Association Internationale de la Savonnerie, de la Détergence et des Produits d'Entretien
International Association for Soaps, Detergents and Maintenance Products

Industry comments on the potential reclassification of sodium hypochlorite

(harmonised classification proposal from Netherlands)

July 2015

Content:

EXECUTIVE SUMMARY

In light of the recommended reclassification of sodium hypochlorite and consequentially of sodium hypochlorite-containing bleach products by the CLP Rapporteur Member State, this document outlines the industry position on this, arguing that the recommended reclassification is not supported by recent scientific information. It does this by reviewing the limitations of the studies used to inform this recommendation as well as highlighting some important alternative studies and proposes some solutions. It is a compilation of several reports from a variety of academic, regulatory and industrial sources.

KEY POINTS

- The data used to formulate the proposed reclassification needs review as it presents an inaccurate opinion of sodium hypochlorite toxicity;
- Higher quality studies are available, they have been used for other regulatory purposes, and are reviewed here;
- Scientifically derived M factors are listed in the summary section.

When looking at all the data in a weight of evidence approach, we believe the classification proposal should be:

For acute aquatic toxicity: Category 1, H400, M=10

For chronic aquatic toxicity: Category 1, H410, M=1

It has to be noted that the environmental classification of sodium hypochlorite is of critical importance for formulators as well as retailers because of its implications due to downstream legislation, notably the Seveso III Directive.

BACKGROUND

The deletion in December 2008 of the Concentration Limit of 25% above which sodium hypochlorite was classifiable N, R50 in Annex I of the Dangerous Substances Directive (DPD) during 'transcription' to Annex VI of CLP Regulation led to sodium hypochlorite-containing mixtures becoming potentially classifiable N, R50 and labelled 'dangerous to the environment' at lower concentrations. There was no clear guidance on the level above which such classification should apply. Partly this arose because ecotoxicity data provided by suppliers on Safety Data Sheets varied widely (the REACH registration process has not started), and no 'M-factor' had then been agreed for sodium hypochlorite. Since then, A.I.S.E. and Euro Chlor have been working together to review all available data and derive classification guidelines for their members.

Various discussions with individual Member States, their ecotoxicological experts and the Commission took place in mid-2009 in relation to the guidance. At that time, the CLP Regulation was new and since it introduced significant changes compared to DPD, A.I.S.E. wanted to discuss the approach to using mixture testing data with EU GHS/CLP environmental experts. There was also no ECHA Guidance on CLP (in relation to the 2nd ATP to CLP which introduced significant changes to environmental classification rules) and it was important to clarify a number of points such as species on which to test mixtures, hierarchy of data under CLP (mixture test data prevail), etc. The discussions were also driven significantly by the need to establish a widely accepted approach to mixture classification in view of potential Seveso implications.

Recently, the CLP harmonised classification process was kicked off with the submission of an Annex XV dossier by the Netherlands. Environmental classification of sodium hypochlorite is part of this dossier.

DETAIL

3.1 PREVIOUS EVALUATIONS FOR REGULATORY PURPOSES

It appears that one potential reason for the proposed reclassification relates to several key studies which were previously analysed as part of the following reports. The following sections (3.1.1 to 3.1.4) focus on issues with invertebrate toxicity studies whilst later sections highlight other trophic levels.

3.1.1 EC RISK ASSESSMENT REPORT (RAR)

"Sodium hypochlorite Risk Assessment Report in the context of Regulation (EEC) 793/93 on the evaluation and control of the risks of existing substances"

In the Risk Assessment Report (2007) prepared by Italy in the frame of (EEC) 793/93 regulation of existing substances, the only acute invertebrate data evaluated as being valid enough for use in the risk assessment of sodium hypochlorite was the article published by P.A. Taylor in 1993. The assessors stated in the RAR (§3.2.1, page 81):

"*Taylor (1993) tested the acute toxicity of various forms of free and combined chlorine to Ceriodaphnia dubia in standard 24h toxicity tests, carried out under static and flow through conditions. Sodium hypochlorite was tested at pH 7 for HOCl (70% HOCl and 30% OCl-) and pH 8 for OCl- (80% OCl and 20% HOCl). In static tests the decay of free chlorine was very rapid (1 minute and 7 hours in tests with or without food, respectively) and the results were not considered valid. Flow-through tests (without food) were carried out to maintain a constant concentration over the exposure time. The toxicity of free chlorine in these tests was much higher:* ***EC50 -24h = 5 and 6 µg/L for HOCl and OCl -****, respectively. These data were judged valid with restriction (rated 2) by RAR Rapporteur Member State because the test concentrations were calculated from measured chlorine concentration of the stock solution and dilution ratios, the number of concentrations/replicates are not specified, the performance of the controls not mentioned, and the 24h LC50s determined by graphical interpolation.*"

This study was considered as the key one for freshwater invertebrates as all others were considered as "not reliable".

3.1.2 REGISTRATION OF SODIUM HYPOCHLORITE UNDER REACh REGULATION (EC) 1907/2006

When preparing the REACh registration dossier, Registrants re-examined the Taylor report.

It was apparent that the report lacked description of several important features of the experiment, which meant that this set of data cannot be used with confidence. For example:

- there was no information on the tested material: "*Stock solutions containing about 20 mg/L of NH_2Cl, $NHCl_2$, or sodium hypochlorite were prepared and then diluted with DMW to make the various test solutions*" (there are issues here as DMW is 20% v/v degassed Perrier© in deionized water and thus hardness or other characteristics are not provided);

- there was little information on the analytical measurements: "*Measurements of free chlorine, NH_2Cl, and $NHCl_2$ concentrations were made with a Wallace & Tiernan (Atlanta, GA) amperometric titrator, using the procedures recommended in the instruction manual*". It was stated that the detection limit of the titrator is 0,01 mg/L (though no indication of whether this referred to total available chlorine, free available chlorine or even test material was given). Given the characteristics of this method and its precision in the low level range targeted here, it would have been of prime importance to get information on limit of quantification and confidence intervals. Below 0,01 mg/L, concentrations were calculated from dilution factors of the stock solutions;

- there was no indication on sample treatment: i.e. number of analytical measurements between 0 and 24 hours, and, most importantly, time between sampling and titration. A significant decay can happen in this period and result in measured concentrations that are lower than those to which the animals are actually exposed;

- it was not indicated if the concentrations mentioned were initial measured, mean of initial and final, or nominal ones. Separate stability experiments described in the same article, performed without animals, show different rates of decay according to conditions, but no information was given on stability during the flow-through exposure of animals itself;

- there were no data on test design such as number of tested concentrations, range of concentrations, separation factors in the flow-through experiments, number of animals, number of replicates, lighting conditions (which plays an important role in stability);

- in contrast to the requirements of the standard OECD TG 202, exposure duration was only 24 hours instead of 48 hours.

