On the validation of grouping health hazard indicators

T. Scheffers, G. Wieling, C. Coucke
DOHSBase v.o.f., Eersel. E-mail: dohsbase@dohsbase.nl

Content

Summary

Objective:
Workplace assessment tools such as Control banding (CB) and Exposure Modeling (EM) use grouped Health Hazard Identifiers (HHI) like R-phrases or H3##-statements to rank chemical substance health hazard in 3 to 5 categories. The aim of this study is to evaluate the validity of HHI grouping.

Methods and materials
HHI grouping schemes are examined on (1) grouping and ranking factors in HHI classification criteria, (2) their mutual differences and (3) the strength by which the ranked categories are related to the quantitative standard they replace: the Occupational Exposure Limit Value (OELV). R-phrases will be phased out in May 2015. Therefore harmonized EU H3##-statements, convertible classifications on carcinogenicity (IARC, Dutch Health Council=DHC, ACGIH), mutagenicity & reprotox (DHC) and the REACH "no Exposure Scenario obligation" and "causing minimal risk" criteria are used as HHIs. Substances with at least one HHI/OELV combination are selected from an occupational exposure database (www.dohsbase.com, version14-01). DNELs, a Biological Limit Values, Kick-off levels and OELVs with non-fitting units (fibers, %, non-TWA 8 hours etc.) are excluded. Non-parametric (Kruskal-Wallis & Page) techniques, unifactorial ANOVA and log-Linear regression are used for the statistical inference on the strength of the relation between the ranked categories and the OELV levels.

Results
The HHI's for inhalation, dermal and oral toxicity (TOX), irritation, corrosion & sensitization (ICS) and carcinogenicity, mutagenicity & reprotoxicity (CMR) are mutually independent and their classification criteria lack a common factor for ranking. HHI classification criteria within the endpoints TOX (e.g. acute H300->333, repeated H370->373 per route), ICS (H314->320) and CMR (H340->362) are ranked to some extend but of different nature (dose, severity, duration, weight of evidence) and measuring rules (discrete, ordinal or categorical) what hampers grouping. The HHI grouping relies to a large extend on subjective expert judgment.

Seven R-phrases and five H-statement based HHI grouping tools are identified. Mutual comparison show that their HHI groupings schemes differ in (1) having 3 to 5 HHI categories, (2) enrolling different HHI's and (3) allocating HHI's in different categories. 84 Classification criteria determine 50 health hazard R-phrases and 38 H3##-statement. For TOX the classification cut-off points of R-phrases and H-statements differ, leading to different hazard categories for individual substances. Several HHI groupings schemes contain errors in the HHI allocation. 40% of the substances with one or more HHIs have a different hazard categories in COSHH compared to Spaltenmodell. For COSHH and EMKG this is 33%.

More than 7300 chemical substances with HHIs are merged with 4500 substances with TWA 8-hours OELVs in PPM's for substances that exceed the OELV as vapor/gas and in mg/m^3 otherwise. This resulted in 970 mutually independent HHI-OELV combinations (630 in PPM and 340 in mg/m^3)

HHI grouping schemes are strongly related to OELVs and explain about 25% (for mg/m3) to 40% (for PPM) of the OELV variance. DGUV_IFA GHS-Spaltenmodell has the strongest power to predict the PPM OELV range and COSHH the mg/m^3 OELV range. Loglinear regression estimates a multiplier of about 10 for the COSHH PPM OELV decrease with 4 increasing hazard categories and 6 for the Spaltenmodell mg/m^3 OELV decrease with 5 categories.

Conclusion
Control banding and Exposure Modeling tools suffer from the subjective expert judgment applied in the hazard categorization of Health Hazard Identifiers (HHI) like R-phrases or H3##-statements. Different schemes lead to substantial differences hazard categories, leading to different control regimes in CB and different risks in EM. This undermines the credibility and worldwide use of the CB and EM tools in Small and Medium Enterprises.

Although there is reason to criticize current HHI grouping schemes, their observational relation with the OELV is strong. Their different performances indicate that there is room for improvement by shifting towards an international accepted, harmonized and optimized HHI grouping scheme with an optimized number of HHI groups, the best fitting HHI categorization and based on the smallest, most distinguishing OELV distributions.

Keywords: H-statements, GHS, CLP, Control Banding, COSHH essentials, BAUA Einfache Maßnahmenkonzept Gefahrstoffe , DGUV_IFA GHS-Spaltenmodell, Small and Medium Enterprises (SME), OELV Hierarchy.

