcinogenicity

No studies on carcinogenicity are available for PMAAA. PMAAA is, however, devoid of any genotoxic potential in-vitro and in-vivo. Apart from some indication of cellular pneumocyte hyperplasia in a 90 d inhalation study, these polymers did not show other cellular hyperplasias upon other routes of exposure. As acrylic copolymers for detergent applications are manufactured to rigorous specification of particle size and exclusion of inhalable particles and as no long high dose inhalative exposure is anticipated from handling and use patterns in

detergent application, especially in the absence of spray applications, a carcinogenic risk appears to be negligible.
Furthermore, the monomers are devoid of alerting groups for a genotoxic or carcinogenic potential.

2.12 Reproductive and developmental toxicity

PMAAA (molecular weight 12.000) was administered to four groups of 25 female rats each by gavage at dose levels of 67, 667 and 6.670 mg/kg-bw/day during days 6-15 of gestation.
On day 20 of gestation the dams were killed. One half of each litter was examined for visceral findings by the Wilson (1965) method and the other half by the Dawson (1926) method for skeletal findings. Conception was considered day 0. There were no deaths in the high-dose group but in the low-dose group there were 8 malformed foetuses all from 1 litter and all with short-thickened bodies with numerous malformations. Animals from the other 23 litters in this test group showed no developmental toxic effects (no foetotoxicity and no teratogenicity). This singular finding was therefore considered to be incidental and not to be treatment related. All other findings with respect to malformations or variations were scattered randomly throughout the groups with no pattern or increased incidence. Therefore, the NOEL for maternal toxicity and developmental toxicity was determined to be 6.670 mg/kg-bw/day).
From these observations a reprotoxic potential appears negligible.

3. Derivation of a drinking water limit for PMAAA

In the 28-day repeated dose study in rats the highest dose without any effect appeared to be 1.871 mg PMAAA/kg-bw/day, based on the repeated dose oral toxicity.

In the ECHA Guidance on information requirements and chemical safety assessment Chapter R.8: Characterisation of dose [concentration]-response for human health (Version: 2.1 November 2012) has been stated how such an acute NOAEL should be translated to a Derived No Effective Level for consumers via extrapolation assessment factors:

rat to human	10
general population	10
28 days to 2 year rat	6

This results into a DNEL of 1.871 / (10*10*6) = 3,12 mg PMAAA/kg-bw/day for humans.

There is an additional limitation in the Netherlands for drinking water. Drinking water may not contribute more than 20% of the total DNEL to the daily body burden in a daily drinking water volume of 2 litres at a body weight of 70 kg.
This means that the total concentration of PMAAA in drinking water may not exceed 20%*70*3,12/2 = 21,8 mg/litre.

4. References

HERA, 2014. Polyacrylic acid homopolymers and their sodium salts (CAS 9003-04-7) https://www.heraproject.com/files/HERA_P-AA_final_v3_23012014.pdf
Toxtree. "Estimation of Toxic Hazard – A Decision Tree Approach"; version 3.1.0.1851, www.ideaconsult.net.

Appendix C
Derivation of the drinking water target value for Polyacrylic acid (pAA)

Summary

The HERA report on polyacrylic acid (PAA) has been used as the basic document for toxicity information. The lowest NOAEL was selected from a range of toxicological endpoints in studies with rodents. The lowest NOAEL was found to be 375 mg/kg-bw/day related to the reproductive and developmental toxicity in rats. This NOAEL was taken as starting point for deriving a maximum concentration in drinking water. For deriving a DNEL (Derived No Effect Level) of PAA for the general population, the following assessment factors were considered:

- subacute to chronic duration (6)
- interspecies variability (10)
- intraspecies variability (10)

Applying above assessment factors to the lowest NOAEL results into a DNEL for the general population of (375/(6*10*10) =) 0,625 mg/kg-bw/day. In addition, the daily dose via drinking water uptake (2 litres at 70 kg bodyweight per day) may not exceed 20% of the DNEL of the general population.
This results in a drinking water limit of (20%*70*0,625/2 =) 4,4 mg PAA per litre (rounded to two digits).