Considering the numerous uncertainties about the validity of this study, it was therefore attributed the reliability rating of "4 (not assignable)" in the IUCLID, although the most appropriate should be "3 (not reliable)" according to the Klimisch scale (sub-category 3a "Documentation insufficient for assessment").

Due to the limitations of the only available invertebrate acute toxicity study, and its unreliability for classification purposes, the sodium hypochlorite REACh Registration Consortium decided a new experiment must be conducted according to current best practice to provide a sound basis for classification. This would conform to OECD TG 202, under GLP conditions, and take into account the specific characteristics of this difficult substance.

In this study, 48–hr acute toxicity of sodium hypochlorite to *Daphnia magna* was studied under flow through conditions in a state-of-the-art study (Gallagher *et al.*, 2009). Daphnids were exposed to the test chemical (a representative industrial batch, duly characterised), at nominal concentrations of 12,5, 25, 50, 100, 200 and 400 µg active chlorine/L for 48 hr. Mortality/immobilisation and sub-lethal effects were observed daily.

Measurements of concentrations were done at t = 0, 1 and 2 days. Quantification was done by derivatisation of active chlorine with o-tolidine followed by HPLC-UV (LOQ = 15 µg active Cl/L). Chromatography ensures separation of chlorinated derivatives from other compounds able to react with o-tolidine. Where measured concentrations were above LOQ (200 and 400 µg/L nominal), it was shown that the concentration remained constant between 0 and 48 h. Even with a ratio of 2 in concentration series, the concentration effect curve is very steep: from 10 to 90% effects observed between 2 consecutive concentrations. The analytical measurements show clearly that a significant amount of hypochlorite reacts with test system (every component which can be oxidized by the test material). The lower the added concentration is, the lower the remaining percent of active chlorine. Toxicity is only observed in the higher concentration range.

The results of this study are summarised in the table below:

Nominal Concentration (µg active Cl/L)	Percent Dead and Immobile *Daphnia magna* (48h)	Mean Measured Concentration (µg active Cl/L)	Mean Measured Percent of Nominal
Negative Control	0	< LOQ	-
12,5	0	< LOQ	-
25	0	< LOQ	-
50	0	< LOQ	-
100	10	< LOQ	-
200	90	48,5	24,3
400	100	232	57,9

The use of nominal concentrations for the calculation of EC50 was based on the recommendation given in the OECD guidance document on aquatic toxicity testing of difficult substances and mixtures (OECD series on testing and assessment, number 23, 2000). In detail, Chapter 5 (p. 43) states:

- *For static and semi-static and flow-through tests, where the concentrations remain within 80-120% of nominal, the effect concentrations can be expressed relative to nominal or measured concentrations;*
- *For static and semi-static tests, where the concentrations do not remain within 80-120% of nominal, the effect concentrations could be determined and expressed relative to the geometric mean of the measured concentrations. A formula for calculating the geometric mean is given in Annex 2;*
- *For flow-through tests, where the concentrations do not remain within 80-120% of nominal, the effects concentrations should be determined and expressed relative to the arithmetic mean concentration; and*
- *For tests with chemicals that cannot be quantified by analytical methods at the concentrations causing effects, the effect concentration can be expressed based on the nominal concentrations.*

The fourth option above applies here as most of the effects are located at exposure levels below limit of quantification. The **EC50-48h** thus was calculated as

being **= 141 µg active chlorine/L.** (A 48-hour NOEC based on mortality/immobilisation was calculated as 50 µg active chlorine /L).

If the third option is used instead (not recommended in this case), calculation based on the mean measured concentrations (for the exposure levels where they are available or set equal to the LOQ where below LOQ) would give an **EC50-48h = 30,5 µg/L** (based on ToxRat© software). In light of this, this study fulfils the criteria for a reliability rating of 1 "Reliable without restriction" (1a Klimisch sub-category). It should therefore be considered as the key study for addressing acute toxicity to freshwater invertebrates.

3.1.3 LITERATURE REVIEW ON THE SENSITIVITY OF AQUATIC SPECIES TO SODIUM HYPOCHLORITE

In the course of A.I.S.E.'s interactions with Member States experts on environmental classification, in 2009, the 'Taylor study' was discussed[1]. A participant expressed concern in relation to species sensitivity: the results of the Taylor study on Ceriodaphnia being much lower than the latest GLP study with *Daphnia magna* might indicate Ceriodaphnia are a more sensitive species than *Daphnia magna* and the tests on the former species should be used for classification. Industry pointed out the weaknesses (listed above) in the Taylor study which might account for the apparent difference and that *Daphnia magna* are clearly indicated as the preferred species for acute daphnia toxicity testing for C&L purposes in the EU guidance on Test Methods and in the OECD test methodology (OECD 202 part 1).

To address the concern, Industry conducted a literature review. Versteeg *et al.* (Chemosphere, 1997, 34, 869-892) published a comprehensive review of those data available for comparing sensitivity of these species to a wide variety of chemicals. They have shown that there is a slight excess of cases where *Ceriodaphnia magna* has a lower EC50-48h value than *Daphnia magna* but the sensitivity ratio is small. Regression analysis shows high correlation (r^2 = 0,96) and a slope of approximately 1,0 (0,97) indicating that *Ceriodaphnia* are similar in sensitivity to other Cladocerans. Furthermore, data suggest that interspecies variability is not greater than inter- and even intra-laboratory variability for these types of tests. The authors proposed "*that toxicity test data from these species be considered equivalent in environmental risk assessment and regulatory decision-making schemes*". This advice has been taken on board in the REACh IR/CSA Guidance Chapter R.7b which states: "*In addition to Daphnia magna, D. pulex, Ceriodaphnia affinis and C. dubia are commonly tested species. Overall, there is no significant*

[1] *Conference call held on 19th November 2009. The participants included Jonas Falck (SE), Els Boels (BE), Richard Luit (NL), Juan Jose Izquierdo and Manuel Carbo (ES), Evita Luschutzky (ECHA), Sylvain Bintein (DG ENV) as well as A.I.S.E. and Euro Chlor.*

difference in sensitivity of D. magna and D. pulex. Good correlation has been reported between acute toxicities of all three species (ECETOC 2003c). All these can be considered as equally accepted preferred species."