1 Introduction

Control banding (CB) and Exposure modeling (EM) are a generic technique for assessing and managing workplace exposure risks, based on the grouped and ranked Health Hazard Identifiers (HHI) for toxicity (TOX), irritation, corrosion & sensitization (ICS), carcinogenicity, mutagenicity & reprotoxicity (CMR) and some others (see Table 12 to Table 15). HHI grouping schemes are developed in different countries and by different institutions to deal with (1) the limited number of Occupational Exposure Limit Values (=OELV), (2) the complex and expensive OELV compliance testing, and (3) Small and Medium Enterprises that want to work safely.

CB is developed in the 90^{ties} of the last century [6,33,3,7,54]. It is incorporated in the working condition regulations of many countries. It is promoted internationally by ILO [28] and ECHA [14]. HHI-grouping schemes are also included in exposure modeling tools like ECETOC TRA[12], Chesar [14], EMKG [30] and Stoffenmanager [49]. The tools are well described in may documents and brochures, easy available in user-friendly software tools and discussed extensively at many conferences and symposia throughout the world [54They are widely used IN many applications (Compliance testing, REACH registration).

A call for international harmonization and validation of CB, EM HHI grouping is done at the BOHS conference in Nothingham 2014 [5] as the number of tools are still growing and tools with the same task provide different outcome. Validation studies are performed in the last decades [54] on CB schemes [50] and their claimed exposure ranges [36]. Scheffers & Wieling [41] found significant within and between differences in the OELV distributions of R-phrase groupings in different CB schemes. Their regression and single factor ANOVA revealed that the German TRGS440 R-phrases based HHI-grouping performed better than the others. They used these results to establish so-called “Kick-off” levels for substances without an OELV but with one or more HHIs [41, in Dutch]. ECETOC performed a comparable exercise to establish estimated OEL’s for data poor substances based on the regression between Hazard categories and the 2005 UK-HSE OELs. And Ruppich [36] researched the overlap between claimed exposure ranges of COSHH and the TRGS900 OELVs distributions [36, in German].

This study focusses on the validation and consistency of HHI grouping and ranking, and on finding the most optimal HHI grouping of H-statements. It uses a larger and more recent OELV HHI dataset but the same methods as the 2005 study of Scheffers and Wieling [41].

2 Material and methods

2.1 Materials

2.1.1 Health Hazard Identifiers

Health Hazard Identifier (HHI) is the generic term used in this study for (1) R-phrases, (2) EU CLP H-statements, (3) GHS hazard class, category and statement codes and (4) other classifications convertible to R-phrases or H-statements. The classification criteria for the HHI's (1) and (2) are listed in Table 12 to Table 15.

The European Dangerous Substances Directive (DSD) [17] provides since1967 a legal framework for the classification of R-phrases [18]. R-phrases will be replaced in Europe on May 31, 2015 by the H-statements of the European CLP system [20]. CLP aligns the EU with the Globally Harmonized System of Classification & Labelling of Chemicals (GHS) [52]. The Global harmonized System (GHS) is introduced in 2003 after an UN mandate (UNCED 1992) and is based upon the "major existing systems" throughout the world [52].

As most tools also include non-dangerous substances in the HHI grouping schemes two additional HHI are added in Table 12 to Table 15 based on criteria for REACH[19]:

- no REACH registration Exposure Scenario obligation
- Considered to cause minimum risk according to REACH Annex IV

Both HHI's indicate a low health hazard for the specific endpoint and these HHI's fit in the lowest HHI group.

IARC (www.iarc.fr), ACGIH (www.acgih.org) and the Dutch Health Council (www.gr.nl) provide classifications on carcinogenicity (IARC, DHC), mutagenicity & reprotoxicity (DHC) that can be converted to, or are already (DHC) reported as R-phrases or H-statements.

2.1.2 HHI Grouping and classification criteria

Since the 1990^{ties} [6] at least 7 R-phrase based HHI grouping schemes are published (see Table 9). Most of the schemes are linked to one or more CB or EM tools. The general principles of allocating R-phrases over the hazard categories are extensively described by Brooke [6]. Since 2009 at least six H3##-statement based HHI groupings are published. Four are linked to Control Banding (see Table 10), one to REACH (2.1.3.6) and one to the NIOSH exposure banding process [48].

Table 12 to Table 15 show the 84 classification criteria use by DSD/CLP/GHS for choosing 50 health hazard R-phrases and 38 H3##-statement. HHI grouping schemes group and rank the 50 health hazard R-phrases or 38 H3##-statements over the hazard categories, in example as simplified pictured in Figure 1.