5. Introduction

Poly-acrylic acid belongs to the category of polycarboxylate polymers. Polycarboxylate polymers were developed to replace the functions of phosphates in cleaning products, which were phased out due to environmental concerns regarding eutrophication. They enhance the efficiency of surfactants by preventing precipitation of calcium salts due to interaction of Ca^{2+}-ions with the carboxylic acid groups. They are constituents of automatic dishwashing detergent and laundry detergent booster-machine cleaning agents. The typical molecular weight is about 4500 (about 62 times the backbone acrylic acid, figure 1).

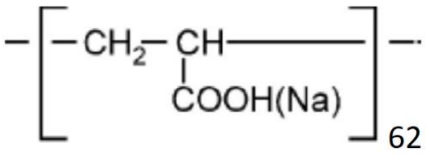

Fig 1: Back bone polyacrylic acid

If the carboxylic groups are occupied by an H^+-ion, the aqueous solution has a low pH and is irritant to the eyes and the skin. If all carboxylic groups contain a Na^+-ion, the pH is about neutral. This is shown in figure 2 for a polymer consisting of 14 acrylic acid backbones.

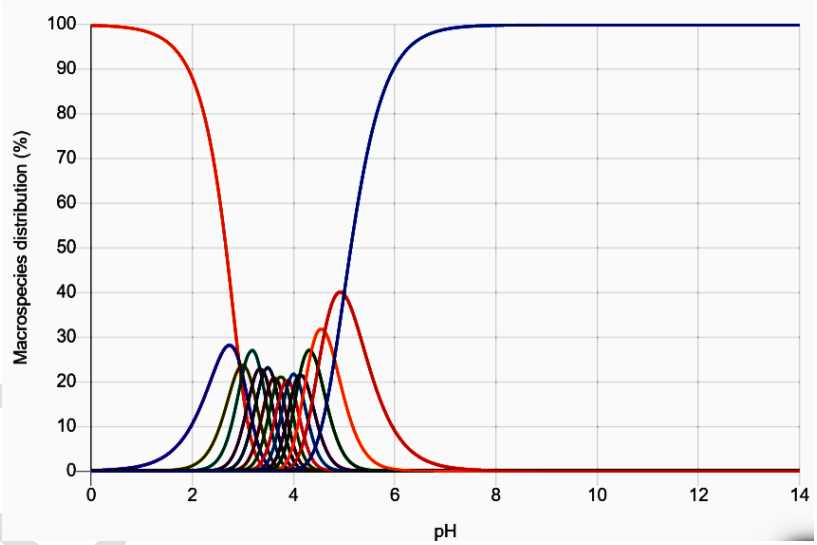

Fig. 2 (ChemAxon estimation model)

In this note the focus is on the sodium salt of polyacrylic acid. The solubility of this salt in water is very high, but in a wastewater treatment plant a lot is adsorbed to the activated sludge. The typical partition ratio (Kd) between activated sludge and water is about 1.825 litres/kg and is dependent on the calcium content of the sludge. If the sludge contains a lot of calcium salts the Kd may be up to one order of magnitude higher.

Nevertheless, the sodium salt of polyacrylic acid is discharged via the effluent of the wastewater treatment plant to surface water. The toxicity for aquatic and benthic organisms is so limited, that it is far above the limit concentrations, which hazard labelling for the environment makes obligatory (DeLeo et al 2020).

River water is also the raw material for drinking water. The technical processes for the preparation of drinking water are not always able to remove completely the polyacrylic acid sodium salt from the drinking water. This note reviews the existing toxicological information of the sodium salt of polyacrylic acid with the aim to derive a limit for the sodium salt of polyacrylic acid in drinking water.

6. Toxicological information on the sodium salt of polyacrylic acid (PAA-Na, CAS 9003-04-7)

The toxicology of PAA-Na has been studied and reported by the HERA (Human and Environmental Risk Assessment) project participants, a European voluntary initiative launched in 1999 by the following organisations:

- A.I.S.E. representing the formulators and manufacturers of household and maintenance cleaning products.
- CEFIC representing the suppliers and manufacturers of the raw materials.