An examination of publications beyond 1997 on the topic tends to confirm the conclusion of Versteeg *et al.* (1997). Most acute toxicity data are in the same order of magnitude for the two species. It seems clear that other considerations than species have to be taken into account to explain variability, such as: clone history and origin, test medium composition (hardness), type of toxicant, etc. Therefore, as stated in the REACh guidance, results on any of these species can be used for classification purposes. Besides, *D. magna* has been used for more than 40 years as a standard species in Europe for this purpose, and is more widespread in testing labs than *Ceriodaphnia*. For testing on any hypochlorite containing mixture, results obtained with *D. magna* are therefore more likely to be made available for classification purposes according to provisions of Regulations EC 1272/2008 and EC 286/2011.

Informal discussions in various fora continued and by April 2010 Member State expert opinion was that a repeat of the *D. magna* study on sodium hypochlorite (Gallagher *et al.* 2009) using *Ceriodaphnia* in the same laboratory and conditions would be the most effective way of clarifying whether there was a significant difference in sensitivity of the two species to hypochlorite or whether the Taylor results should be considered as an outlier. Despite the view that the Gallagher (2009) study was already the most appropriate, valid and reliable base for classification, Industry agreed to repeat that study as closely as possible using Ceriodaphnia as the test species to resolve the issue.

3.1.4 CERIODAPHNIA STUDY

In spite of this literature analysis of species sensitivity, the consortium of registrants decided to commission a new study on *Ceriodaphnia dubia*, in conditions strictly similar (OECD 202, flow-through conditions, GLP) to those applied in the Gallagher (2009) study on *D. magna*. Exposure duration was set to 48 hours, which is challenging without feeding animals, particularly knowing that *C. dubia* succumb to starvation stress more quickly than larger species like *D. magna*. Nevertheless the study successfully met the validity criteria of OECD TG 202.

The results of this study are summarised in the table below:

Nominal Concentration (µg active Cl/L)	Percent Dead and Immobile *Ceriodaphnia dubia* (48h)	Mean Measured Concentration (µg active Cl/L)	Mean Measured Percent of Nominal
Negative Control	5	< LOQ	-
25	0	< LOQ	-
50	100	25,8	52
100	100	55,7	56
200	100	106	53
400	100	181	45

(LOQ = 15 µg active Cl/L)

The results (Gallagher, 2011) show an **EC50-48h = 35 µg/L** and NOEC = 25 µg/L, based on nominal concentrations, or, when based on mean measured concentration (with 25 µg/L nominal set at LOQ = 10µg/L) an **EC50-48h = 16 µg/L** and NOEC = 10 µg/L.

Again, this study is to be rated as fully reliable (rated Klimisch 1; reliable without restrictions) and considered as a key study for classification and risk assessment.

The results (Gallagher, 2011) confirmed an M-Factor of 10 for acute aquatic toxicity to be appropriate and the study results were incorporated in the joint REACh Registration Dossier.

With regards to other trophic levels used for classification according to CLP criteria:

Fish:

In the searched literature, adequate standard acute tests with fish are lacking, as many reliable studies have been performed under intermittent exposure. From these latter studies, the trout was shown to be the most sensitive species; three 40 minute pulses per day produced an **LC50 = 60 µg TRC/L after 96h** and an LC50 = 33 µg TRC/L after 168h.

Algae:

As part of the requirements under the biocidal product registration, a recent study on the freshwater algae *Pseudokirchneriella subcapitata* (Liedtke, 2013) was

carried out according to OECD TG 201 under GLP conditions. Nominal concentrations were set from 0,017 to 0,27 mg available chlorine/L. Measured concentrations at the start of the test ranged from below the limit of quantification (LOQ = 0,0108 mg available chlorine/L) for the low nominal concentrations to 0,256 mg available chlorine/L corresponding to 93% of the nominal values at the start of the test. During the test period of 72 hours, the reduction of available chlorine in the test media was of the same order for samples with and without algae. At the end of the test, the measured values were below the limit of quantification. This confirms the difficulty of keeping the exposure to hypochlorite constant in a static ecotoxicity test, under the light intensity needed for algae growth. The report provides results according to both initial measured concentrations and nominal concentrations. The test item is known to be a potent oxidizing agent in aqueous solution. This is confirmed by the strong toxic effects observed within the first 24 hours of exposure. In the two highest test concentrations, the damage of the algal cells observed during the first 24 hours was complete; consequently, no algal biomass could be determined after 24 hours of exposure. In the two lowest test concentrations, the decrease of available chlorine was accompanied by a slight recovery of the algae during the last 48 hours of exposure. Due to these observations, the biological results were considered to be mainly referring to the concentration of the test item measured at the start of the test (initial measured). On the other hand, as explained above, according to the OECD Guidance on Aquatic Toxicity Testing of Difficult Substances and Mixtures, section 5 - Calculation and expression of test results, it is recommended that: "for tests with chemicals that cannot be quantified by analytical methods at the concentrations causing effects, the effect concentration can be expressed based on the nominal concentrations". Based on nominal available chlorine concentrations, the following values were obtained:

- **ErC50-72h = 0,0499 mg available chlorine/L**,
- **ErC10-72h = 0,0299 mg available chlorine/L** and
- **NOECr = 0,0171 mg available chlorine/L.**

Based on initial measured available chlorine concentrations the following values are obtained:

- **ErC50-72h = 0,0365 mg available chlorine/L,**
- **ErC10-72h = 0,0199 mg available chlorine/L** and
- **NOECr = 0,0054 mg available chlorine/L.**

3.2 OTHER RELEVANT STUDIES/ EVALUATIONS

3.2.1 MIXTURES

In 2009, in parallel to the Gallagher study, A.I.S.E. conducted a test under GLP conditions on a representative model sodium hypochlorite containing bleach mixture as provided for under both DPD and CLP, to form the basis of more specific guidance on classification in relation to sodium hypochlorite containing bleach and similar products sold for cleaning and hygiene uses.