Hazard category	Health Hazard Identifiers (HHI) like R-phrases, H- & EUH statements and REACH & CMR classifications (IARC, etc.)
5/E	Human Carcinogen R45, 49, H350(i), IARC 1, 2a
4/D	Very toxic, R26, H330, Possible Carc. R40, H351 , IARC 2b.
3/C	Toxic R23,H331, Corrosive 34, 35, H314, EUH071
2/B	Harmful R20, H332; Irritation R37, H335
1/A	Harmless. R36, 38; REACH non ES obligation, Annex IV

Figure 1 Simplified hazard grouping of health hazard identifiers (HHI)

HHIs are substance specific properties. The HHI with the highest hazard category is leading for substance hazard. Higher hazard categories leads in a CB to a more structural and stringent control regime and in EM to a higher risk of non-compliance.

2.1.3 HHI grouping schemes

2.1.3.1 R-phrase grouping schemes

R-phrase based groupings are displayed in Table 9. The UK COSHH CB scheme [9, 27] uses 5 hazard bands (A to E). The scheme is developed and described in the 90^{ties} by Brooke [6], Maidment [31] and Guest [24]. It is based on earlier work by Naumann (1996) [33], British Pharmaceutical Industry [3] and the Chemi-

cal Industries Association [7]. It allocates the R-phrases assigned under the 26th ATP European Union DSD classification system. The CB scheme was evaluated using the occupational exposure limits of 111 substances [6].
The R-phrases based schemes of TRGS600 [8] and its predecessor TRGS440 [51] allocates R-phrases different from COSHH_R 2009 [27]. ECOTOC [12] excluded the Carcinogenic, Mutagenic or Reprotoxic category 1,2 (R45,46,49,60 &62; 28th ATP) from the grouping scheme . ECOTOC [12] and SOMS [47] allocates the R-phrases in 3 HHI categories and also different from all others.. ECOTOC [12] and the Dutch SOMS system [47] suffers from overrepresentation of R-phrases in the two lowest and the two highest HHI categories, respectively.
TRGS440 [51] was used by Scheffers and Wieling [41] to establish Kick-off levels as this grouping provided the best discriminating OELV distributions. The upgraded R-phrase groupings (COSHH, TRGS) are reanalyzed and the results are available as consultancy on request. As the R-phrases will be phased out in May 2015 the results are not reported here.

2.1.3.2 BAUA Einfaches Maßnahmenkonzept Gefahrstoffe (2009/2012)

The `Einfaches Maßnahmenkonzept für Gefahrstoffe" (=EMKG; Easy-to-use workplace control scheme for hazardous substances") is developed by the Bundesanstalt für Arbeitsschutz Und Arbeitsmedizin (=BAUA; Federal institute for Occupational Safety and Health) [30, 4, 36].
The health hazard H-statements for workplace air (see Table 1) are separately grouped from the skin related H-statements (H312**; H315, H317, H371*; H373*, H311; H314 (Hautätz. 1B, 1C); H341*; H351*; H361*; H370*; H372*, H310; H314 (Hautätz. 1A); H340*; H350*, H360*) [4].

Table 1 BAUA EMKG hazard groups (Gefährlichkeitsgruppen) for H-statements (H-Sätzen) through inhalation [4].

Gefährlichkeitsgruppe	zugeordnete H-Sätze
A	Kein gesundheitsbezogener R-Satz, H319, H335, H336, H304
B	H302, H332, H318,
C	H301**, H331**, H314, H334, H341*, H351*, H361f*, H361d*, H370*, H371*, H373*, EUH031;TRGS 907
D	H300, H330, H360D*, H372*; EUH032
E	H340*, H350*, H350i, H360F*, TRGS 905, TRGS 906

In table 3 hazard group A contains the phrase "Kein gesundheitsbezogener R-Satz," (no health related R-phrases) where probably H-statements is meant. H314 (*Skin corrosion/irritation, Hazard Category 1A, 1B and 1C*) is the only H-statement included in both inhalation and skin/dermal hazard.

2.1.3.3 DGUV IFA GHS-Spaltenmodell (2011)

The German Research Institute for Occupational Health and Safety of the Social Accident Insurance (Institut für Arbeitsschutz [IFA] der Deutschen Gesetzlichen UnfallVersicherung [DGUV]) has developed the so called Spaltenmodell (=Gap model) [45]. The model translates the TRGS440/600 R-phrase grouping [51, 8] to the GHS H statements and the CLP EUH statements (see Table 10). COSHH H-statement grouping (2009)

2.1.3.4 COSHH

The original R-phrases COSHH essentials CB scheme [9] (see 2.1.3.1) is in 2009 upgraded including the GHS H-statements [27], see Table 2.