HERA has issued the 3rd version of the report on the Human and Environmental Risk Assessment in 2014. This report is to be downloaded from https://www.heraproject.com/files/HERA_P-AA_final_v3_23012014.pdf

The report shows that PAA-Na has such a low toxicity, that there is no obligation to classify this substance as a hazardous substance according to the REACH-CLP requirements (CLP= Classification, Labelling and Packaging).

The toxicological findings form the HERA report have been summarized in the following paragraphs:

2.1 Acute oral toxicity (rat)

The acute oral toxicity was studied in rats for PAA-Na with different average molecular weight (1.000 through 7.800). The LD50 appeared to be larger than 5 grams per kg bodyweight.

2.2 Acute dermal toxicity(rabbit)

The acute dermal toxicity was studied in rabbits for PAA-Na with different average molecular weights (1.000 – 4.500). The acute dermal LD50 was found to be larger than 5 grams per kg bodyweight.

2.3 Acute inhalation toxicity (LC50 4 hours)

No references found to this type of study.

2.4 Skin Irritation

Several skin irritation studies on rabbits were done with PAA-Na of different molecular weights (1.000-78.000), in concentrations between 15-45% or neat undiluted material. Exposure was for 4 h -24 h with occlusive or semi-occlusive dressing. All studies show no skin irritation potential.

2.5 Skin sensitisation

PAA-Na with an average molecular weight of 4.500 or 78.000 were tested for skin sensitisation in the guinea pig maximisation test (GMPT). The test concentrations in contact with the skin were between 5 and 20%. PAA-Na showed no sensitising potential in the GMPT as a low or high molecular weight polymer.

2.6 Repeated dose toxicity (oral)

Polyacrylic acid (average molecular weight 2.500, neutralized with sodium hydroxide) has been tested in a Non-Guideline study with substance application via oral feed for 28 days to examine the effect of the test substance on mineral homeostasis.
Six male rats were fed 2,5% of the test substance in the diet (about 1.136 mg/kg-bw/day). Growth, weight and appearance of the animals were normal throughout the study. In the last week, a small but significant decrease in the total weight of bone minerals was detected and confirmed by radiographic and histological examination. The concentration of magnesium in the bones and the plasma of the treated animals were significantly decreased. Calcium loss was slight and not statistically significant. Urinary excretion of sodium and phosphorus was markedly increased. Excretion of calcium was slightly increased. The result was interpreted by the authors to be due to a metabolic or nutritional imbalance rather than to a systemic toxicity. The excretion of sodium might have been increased by the high uptake of the sodium-neutralized test substance. The applied dose was therefore interpreted as a NOAEL (No Observed Adverse Effect Level).

2.7 Repeated dose toxicity by inhalation

The maximum dose level in rodent inhalation studies (maximum 5 mg/m3) for 6 hours per day (inhalation volume of 0,3 m3/kg-bw/day) result into a daily systemic exposure of 1,5 mg/kg-bw/day and is much lower than in the oral study. Inhalation studies on PAA-Na are irrelevant for deriving a DNEL via ingestion.

2.8 Repeated dose toxicity by dermal exposure (bath water)

The molecular weight of PAA-Na of from 1.000 through 70.000 is too high to permeate through the stratum corneum of the human skin. Repeated dose toxicity studies via dermal exposure are not available.

2.9 Genetic toxicity in vitro

PAA-Na (molecular weight 100-4.500) were tested for mutagenic activity in vitro in the Ames test, mouse lymphoma assay, chromosome aberration assay, unscheduled DNA assay etc. These tests are able to detect point and frameshift mutations and chromosome breaks. No mutagenic activity was observed in these in vitro tests.