The results of the mixture test (detailed in Annex 1) show an EC50 above 1 mg/L for the mixture confirming that the model mixture would not be classifiable N, R50 (H400). The test results further show that eco-toxicity is determined by the level of sodium hypochlorite in the product and the EC50 indicates that products containing up to 5,2% sodium hypochlorite (4,9% active chlorine) would not need to be classified N, R50 on the basis of their sodium hypochlorite content, provided other constituents would similarly not contribute to aquatic toxicity.

This finding is entirely consistent with the M-factor derived by the REACh consortium, which leads to products containing up to 2.5% active chlorine **not** being classifiable N, R50 (H400) using the calculation method based on the substance content: the higher value of 4,9% simply reflects refinement of the default calculation method provided by using data from mixture testing which is not artificially constrained into M-factor driven discrete bands (0,25% - 2,5% etc).

In addition to the above test, A.I.S.E. has been advised of the results of a similar test conducted by one of their member companies, for classification purposes, in the frame of a biocidal product registration during the transitional period in the Netherlands. In this test conducted according to the OECD 202 protocol in which *D. magna* were exposed for 48 hours in semi-static conditions to a formulated bleach product containing approximately 5,5% active chlorine and 8% organic substances, the EC50 was also greater than 1 mg/L. This test supports the findings of the A.I.S.E. test.

3.3 SUMMARY OF RELEVENT AQUATIC TOXICITY DATA

High quality studies concerning the acute toxicity of sodium hypochlorite to both aquatic invertebrates and algae have recently been carried out as described above in order to upgrade the data set available, in the frame of the substance dossiers submitted under REACh and the Biocidal Products Regulation (BPR). Relevant studies incorporating these results set out are summarised in the table below..

Summary of acute toxicity data for sodium hypochlorite

Year	Author	Test details	Test organism	Result (active chlorine)
2013	Liedtke	freshwater	*Pseudokirchneriella subcapitata* (Algae)	ErC_{50} = 0.0499 mg (nominal)/L ErC_{50} = 0.0365 mg (initial measured)/L
1984	Watkins	freshwater	*Myriophyllum spicatum* (freshwater vascular plant)	ErC_{50} = 0.1 mg/L
2009	Gallagher	short-term, freshwater	*Daphnia magna*	EC_{50}-48h = 0.141 mg/L
2011	Gallagher	short term, freshwater	*Ceriodaphnia dubia*	EC_{50}-48h = 0.035 mg/L
1978	Roberts	short-term, saltwater invertebrate	*Crassostrea virginica* (oyster)	LC_{50} = 0.026 mg/L
1978	Heath	short-term, freshwater	Fish	LC_{50} = 0.06 mg/L
1978	Thatcher	short-term, saltwater	Fish	LC_{50} = 0.032 mg/L

The above data show that algae, invertebrates and fish are equally sensitive to the toxic effects of sodium hypochlorite and this allows us to conclude that the acute toxicity of sodium hypochlorite to marine and freshwater species lies in the range: **$0{,}01 < L(E)C_{50} \leq 0{,}1$ mg/L.** With respect to classification rules defined in Annex I, Table 4.1.3 of Regulation (EC) No. 1272/2008 (CLP), concerning multiplying factors for highly toxic components of mixtures, **this means that an "M-factor" of 10**

should be assigned to sodium hypochlorite with regards to acute toxicity classification.

Developing from this; sodium hypochlorite is produced as an aqueous solution. According to Table 4.1.1 of the Regulation (EC) No. 1272/2008, pure solutions (i.e. dilutions in water) or mixtures have to be classified depending on the concentration of active chlorine. For mixtures, the acute M-Factor = 10 has to be used unless test data for the complete mixture or similar mixtures are available at the formulator level, as described in Figure 4.1.2 of the CLP Regulation. Where test data are available, classification of a mixture derived using test data for the complete mixture or similar mixtures will take precedence over classification derived from calculation.

As regards chronic toxicity, the 2nd Adaptation to Progress of the CLP regulation (Regulation (EC) No 286/2011) of 10 March 2011 further modified the classification criteria for aquatic chronic toxicity. This means that for substances, as well as for mixtures, aquatic chronic toxicity data are taken into account for long-term hazard classification. The key studies for chronic aquatic toxicity of sodium hypochlorite are presented in the following table.

Summary of chronic toxicity data for sodium hypochlorite

Year	Author	Test details	Test organism	Result (active chlorine)
2013	Liedtke	freshwater	Algae (*Pseudokirchneriella subcapitata*)	ErC_{10} = 0,0299 mg (nominal)/L, NOECr = 0,0171 mg (nominal)/L ErC_{10} = 0,0199 mg (initial measured)/L, NOECr = 0,0054 mg (initial measured)/L
1990	Cairns	long-term, freshwater	Algae (periphyton)	NOEC (7 d) = 0,0021 mg/L
1978	Liden	long-term, marine water	Oyster	NOEC (7 d) = 0,007 mg/L
1983	Goodman	long-term, marine water	Fish	NOEC (28 d) = 0,04 mg/L

The above results show NOEC values between 0,002 and 0,04 mg/L, as active chlorine. According to Table 4.1.0 (b)(ii) of the CLP Regulation, as a rapidly degradable substance, a classification as Chronic Category 1 (H410, very toxic to aquatic life with long lasting effects) applies to sodium hypochlorite solutions. Furthermore, using Table 4.1.3, concerning multiplying factors for highly toxic components of mixtures, an "M-factor" of 1 has to be assigned to sodium hypochlorite with regards to chronic toxicity (0,001 < NOEC ≤ 0,01; RD component).

For dilutions and mixtures containing sodium hypochlorite, provided there is no other component classified as hazardous to the aquatic environment, the proposed classification for acute and chronic toxicity of sodium hypochlorite is outlined in the following two tables. This proposal is based on the key studies and discussion above and taking into consideration the classification criteria set down in Regulation (EC) No. 1272/2008.

Proposed acute environmental classification

Concentration of sodium hypochlorite solutions (as % active chlorine)	Acute Classification	H Statements	M Factor
≥ 2,5 %	Acute Category 1	H400 (very toxic to aquatic life)	10
< 2,5 %	None	None	N/A

Proposed chronic environmental classification

Concentration of sodium hypochlorite solutions (as % active chlorine)	Chronic Classification	H Statements	M Factor
≥ 25 %.	Chronic Category 1	H410 (very toxic to aquatic life with long lasting effects)	1
< 25 % but ≥ 2,5 %	Chronic Category 2	H411 (toxic to aquatic life with long lasting effects)	N/A
< 2,5 % but ≥ 0,25 %.	Chronic Category 3	H412 (harmful to aquatic life with long lasting effects)	N/A

OTHER ISSUES WITH NL CLH REPORT

This section lists industry concerns about the January 2015 report from RIVM/ VSP "CLH report proposal for harmonised classification and labelling for sodium hypochlorite" (here-after referred to as 'the report').