Table 2 COSHH (2009) [27]. Grouping R-phrase and GHS H-statements and their corresponding airborne concentration range identified as providing adequate control

Hazard Group	Type	Concentration range	Units	R-phrases	H-statements
A	Dust	>1 to 10	mg/m³	R36, R38 and all R-numbers not otherwise listed	H303, H304, H305, H313, H315, H316, H318, H319, H320, H333, H336 and all H-numbers not otherwise listed
	Vapour	>50 to 500	ppm		
B	Dust	>0.1 to 1	mg/m³	R20/21/22 and R68/20/21/22	H302, H312, H332, H371
	Vapour	>5 to 50	ppm		
C	Dust	>0.01 to 0.1	mg/m³	R23/24/25, R34, R35, R37, R39/23/24/25, R41, R43, R48/20/21/22, R68/23/24/25	H301, H311, H314, H317, H318, H331, H335, H370, H373
	Vapour	>0.5 to 5	ppm		
D	Dust	<0.01	mg/m³	R26/27/28, R39/26/27/28, R40, R48/23/24/25, R60, R61, R62, R63, R64	H300, H310, H330, H351, H360, H361, H362, H372
	Vapour	<0.5	ppm		
E	Dust	-	mg/m³	R42, R45, R46, R49, R68	H334, H340, H341, H350
	Vapour	-	ppm		

In Table 2 H-statement H318 (Eye damage 1) is allocated in two hazard categories: A and C. Email correspondence (HSE 2014 Jan 16) learned that the allocation in A is correct, what is used in this study. As mentioned on page 29 of COSHH (2009) and confirmed by email the EUH-statements of Table 3 are included in COSHH although not mentioned in Table 2

2.1.3.5 ILO-CCT

The ILO-CCT [28] "International Chemical Control Toolkit" (http://www.ilo.org/legacy/english/protection/safework/ctrl_banding/toolkit/icct/hgroup.htm) is an upgrade to global GHS of an expanded and adjusted UK COSHH CB scheme with the R-phrases changes introduced with the 28th ATP. It allocates both the R-phrases and Global Harmonization System (GHS) class/level values in five hazard categories.
The hazard grouping of ILO is not included in the study because:

- The differences between ILO and COSHH R-phrase grouping is limited [29] (see Table 9)
- There are errors in the R-phrases R40/20/21/22 does not exist.
- The GHS H-statements codes are not mentioned and EUH-statements are not included.
- ILO may have stopped supporting the Toolkit[40], as did not react on requests for clarification.

2.1.3.6 ECHA Hazard bands

In the step-wise approach for the qualitative assessment [14, chapter E.3.4.3) of the REACH registration a three band hazard grouping scheme for systemic and local effects is proposed for general risk management measures and operational conditions (RMMs/OCs) and PPE to be considered when developing exposure scenarios if no DNEL or DMEL can be set. On page 28-32 Table E.3-1 presents Hazard bands of systemic and local effects. R-phrases and H-statements, grouped in 3 bands of High, Moderate and Low hazard.
The scheme is not included because:

- The hazard grouping is limited to three groups of which the low hazard group is quite underrepresented as only the individual low irritant hazards are included.
- Further the following R-phrases and H-statements are not included in the HHI grouping
  - R60, R61, H360, H361 (reproduction toxicity)
  - H302, H312 and H332 (acute toxicity 4),
  - R48/20 thru 25 H372 & H373 (repeated dose toxicity 1& 2), H362 (lactation),
  - H336 (drowsiness) and
  - all EUH statements: 029, 031, 032, 066, 070 & 071

ECHA indicates that the grouping is based on expert judgment and that the reason for exclusion is that for substances with these HHI's a DNEL can be derived [38].

2.1.4 substance information

The information on substance identity (name, CAS#, EG#, ID#), physical state, Mol. mass, R-phrases, H-statements and OELVs are retrieved from DOHSBase14-01 (see 2.1.4.3)

2.1.4.1 Harmonized R-phrases and H-statements

EU competent authorities produce tables with harmonized classification and labeling of certain hazardous substances. The harmonized classifications and labeling up to October 2013 (ATP5) are published [16] as Table 3.1 (CLP) and Table 3.2 (DSD) and include about 4100 ID#. Multiple (like the Xylene isomers) or group (like the organic lead compounds) substance classification and labeling are produced if the substances involved are considered of equal hazards. The unique Index Number (ID#) refer to the EU classification dossier.