2.10 Genetic toxicity in vivo

PAA-Na (molecular weight 2.000) has been tested in a mouse micronucleus assay using groups of 5 male and 5 female mice. The test substance or sterile distilled water (control vehicle) was administered by gavage at a volume of 20 ml/kg. Animals were dosed by gavage with the maximum tolerated dose (13.850 mg/kg bw) and observed over a 3-day period. Positive control animals were i.p. injected with mitomycin C that was prepared in sterile 0,9% saline at a concentration of 0,2 mg/ml. Animals were killed at 24, 48 and 72 h after dosing, bone marrow cells were harvested and 1.000 cells per animal were examined for micronuclei in polychromatic erythrocytes and also for the ratio for polychromatic to normochromatic erythrocytes.
During the experiment 3 female mice died, 1 at each of the harvest times. Clinical signs of piloerection, hunched posture and lethargy were observed following dosing. No increase in micronucleus induction was observed in the groups administered the test substance at any of the harvest times, when compared with the controls.

2.11 Carcinogenicity

Carcinogenicity studies have not been performed for PAA-Na. Carcinogenicity studies are not considered to be relevant considering the chemical structure and the absence of any mutagenic activity in experimental studies in vitro and in vivo.

2.12 Reproductive and developmental toxicity

Test results

Developmental toxicity (teratogenicity) of PAA-Na has been studied in rats for an average molecular weight of 4.500 and 90.000. The doses were applied by gavage during the period of organogenesis (8 – 10 days). PAA-Na (MW 4.500) was applied at dose levels of 0, 500, 1.000, and 3.000 mg/kg-bw/day and PAA-Na (MW 90.000) at dose levels of 0, 125, 375 and 1.125 mg/kg-bw/day.

Seven dams died during the last study (PAA-Na MW 90.000), of which 4 mortalities were caused by mal-intubation. However, the authors of the latter study attributed 3 mortalities at the highest dose group to treatment with PAA-Na (MW 90.000). This is probably not a correct interpretation of the test results as PAA-Na (MW 90.000) is at least 10 times less absorbed from the intestines due to the 20 times higher molecular weight (90.000 versus 4.500, see Loehry et al. 1970).

The highest dose level of PAA-Na (MW 4.500) was applied at 3.000 mg/kg-bw/day, while PAA-Na (MW 90.000) was given at a dose of 1.125 mg/kg-bw/day. Despite the fact that there was not any effect observed at the highest dose level of 1.125 mg/kg-bw/day on the body weight of the dams and pups and body weight gain of the dams compared to the control group, the NOAEL for PAA-Na 90.000 is set at 375 mg/kg-bw/day.

The NOAEL for PAA-Na (MW 4.500) appeared to be 3.000 mg/kg-bw/day related to maternal and to developmental toxicity.

7. Derivation of a drinking water limit for the sodium salt of polyacrylic acid

In the 28-day repeated dose study in rats the highest dose without any effect appeared to be 375 mg/kg-bw/day, based on the repeated dose oral toxicity.

In the ECHA Guidance on information requirements and chemical safety assessment Chapter R.8: Characterisation of dose [concentration]-response for human health (Version: 2.1 November 2012) has been stated how such an acute NOAEL should be translated to a Derived No Effective Level for consumers via extrapolation assessment factors:

rat to human	10
general population	10
28 days to 2 year rat	6

This results into a DNEL of 375 / (10*10*6) = 0,625 mg/kg-bw/day for humans.

There is an additional limitation in the Netherlands for drinking water. Drinking water may not contribute more than 20% of the total DNEL to the daily body burden in a daily drinking water volume of 2 litres at a body weight of 70 kg. This means that the total mass of PAA-Na in drinking water may not exceed 20%*70*0,625/2 = 4,38 mg/litre.

8. References

DeLeo PC, Summers H, Stanton K, Lam MW, 2020. Environmental risk assessment of polycarboxylate polymers used in cleaning products in the United States. Chemosphere. 258:127242.

HERA, 2014. Polyacrylic acid homopolymers and their sodium salts (CAS 9003-04-7) https://www.heraproject.com/files/HERA_P-AA_final_v3_23012014.pdf

Loehry CA, Axon AT, Hilton PJ, Hider RC, Creamer B, 1970. Permeability of the small intestine to substances of different molecular weight. Gut. 11(6):466-70.