- Section 5.1.1 – Stability – Stability in Water: The report states that "sodium hypochlorite solutions are stable in pure water and at low concentration, in the dark at low concentration". These are not (normal) "environmentally relevant conditions" against which 'rapid degradability' should be assessed according to the guidelines;
- Section 5.1.1 – Stability – Photo-transformation in water: The report states that "direct sunlight may cause rearrangement and decomposition to form chlorate and oxygen". This is mentioned in RAR section 2.4.2. Section 2.6 of the RAR also mentions: "exposure to sunlight or strong light accelerating the transformation of hypochlorous acid to into chloride. Agitation of the sample also accelerates this process". As such samples should be analysed immediately after collection, whilst avoiding light and agitation and as such cannot be stored;
- Section 5.1.3 – Summary and discussion of degradation – Against: The report argues that the "degradation products chlorine and sodium chlorate have a harmonized classification as hazardous to the environment; chlorine being classified as Aquatic Acute 1 (M-factor 100)". This is inappropriate as chlorine is classified for the environment based on data on hypochlorite but the harmonized classification of chlorine was set BEFORE those new valid data were collected;
- Section 5.1.3 – Summary and discussion of degradation – Against: The report argues that "hypochlorite solutions (kept away from sunlight and at a constant 15^{o}C are relatively stable (with a low rate of hydrolysis). Especially at low concentration levels the losses being minor". As previously stated, this is not relevant to environmental conditions. It is further evident that M factors here are based on older values for chlorine. It should be that any M factor for sodium hypochlorite must be based on the new, high quality data obtained for the purpose;
- Section 5.1.3 – Summary and discussion of degradation – Conclusion: The relevance of 'degradation' in relation to environmental classification is explained in the introduction to Annex II of the Guidance to CLP on Rapid Degradation which states:

> "Degradability is one of the important properties of substances that have impact on the potential for substances to exert an aquatic hazard. Non-degradable substances will persist in the environment and may consequently have a potential for causing long-term adverse

effects on biota. In contrast, degradable substances may be removed in the sewers, in sewage treatment plants or in the environment"

Annex I to CLP, paragraph 4.1.2.9.1 states that:

> "Substances that rapidly degrade can be quickly removed from the environment. While effects of such substances can occur, particularly in the event of spillage or accident, they are localized and of short duration."

While CLP chooses to define degradability as applying to organic molecules, it is obvious that the characteristics of decomposition and removal from the environment are equally shared by many inorganic substances. Annex I to CLP, section 4.1.2.10.1, while considering that the term 'degradability' has limited or no meaning for inorganic substances, recognises that "such substances may be transformed by normal environmental processes to either increase or decrease the bioavailability of the toxic species". The guidance addresses transformation for inorganic metal compounds, where the toxicity is often dependent upon the speciation of the metal ion or where solubility is a critical limiting factor. The metal remains present, but not in a form which is bioavailable. Often there is potential for such transformations to be reversible. For some reactive non-metal inorganic substances however, not addressed by the guidance, including hypochlorite, the transformation to mineral ion is irreversible.

The report acknowledges that in natural waters free chlorine is "very rapidly and totally transformed" but it perhaps suggests that the implicitly stable product is combined chlorine, *which is not the case*. In practice, the major ultimate breakdown product is chloride ion. Though combined chlorine decays somewhat less rapidly than free chlorine, it is itself short lived in the presence of oxidisable substrates, which are commonly present in the aquatic environment and the major end product is chloride ion. Half-lives are typically hours rather than days and much shorter than the standards set for being considered 'rapidly degradable' set out in Annex I to CLP, section 4.1.2.9.

Of interest here, we are also aware of a Canadian EA document:

(available online

http://www.hc-sc.gc.ca/ewh-semt/alt_formats/hecs-esc/pdf/pubs/contaminants/psl2-lsp2/inorg_chloramines/chloramines-eng.pdf

- checked June 2015) based on work by Pasternak (2000), which reports that "a focused review of the literature revealed that the first and third quartiles of reported overall decay rate constants for CRC, TRC and TRO

were approximately 0,70 and 20,0 per day (half-life of 0,03-1,0 days) respectively".

The reclassification report states that "given the fact that hypochlorite solutions (kept away from sunlight and stored at low temperatures) are stable and that some degradation products are also hazardous to the environment it is stated that sodium hypochlorite cannot considered being rapidly degradable for classification purposes". As regards some degradation products being hazardous to the environment, apart from combined chlorine which is rapidly broken down as commented above, the quantities of chlorinated organics and other long-lived species produced during the breakdown of hypochlorite in the environment will be small, of the order of 1% or less. Though it is often stated that a substantial proportion of such by-products are unidentified, whole effluent testing performed as part of the EU Risk Assessment process showed that the species formed are themselves relatively biodegradable. It also showed that the production of such by-products from a raw sewage matrix for example did not increase the ecotoxicity of that matrix. In summary, the ultimate mixture of breakdown products of hypochlorite in the aquatic environment would be predominantly chloride ion and even after, for example 28 days, minor species present and as yet 'undegraded' would not result in the mixture being classifiable for the environment;

- Section 5.4.2.1 – Study 1 – It is stated in the report that "since no reassessment is made and the study is assigned in the EU-RAR as key-study for classification, the study is still considered as key-study despite the shortcomings reported by industry". This suggests that, once these data have been considered as being usable in the past, there is no room for improvement even though more recent, higher quality data are available and classification rules have evolved (e.g. for chronic aquatic toxicity). **Recent studies concerning the same endpoint, carried out under strict OECD guidelines and compliant with GLP requirements ought to be duly considered by authorities in the CLH process**. They represent the latest scientific body of evidence. The CLH process should be driven by science, not by procedural considerations preceding CLP;
- Section 5.4.2.1 – Study 2 – It is stated that "given the uncertainty in average actual measured concentrations, the conclusion that the 48h EC50 <25.8 µg active Cl/L (since the 48h EC100 equals to 25.8 µg active Cl/L) seems appropriate". This is not a representative summary of the study reports. The report actually states that the EC50 48h is 35 µg/L based on nominal concentrations (as recommended in OECD guideline 23 on difficult substances). Further to the RIVM request, calculations on mean measured concentrations have been provided (EC50 48h = 16 µg/L). In addition, there is no reporting here of the study carried out on *D. magna* under the same

conditions having provided the data EC50 48h = 141 µg/L (nominal) and 30.5 µg/L (mean measured);