2.1.4.2 Occupational Exposure Limit Values (OELV)

There are worldwide an overwhelming number of OELVs developed by many different countries and institutions. These OELVs differ in quality, in assessment approach and in the influence of interest groups. Different hierarchies are proposed with which you can chose the most appropriate if there are more than one OELV per substance.
In this study we use an EU oriented hierarchy with the Health based only OELVs on top (see Figure 2). If no SCOEL (the EU Scientific Committee on Occupational Exposure Limits) or DHC (Dutch Health Council) OELV exits a replacement is chosen according to the hierarchy. OELVs dating after 1996 are used by preference, as most OELV setting organizations did not use a quality system before that time and corporate influence could not be excluded.

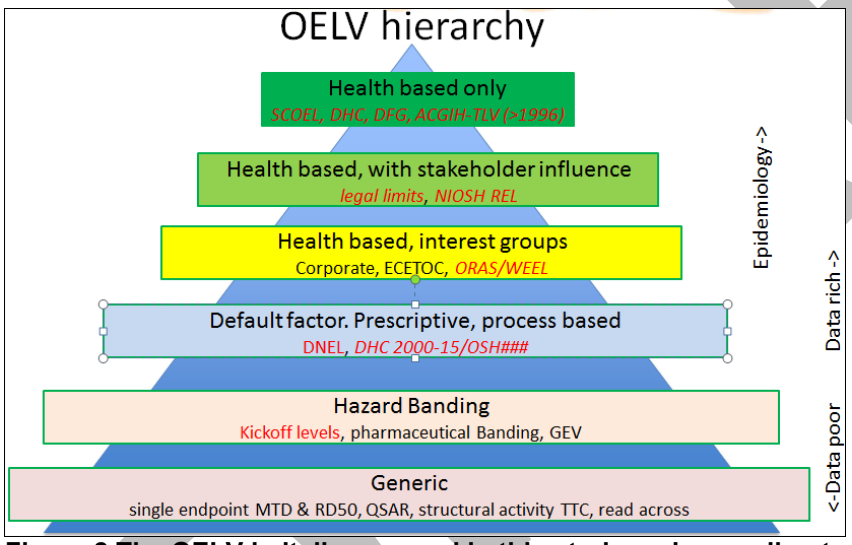


Figure 2 The OELV in italic are used in this study and according to the hierarchy presented.

2.1.4.3 DOHSBaseCompare

The information on substance identity (name, CAS#, EG#, ID#), physical state, Mol. mass, R-phrases, H-statements and OELVs is retrieved from DOHSBase14-01 (www.dohsbase.com). DOHSBase is a comprehensive database with more than 170,000 chemical substances linked to more than 6000 workplace air and biological monitoring exposure limits (OEL's). and over 2,500 internationally renowned sampling methods

DOHSBase's name refers to its origin: it's a spinoff product from the Dutch Occupational Hygiene Society (NVvA, http://www.arbeidshygiene.nl/english-summary/). Current distributor DOHSBASE v.o.f. (a limited liability company under Dutch law) is founded in 1994 by members of the NVvA 'Threshold Limit Values and Measurement Methods' committee (http://www.dohsbase.nl/en/about-us/history/).

DOHSBase contains:

- More than 7300 chemical substances with harmonized classification according to the ATP4 C&L/CLP/GHS [15], a IARC (www.iarc.fr) or DHC (http://www.gr.nl/en/publications/healthy-working-conditions) classifications or a the REACH Annex IV status (causing minimal risk) [13]
- more than 4500 substances with at least one $TWA_{8\ hour}$ OELV

The chemical substances with HHIs are merged with the substances with TWA 8-hours OELVs. This resulted in 970 mutually independent HHI/OELV combinations for which the physical state at OELV exceedance

is known : 630 in PPM and 340 in mg/m3. This is nearly 10 times the number used for the evaluation of the COSHH R-phrase grouping [6].

2.2 Methods

Scientific knowledge can be characterized as a common belief among experts based on reproducible outcome. The scientific method to evaluate a deterministic or empirical model, like a ranking of chemicals on their health hazard properties is to find and validate the common factors that determine the model or to compare the model with a "golden" standard. Three methods are used here to evaluate the grouping and ranking of the HHI's in an ordinal scheme (3 to 6 categories, see Figure 1):
(1) Finding common grouping factors.
(2) Comparing different grouping schemes.
(3) A comparison with the standard it replaces: the OELV.