Appendix D Flowcharts for the derivation of the TDI

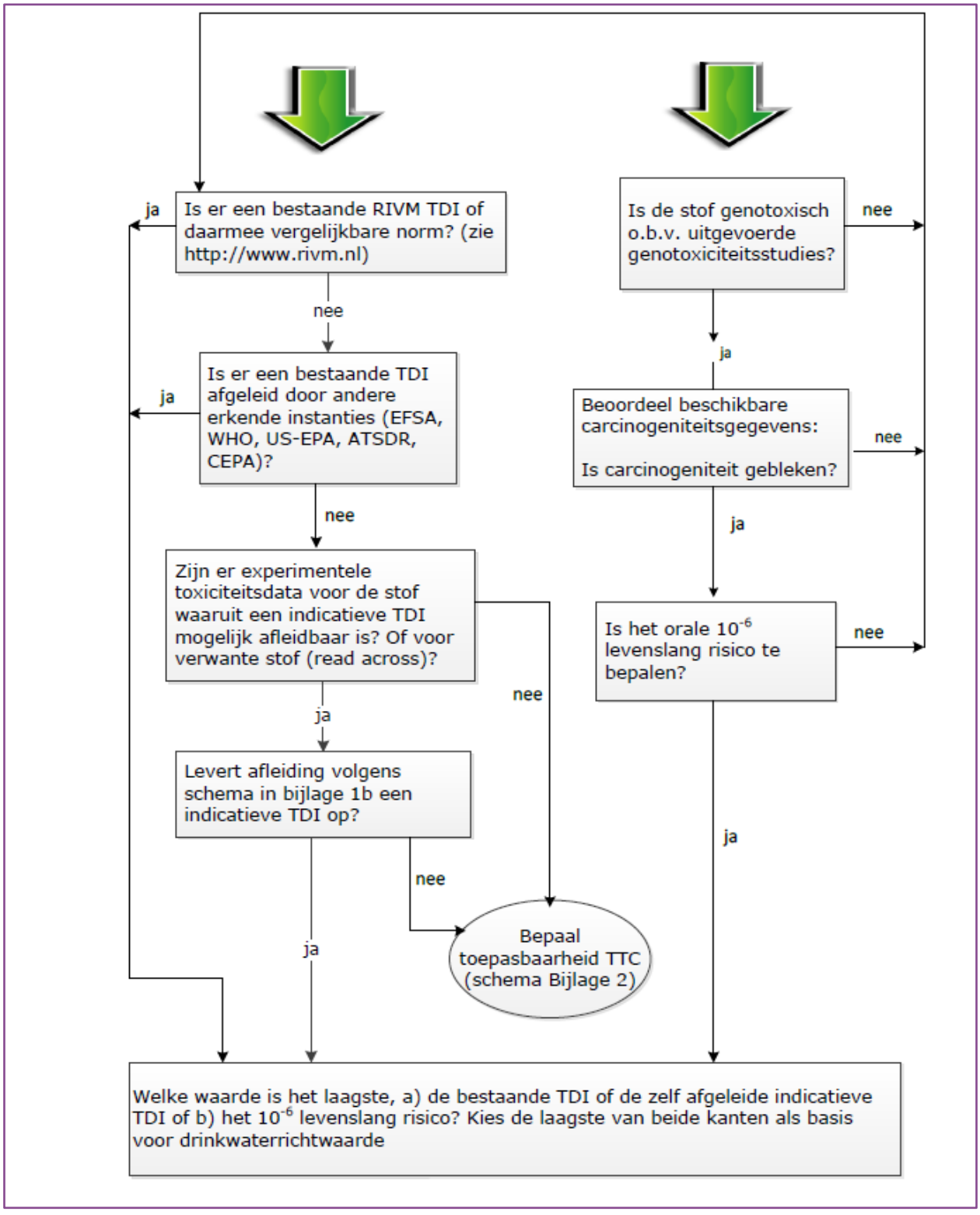

Figure D.1 Flow diagram to determine the necessity of