- Section 5.4.2.1 – Study 3 – The report states that the Williams study is "assigned as a key study for classification, whilst in the dossier the reliability of the study was scored 4 (not assignable)". In the REACh registration it is concluded about these data: "the study was carried out in artificial streams, but the report lacks some key information such as hydraulic retention times and analytical measurement results. Although it is difficult to assign a Klimisch rating for the study, a rating of 3a or 4e (document insufficient for assessment is proposed)". This is the actual reason why the study is not considered reliable for the assessment of acute toxicity to invertebrates;
- Section 5.4.2.x – Missing study – The report fails to include invertebrate studies from brackish/ sea water and freshwater environments (as it does for fish). The report (by Roberts and Gleason) on oysters is considered to be a key study for assessment under RAR and REACh and so should be evaluated and included;
- Section 5.4.3.1 – Toxicity to algae and aquatic plants – The report misquotes the study. The study states that ErC50 72h = 49.9 µg/L based on nominal active chlorine and 36.5 µg/L based on initial measured. However, the report claims that "After 24 hours only for the highest nominal test substance concentration of 2 mg/l FAC/L, some active chlorine could be detected. In all other test substance concentrations the levels are below the LOQ. After 24 hours the inhibition of the growth rate for the initial measured concentration of 23.3 µg FAC/L is 60%. After 24 hours the measured concentration is below the LOQ. Half of the LOQ is assumed for derivation of a mean measured concentration by the authors of this study, than the geometric mean measured concentration equals to 11 µg FAC/L. It can be concluded that the 24h EC50r is <23.3 µg FAC/L". This is not representative of the study findings;
- Section 5.4.3.2 – Long term toxicity to algae and aquatic plants – The report does not appreciate the difficulties in maintaining stable active chlorine concentrations in test media, difficulties which show how inappropriate it would be that sodium hypochlorite be considered to be "not rapidly degradable" as quoted in the report;
- Section 5.4.3.2 – Study 3 – The report states "conclusions are supported by the comparison of the long term zooplankton NOEC from this test (24d NOEC = 1.5 µg FAC(or TRC)/L) with the laboratory short-term toxicity to daphnia (24h LC50 = 5 µg FAC/L) which suggests that a continuous long term exposure of 1.5 µg FAC/L might dramatically affect daphnia populations". This is very speculative as it attempts to draw a link between a mesocosm study and the study by Taylor on *Ceriodaphnia* to generate conclusions relevant to classification;

- Section 5.5 – Comparison with criteria for environmental hazards – The report uses a weight of evidence based approach to deduce the critical concentration effects. Observations of Table 13 in the report actually suggest that, for fish, all but one data point is above 10 µg/L, for invertebrate data the two points below 10 µg/L are unreliable as per their Klimisch score which is why new data have been produced according to international standards with EC50s in the range of 10-100 µg/L and for algae, the figure reported is not consistent with the reported data from the actual source material (which reports between 10-100 µg/L). In addition, the report states that whilst some studies do not allow for an estimation of endpoints useful for assessment, alternatives are available such as the Goodman report which has a Klimisch score of 1 (Table 13). Finally, in this section a lowest NOEC range between 1 and 10 µg/L is recommended *but having acute and chronic toxicities in the same range is unusual but it may have arisen due to the data selection bias inherent to this report*;
- Conclusions – Whilst the report states that the lowest LC50 are between 1-10 µg/L (leading to an acute M factor of 100), based on the evidence presented here, the relevant range is actually 10-100 µg/L, corresponding to an M factor of 10. The same is true for the chronic M factor, which the report claims (based on lowest NOEC values of 1-10 µg/L and the substance being non-rapidly degradable in unrealistic conditions) should be 10, the range should be defined on the basis of its degradability which corresponds to an M factor of 1.

SUMMARY

Taking into account all the above information, it is apparent that the Taylor study results are not consistent with data generated in the more recent, precisely-controlled studies on *Ceriodaphnia dubia* and *Daphnia magna* which were specifically commissioned because of concerns about its limitations and reliability.

Together, the two newer, reliable studies confirm that the range of invertebrate acute toxicities to be used for classification and labelling purposes is 10 -100 µg/L. Further studies on algae and available datasets on fish indicate that when **all reliable acute ecotoxicity data are used for classification of sodium hypochlorite, it is situated in the range 0.01 < L(E)C50 ≤ 0.1 mg/L, which corresponds to "Acute category 1" with M = 10.** This finding is entirely consistent with the M-factor derived by the REACh consortium, which leads to solutions containing less than 2.5% active chlorine **not** being classifiable N, R50 (H400) using the calculation method based on the substance content. The available chronic data and the very rapid degradability of sodium hypochlorite warrants the following classification according to sodium hypochlorite concentration.

Concentration of sodium hypochlorite solutions (as % active chlorine)	Chronic Classification	H Statements	M Factor
≥ 25 %.	Chronic Category 1	H410 (very toxic to aquatic life with long lasting effects)	1
< 25 % but ≥ 2.5 %	Chronic Category 2	H411 (toxic to aquatic life with long lasting effects)	N/A
< 2.5 % but ≥ 0.25 %.	Chronic Category 3	H412 (harmful to aquatic life with long lasting effects)	N/A

Annex I – A.I.S.E. *Daphnia magna* study on a model bleach preparation

To provide the basis for guidance on classification of sodium hypochlorite containing bleach products A.I.S.E. commissioned a 48-hr acute *D. magna* immobilisation test on a representative model sodium hypochlorite containing bleach mixture (see Table below) according to the OECD 202 protocol and conducted to GLP standards. This model mixture contained 5% sodium hypochlorite (=4,75% active chlorine), significantly representing the ingredient with substantially the highest ecotoxicity, and a range of other ingredients to constitute a typical formulation for a more complex sodium hypochlorite containing bleach product.