2.2.1 A common grouping factor and mutual comparison

The HHI classification criteria are examined on the existence of a common toxicological or other health hazard factor criteria to which all HHIs depend. The null hypothesis for mutual comparison is that if HHI grouping is a universal entity, then HHI grouping schemes developed by different institutes must be equal. However if HHI grouping schemes differ, then institutional influence or other factors must play a role as well. So the similarity and differences of the HHI grouping schemes is used as a measure of the HHI grouping validity.

2.2.2 Comparison with a standard

A "golden" standard to compare HHI grouping schemes does not exist. In this and other studies [12, 11, 6, 50, 41] Occupational Exposure Limit Values (OELV) are used for comparison. The relation between substance HHI grouping and OELVs for vapor/gas in PPM and for aerosols in mg/m^3 is evaluated (see 2.2.3 through 2.2.5) using a comprehensive database with substance information on HHI and OELVs (see 2.1.4)

2.2.3 Substance selection

From the occupational exposure DOHSBase database NLXtend version 14-01 with substance OELV and HHI information, the chemical substance records are selected with the following properties:

- a OELV TWA of at least 8 hours with a level >0 with the exception of the:
    - Kick-off levels 2005
    - disseminated DNELs
    - provisional nano levels
- a IARC classification on carcinogenicity
- a Dutch Health Council (DHC) classification on carcinogenicity, mutagenicity or reprotoxicity
- Classified by ECHA Annex IV "Considered to cause minimum risk" [13]
- Information on the physical state when exceeding the OELV

Ae database table is constructed in several steps (see Table 11) with all mutual independent OELV/HHI combinations.

2.2.4 OELV distributions per HHI grouping for dust and gas/vapor

Gasses and vapors are defined as [nearly-]molecular distributed masses of a substance in the workplace air and are quantified in all HHI grouping schemes in PPM. Dusts and aerosols are non-nano conglomerates of solid or liquid molecules and are quantified in mg/m^3. The OELVs are separated first in:

- The PPM OELVs for substances with a saturation concentration (= the theoretical maximum concentration C_{sat} in mg/m^3 by evaporation in the workplace air based on its vapor pressure) that is larger than the OEL.
- The mg/m^3-OELVs of substances that can only reach the concentration level of the OELV as (in part) an aerosol. In other words the vapor pressure of these substances is below the OELV

Some solids (like Phenol) have a PPM OELV as their C_{sat} exceeds the OELV at room temperature and 1 bar and some liquids (like Sulfuric acid) have an mg/m^3 OELV as their C_{sat} is too low to exceed the OELV as a vapor.

2.2.5 The statistical analysis

2.2.5.1 The shape of the OELV distribution

OELVs for chemicals are by definition positive (>0) for all units of measurement. OELV levels vary about 11 orders of magnitude. OELVs are grouped around the median and there distributions are skewed. The medi-

an for dust/aerosol lies at 0,1 mg/m3 and for gas/vapor at 0,05 PPM (DOHSBaseCompare 14-01) and their ranges include values between 10^{-8} to 10^{+4}. Some publications assume that OELV distributions have a Lognormal shape [36, 12, 41] but no scientific evidence for this assumption exists.

The PPM is by definition censored at 10^{+6} and physically censored at the saturation concentration. Extreme low and high OELV values are exceptional. The 5000 PPM for CO2 is highest known value for vapor and gas. REACH DNELs for solids over 100 mg/m^3 exist as they are based on the toxicity properties only. In working condition policy OELV values for inhalable dusts are normally censored at a level of 10 mg/m^3, not on health considerations but due to the safety risk of a visibility disturbance and the inability to read safety and escape at or above this level. Further OELV are often rounded to preferred values like 1E-/+## (inhalable Nickel 0,01 mg/m^3) or 5-/+## (CO2 5000 PPM) making OELV distributions appear discrete graphically.

As the OELV distribution deviate in its tails, nonparametric statistical techniques are used first [44] to test the differences between the OELV distributions, graphically the 90%-tile range is displayed and parametric test are only used to approximate a desired estimator (see 2.2.5.5.)

2.2.5.2 Nonparametric techniques

In nonparametric statistics the OELV levels are replaced by their sample ranks and these ranks are used for the mutual comparison of the OELV samples within the schemes and for the estimation of the OELV distribution %-iles.

Kruskal Wallis & Page
The ordinal Kruskal-Wallis test [23] is the distribution free alternative for the parametric ANOVA test (see 2.2.5.5), if the assumption of (transformed) normality is not acceptable. It tests if the ranks of the OELVs over all HHI groups origin from the same rank distribution. The ordinal Page test [34] verifies if there is an impaired trend in the ranks over the HHI groups.