derivation of the TDI

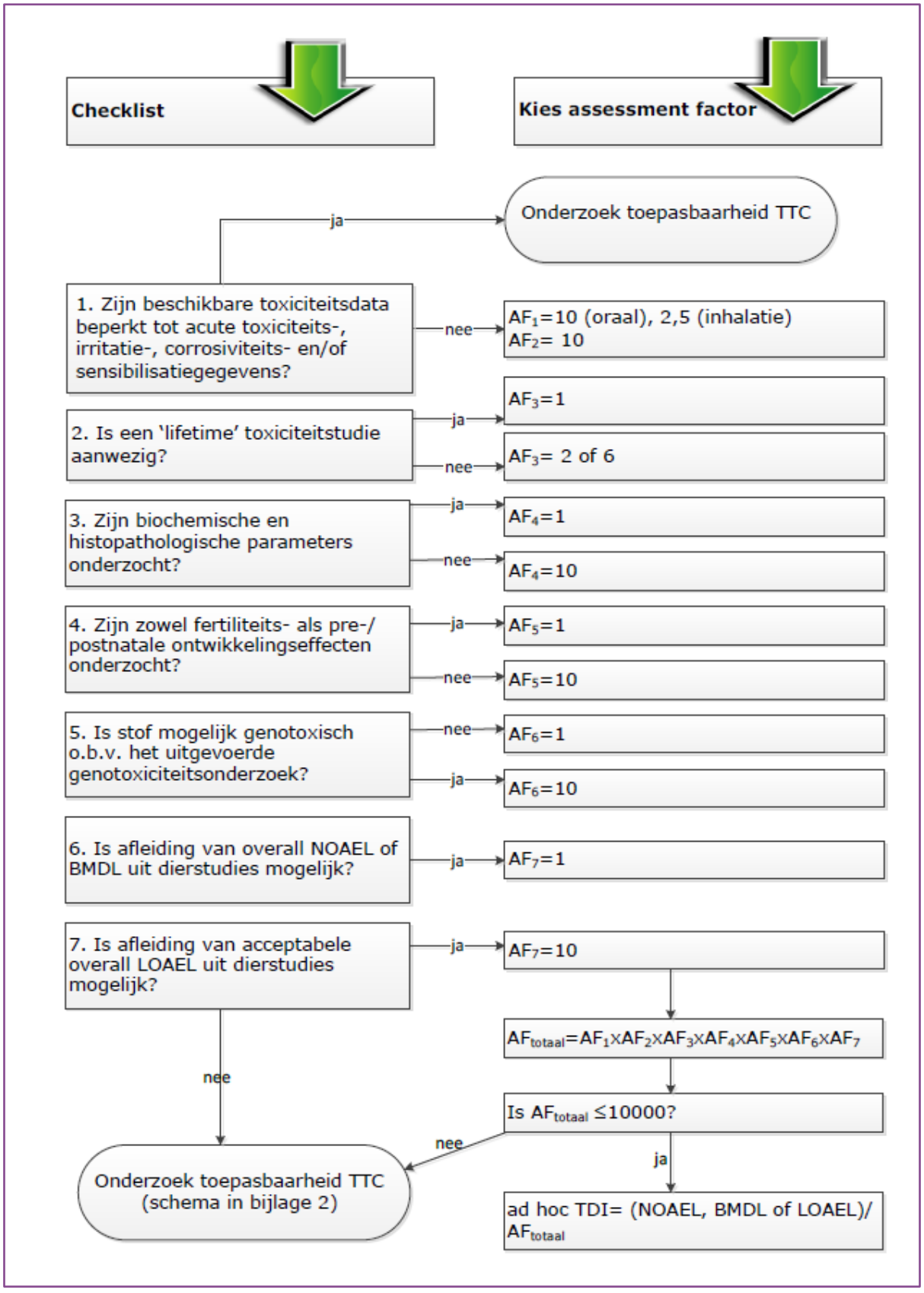

Figure D.2 Flow diagram to derive the TDI for a chemical using assessment factors