Composition of A.I.S.E. model bleach preparation tested

Sodium hypochlorite	5%
Sodium hydroxide	1%
Sodium silicate	0,2%
Sodium carbonate	4,5%
Anionic surfactants	2%
Perfume	0.05%
Water	to 100%

The levels chosen in respect of both sodium hypochlorite and other ingredients were at the top of the ranges typically used in the most common sodium hypochlorite containing bleach products. The conclusions of the study report by Covance (Report number 8200595-D2149, 1 April 2009) are presented in Annex I, and the full study report is available upon request at the A.I.S.E secretariat.

The following summarises key points in relation to the design, conduct and results of the test:

a) The role of preparation testing as described in the DPD legislation under which it was conducted is to assist in deriving classification of a preparation as regards acute ecotoxicity. Indeed, it should be borne in mind that sodium hypochlorite contained in packed cleaning and hygiene products does not reach the aquatic environment during normal use and disposal because it is rapidly decomposed, so that its ecotoxic hazard is not in fact manifest in normal circumstances. The Risk Assessment Report for sodium hypochlorite conducted under the EU Existing Chemicals Legislation confirms that during normal use and disposal down a drain, sodium hypochlorite will be entirely decomposed in the sewer system. Since sodium hypochlorite decomposes rapidly in the aquatic environment especially on contact with organic matter, and since it is inorganic

with no potential for bioaccumulation, there is no possibility of long-term hazard for the environment arising from hypochlorite in cleaning products. Acute testing alone is thus necessary.

b) Environmental classification requires a consideration of toxicity in relation to each of the main species groups – algae, daphnia and fish, though classification of substances ultimately is often derived from one set of data relating to the 'most sensitive' species group. While classification based on preparation testing under the DPD normally requires tests to be conducted on all three species groups, the spirit of current regulatory thinking is to minimise testing generally for C&L purposes. In particular, minimising testing on animals is regarded as essential good practice nowadays.
In this context, fish are regarded as animals on which testing is to be avoided where possible, though daphnia are not. Since the available data on ecotoxicity of active chlorine indicate that invertebrates (i.e. daphnia) are similar in sensitivity to fish, testing on fish is not necessary and should not be conducted as it would be unlikely to have any bearing on the classification of the preparations concerned. This is also the conclusion reached by the sodium hypochlorite REACh Consortium[2].

Thus, taking into account the whole body of existing data, including the concurrent assessment of an M-factor by the REACh consortium, and in accordance with regulatory recommendations for obtaining data for classification, a 48-hr acute daphnia magna immobilisation test according to the OECD 202 protocol and conducted to GLP standards is thus seen as adequate and appropriate for testing sodium hypochlorite containing bleach preparations for classification purposes.

c) The daphnia immobilisation test was conducted in low light conditions to minimise degradation, with renewal of the test preparation at 24hr intervals. This semi-static regime was established as adequate according to the OECD 202 protocol by range-finding tests in which free available chlorine (HOCl and OCl^-), expected and subsequently confirmed to be the driving toxicants, were shown to be quite stable at the most relevant test concentration (~1mg/L).

In the definitive test, analytical data obtained during the test confirmed that exposure to active chlorine was essentially stable within the limits (+/- 20%) that would permit EC50 results to be calculated from nominal concentrations (i.e. the amounts added) allowing fluctuations of exposure to be ignored. This approach based on nominal concentrations of sodium hypochlorite would give

[2] *The classification and labelling of solutions of sodium hypochlorite as "Dangerous to the Environment"; important new guidance for manufacturers and users. September 2011. Sodium Hypochlorite REACh Consortium.*

an effective ceiling for non-classification of about 5,6% sodium hypochlorite (5,3% active chlorine). A more conservative interpretation of the data which corrects even for this modest observed decay using a 'geometric mean' adjustment, indicates a ceiling of 5,2% sodium hypochlorite (4,9% active chlorine).

In addition to the above test, A.I.S.E. has been advised of the results of a similar test conducted by one of their member companies, for classification purposes, in the frame of a biocidal product registration during the transitional period in the Netherlands. In this test conducted according to the OECD 202 protocol in which daphnia magna were exposed for 48hr in semi-static conditions to a formulated bleach product containing approx. 5,5% active chlorine and 8% organic substances, the EC50 was also greater than 1 mg/L. This test supports the findings of the A.I.S.E. test[3].

To provide the most secure basis for this guidance, this more conservative value of 5,2% sodium hypochlorite (4,9% active chlorine) obtained in the A.I.S.E. test has been adopted.

The results of the mixture test showed an EC50 above 1 mg/L for the mixture confirming that the model mixture would **not** be classifiable N, R50. The test results further show that eco-toxicity is determined by the level of sodium hypochlorite in the product and the EC50 indicates that products containing up to 5,2% sodium hypochlorite (4,9% active chlorine) would not need to be classified N, R50 on the basis of their sodium hypochlorite content, provided other constituents would similarly not contribute to aquatic toxicity.

[3] *As they are owned by an individual company, detailed results of these tests cannot be reported in this paper but in case a group is interested in it, A.I.S.E. can facilitate contacts between organisations.*

Annex II – A.I.S.E. Bleach 1 (framework preparation): Acute toxicity to *Daphnia magna* – Study Conclusions

CONCLUSIONS

The objective of the study was to determine the 48-hour acute toxicity according to OECD 202 of a framework preparation based on 5% sodium hypochlorite (AISE bleach 1) to the freshwater planktonic crustacean, *Daphnia magna*.

AISE bleach 1 was found to be toxic to *Daphnia magna* at nominal concentrations exceeding 0.50 mg product/L (equivalent to 0.025 mg/L NaOCl) under the conditions of this definitive test.

The 24 and 48-hour [6]EC_{50} toxicity values, along with the corresponding [7]NOEC values are presented below:

Based on nominal product	24-hour	48-hour
EC_{50}	2.19 mg product/L	1.11 mg product/L
NOEC	1.0 mg product/L	0.5 mg product/L

95% confidence intervals could not be set

Based on nominal NaOCl	24-hour	48-hour
EC_{50}	0.109 mg/L	0.056 mg/L
NOEC	0.05 mg/L	0.025 mg/L

95% confidence intervals could not be set

Based on geometric mean measured TFC	24-hour	48-hour
EC_{50}	0.0639 mg/L	0.0490 mg/L
NOEC	0.0476 mg/L	0.05 mg/L*

95% confidence intervals could not be set

* Treat with caution due to proximity with LOD (0.020 mg/L)

[6] Concentration resulting in 50% immobility of exposed daphnia
[7] No observed effect concentration

Based on measured NaOCl calculated using geometric mean measured TFC	24-hour	48-hour
EC_{50}	0.0668 mg/L	0.0520 mg/L
NOEC	0.05 mg/L	0.05 mg/L

95% confidence intervals could not be set

The lowest measured free chlorine concentration at which 100% immobility occurred was 0.0671 mg/L (equivalent to a nominal concentration of 2.5 mg product/L and a calculated achieved product concentration of 1.41 mg product/L).