Extrapolation to population level: percentiles
As estimator of the population percentile is the OELV belonging to the rank corresponding with sample percentile used.

2.2.5.3 Lognormal goodness-of-fit

“Digital” Lognormal probability paper, meaning a graphical picturing of Log-probability paper on screen, is used to examine the distributions per HHI per state. Normal order statistics (Harter [25]) are used for the unbiased positioning of OELV on the probability axis as the OELV samples sizes within the HHI schemes are varying and are relatively small (10 to 200). The Lognormal goodness-of-fit of the OELV distributions per hazard category and state is tested:

- visually on Lognormal probability paper (see TABLE 6)
- with the Shaprio and Wilks’ omnibus W test [43].

The graphical and W-test goodness-of-fit examination is applied using HYGINIST[7] (http://www.tsac.nl/hyginist.html)
As behavior of the OELV in the tails of the distribution as described in 2.2.5.1 makes rejection of the distribution with the W-test [35] more probable, its P-value must be considered as true but as supportive to the graphical examination

2.2.5.4 Censoring

Censoring is the situation that a population values are limited in the upper or lower tail of the distribution [42]. OELV values are censored (see for inhalable dusts are known to be censored at a level of 10 mg/m^3, not on health considerations but due to the safety risk of a visibility disturbance and the inability to read safety and escape at or above this level. Preferred values in the of the distribution may appear as pseudo-censored Adjusting for censoring is done with HYGINIST (http://www.tsac.nl/hyginist.html) as demonstrated on http://youtu.be/u8-Hgs9LG3g.

2.2.5.5 Parametric techniques

The OELV samples are extrapolated and tested using parametric techniques, if the shape of the log-transformed sample is approximately bell(Gaussian)-shaped. Adjustments for censoring are made when deviations in the tail make this necessary (see 2.1.4.2.)

ANOVA & regression [46]

Single factor ANOVA tests if the log-transformed OELV samples per HHI grouping and state origin from the same population and makes it possible to approximately estimate the proportion of the OELV distribution explained by the HHI grouping.
Regression tests if the log-transformed OELVs follow an impaired linear trend over the HHI groups. A small slope probability indicates that the impaired trend over the HHI categories is straight and steep.

Percentage variance explained and OELV hazard category multiplier.
ANOVA is considered to be robust against a limited violation of its prerequisites [46]. Therefore the variance fraction of hazard grouping, is used as an estimator of the power that the hazard grouping predicts the OELV range. The ten power of the regression slope value is used as estimate of the average multiplication factor between decreasing hazard category and increasing OELV distribution.

Extrapolation to population level: Tolerance limits
The Geometric Mean (GM) is the unbiased measure of location of the OELV distribution. The Geometric Standard Deviation)GSD' is the measure of OELV dispersion. As OELV samples have different and relatively small sample sizes (10 to 200) the OELV population percentiles (%-ile) per HHI per state are estimated using the unbiased Wilk tolerance limit factor k [22]: $OEL_{\%}=GM*GSD^{\wedge k}$.

3 Results

3.1 The grouping and ranking factors

3.1.1 The classification criteria

The classification criteria for the health hazard R-phrases [17,18] and H3##-statements [20, 15, 16] in Table 12 to Table 15 show that the HHI's for inhalation, dermal and oral toxicity (TOX), irritation, corrosion & sensitization (ICS) and carcinogenicity, mutagenicity & reprotoxicity (CMR) are mutually independent as their classification criteria lack common factors for grouping or ranking.
For example the CMR classification criterion 'weight of evidence to be a human health hazard' does not exists in TOX and ICS. And the dose criteria of TOX do not exist in CRM. This accounts also for most of the other, single HHI's (like lactation) with unique classification criteria.

The Table 12 to Table 15 also show that within HHI classification criteria within the endpoints TOX (e.g. acute H300->333, repeated H370->373 per route), ICS (H314->320) and CMR (H340->362) the HHI classification criteria are ranked to some extend but of different nature (dose, severity, duration, weight of evidence) and different scales on the measuring rules (discrete, ordinal or categorical). The endpoints can have two to five ranked HHI's. Acute Toxicity R-phrases for example are in some schemes allocated in 3 to 5 discreet groups based on the dose level cut-off criteria (see Figure 3).