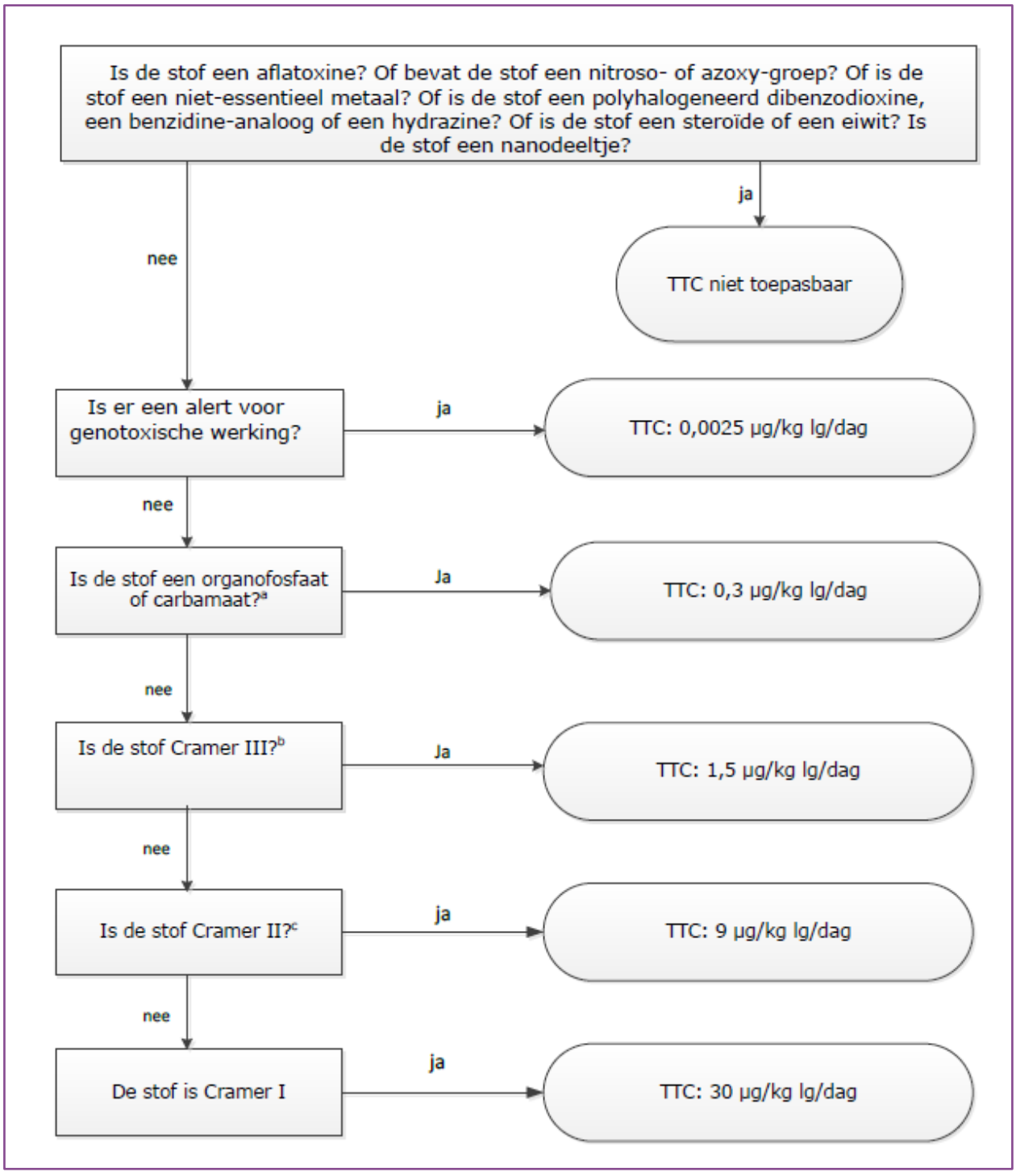

Figure D.3 Flow diagram to derive the TDI based on generic properties