The validity criteria for control immobility (≤10%) and dissolved oxygen (>60% air saturation value) were both satisfied. The test is therefore considered valid.

Annex III – Classification of sodium hypochlorite containing bleach preparations using data from the A.I.S.E. Bleach 1 preparation test

The DPD Article 7 provides that the hazards of a preparation for the environment may be assessed by appropriate ecotoxicological tests on the preparation (article 7.1(b)).

Article 7.3 then sets down criteria that determine when a new hazard assessment is required if the preparation being classified varies in composition from that which was tested. There is a table which defines limits within which the concentrations of ingredients may vary before a new hazard assessment is required (the 'permitted variations'). Any change of ingredient, whether hazardous to the environment or not, would require a new assessment.

However, article 7.3 then concludes by stating that a new evaluation in respect of such variations in formulation is not required where "there is valid scientific justification for considering that a re-evaluation of the hazard will not result in a change of classification."
In the case being considered here of sodium hypochlorite bleach preparations, an analysis of the potential contribution to toxicity of the various ingredients in the model preparation using a 'Toxic Units' approach (Table) shows that sodium hypochlorite would be expected to be the driving toxicant by a wide margin.

Comparative ecotoxicity of ingredients in the model sodium hypochlorite containing bleach mixture.

Ingredient	% in product	Fish		Daphnia		Algae	
		LC50	TU (norm)	EC50	TU (norm)	EC50	TU (norm)
Sodium hypochlorite	5	0.032	1000.000	0.032	1000.000	0.6	53.333
Sodium carbonate	4.5	300	0.096	270	0.107	140	0.206
Sodium hydroxide	1	190	0.034	100	0.064	100	0.064
Anionic surfactants	2	17	0.753	95	0.135	3	4.267
Sodium silicate	0.2	3200	0.0004	1700	0.001	213	0.006
Perfume	0.05	32	0.010	32	0.010	32	0.010

The toxic unit (TU) as a relative measure of potential contribution to ecotoxicity is defined as the reciprocal of the toxicity (e.g. LC50 or EC50) multiplied by the percentage abundance of the component in the preparation. For the ease of comparison, the TU's are normalized (TU norm) to the toxicity of hypochlorite to Fish and Daphnia set at 1000 (TU=1000). See Annex for data sources.

Such 'toxic units' calculations are established methods for assessing the environmental hazards of mixtures. They are used for example in environmental risk assessment of substances that are in reality complex mixtures of similar components (e.g. the EU EUSES Hydrocarbon Block Method for hydrocarbon-based substances[i], the HERA methodology for surfactants[ii] and RIVM derivation of risk limits for soil, sediments and groundwater[iii]). The concept is also now applied to classification and labelling as part of the GHS methodology for classification of mixtures[iv]

Toxic Unit calculations make the assumption that toxic effects of component substances in a mixture are additive. This can be realistic where the components are closely similar substances that share a common mode of toxic action, but is a conservative assumption where the components are dissimilar. The calculation will be especially conservative, as here, where the concentrations of the less toxic ingredients are far below the levels at which they might begin to exert toxic effects in isolation.

The toxic units calculation for the tested model bleach preparation thus indicates that the ingredients other than hypochlorite would be expected to contribute insignificantly, if at all, to the toxic effects of the preparation. This expectation is directly confirmed by the results of the preparation test which show the measured EC50 of the preparation to be typical, and central within the range, of those observed for hypochlorite alone.

When classifying hypochlorite bleach preparations containing less than 5.2% sodium hypochlorite therefore, if it can be shown that the other ingredients in the formulation would make a similarly insignificant contribution to toxicity, the manufacturer would have "valid scientific justification for considering that a re-evaluation of the hazard will not result in a change of classification". The product could be classified using the test data on the A.I.S.E. model bleach.

For bleaches having lower concentrations of the same ingredients present in the model bleach, or indeed for simple dilutions including no additional ingredients, the similarly insignificant contribution to toxicity would be self-evident. Where

different ingredients are substituted, classification could be confirmed for example using a toxic units calculation as above.

In the future, when companies classifying their mixtures according to the CLP Regulation compare the composition of their mixture to the composition of the tested model bleach mixture using the 'Toxic Units' approach, they would in effect be applying expert judgement in conjunction with the CLP 'Bridging Principles' (e.g. 'substantially similar mixtures').

Action to remedy this situation and provide guidance has been taken both by the Sodium Hypochlorite REACh Consortium and by A.I.S.E. The REACh consortium has issued advice that an M-factor of 10 should apply to sodium hypochlorite. This is based on a re-examination of available ecotoxicity data on sodium hypochlorite and on additional tests on *Daphnia* and *Ceriodaphnia* conducted under GLP to provide a sound basis for environmental classification of the substance. These data were submitted in the joint REACh Registration dossier.

References

[i] European Union System for the Evaluation of Substances (EUSES)
http://ecb.jrc.ec.europa.eu/documents/Existing-Chemicals/EUSES/EUSES_2.1/EUSES_2.0_documentation/Euses2.0IIdescription_def.doc Section II.8

[ii] HERA Project (Human & Environmental Risk Assessment on Ingredients of Household Cleaning Products) Guidance Document Methodology February 2005
http://www.heraproject.com/files/HERA%20TGD%20February%202005.pdf

[iii] Technical evaluation of the Intervention Values for Soil/sediment and Groundwater. Human and ecotoxicological risk assessment and derivation of risk limits for soil, aquatic sediment and groundwater J.P.A. Lijzen, A.J. Baars, P.F. Otte, M.G.J. Rikken, F.A. Swartjes, E.M.J. Verbruggen and A.P. van Wezel. RIVM report 711701 023 February 2001
http://rivm.nl/bibliotheek/rapporten/711701023.pdf

[iv] UNECE Globally Harmonised System of Classification and Labelling of Chemicals (GHS) Part 4 Environmental Hazards: Section 4.1.3 Classification criteria for mixtures.
http://www.unece.org/trans/danger/publi/ghs/ghs_rev02/English/04e_part4.pdf