The EUH-statements of Table 3 are included in the COSHH HHI grouping scheme

Table 3 additional EUH statements in the COSHH HHI grouping

Hazard group	EUH statement	Description
A	EU66	Repeated exposure may cause skin dryness or cracking
C	EU71	Corrosive to the respiratory tract
E	EU70	Toxic by eye contact

3.1.2 Expert judgment

COSHH [6] and the ECHA [38] indicate that the grouping and ranking of HHI in hazard categories is based on "expert judgment". Expert judgment explains most of the qualitative differences found in 3.2.1

COSHH and Spaltenmodell group the TOX HHI's for the different routes of exposure (inhalation, dermal and oral). but EMKG groups only the oral and inhalation dose categories and developed a separate scheme for the dermal hazards. In EMKG [4] the H-statements H362 (lactation) and the EUH statements 029, 066, 070 & 071 are not included.

All schemes include substances with limited health hazard outside the classification criteria but use different descriptions and grouping and ranking. The category 0/A/Vernachlässigbar in the Spaltenmodell with the only harmless substances contains a such a limited number of substances that it is decided to merge category 0/A/Vernachlässigbar with category 1/B/Gering

The grouping and ranking differences of all HHIs are displayed in Table 9 and Table 10.

3.1.3 Classification criteria shift in the R-phrases to H-statement conversion.

For TOX the classification cut-off points differ between R-phrases and H-statements.
Some HHI groupings schemes introduced errors when shifting from R- to H-grouping (see Table 10).

Table 12 shows that the classification cut-off points for the TOX R-phrases [18] differ from the EU H3##-statements [20]. Figure 3 shows the different cut-off points for the acute oral LD50. For H-statement H300 the cut-off is at 50 mg/kg while for R-Phrase R28 is 25 mg/kg. The changed classification cut-off points for TOX make H3##-statements in most cases more hazardous than the corresponding R-phrases

Dose mg/kg	R-phrase	hazard group	CLP hazard class & -category	H-Statement	Hazard group
<5	28	D	Acute Tox 1	300	D
5-25	28	D	Acute Tox 2	300	D
25-50	25	C	Acute Tox 2	300	D
50-200	25	C	Acute Tox 3	301	C
200-300	22	B	Acute Tox 3	301	C
300-2000	22	B	Acute Tox 4	302	B

Figure 3 Oral LD50 classification criteria for R-phrases and H-statements leading to a different HHI grouping

. For CMR and ICS R-phrases and H-statements the same classification criteria are more or less the same. The COSHH (see Table 2) EMKG [30, 36] and ILO (see **Fout! Verwijzingsbron niet gevonden.**) Control Bandings are not adjusted for the different HHI classification criteria when shifting from R-phrases to H-statements. BAUA [45, 4] made the changes in the allocation of the R-phrases and there corresponding H-statements (see also Table 4) but it is unclear if this is caused by the changed cut-off points:

- the R-20, 21, 22, 23, 24 and 25 (toxicity) combined with the R-48 (repeated dose) are ranked one group up in TRGS440/600, while in the Spaltenmodell the corresponding repeated dose toxicity H-statements 372 (for 48/23,24,25) and 373 (for 48/20,21,22) are placed in same hazard category as the acute toxicity.
- R-35 and H314 for Corrosion skin burns and R-41 and H318 for Corrosion eye damage have received other hazard categories.

Table 4 R-phrases in TRGS440/660 different allocated as H-statement in DGUV Spaltenmodell

Hazard group/ Gefahr	TRGS440 [51] & TRGS600 [8]	DGUV IFA Spaltenmodel [45]
4/E/Hoch	48/23,24,25	
3/D/Mittel	48/20,21,22 35	H372 H318
2/C/Gering	41	H373 H314

3.2 Comparing grouping schemes

3.2.1 Qualitative differences

The experts that have developed the different HHI schemes group and rank H-statements in different hazard categories as pictured in Figure 4

Hazard category	DGUV IFA Spaltenmodell (TRGS600)	COSHH Essentials	BAUA EMKG (Einfaches Maßnahmenkonzept) (inhalation)
4/E	H300, H310, H330, EU032 H340 (AGS Mut 1AB) H350, H350i (AGS K1/2 & TRGS 906)	H334, H340, H341, H350, H350i	H340, H350, H350i, H360F (TRGS 905 & 906)
3/D	H301, H311, H331 EUH070, EUH029, EUH031 H370, H317 (Sh), H334 (Sa), H318 $H360_{xy}$ (AGS R_{EF}1/2) H351 (AGS K3), H341 (AGS M3), H372	H300, H310, H330 H351, $H360_{xy}$, H361, H362, H372	H300, H330, H360D, H372, EUH032
2/C	H302, H312, H332 H314 (pH ≥ 11,5, pH ≤ 2), H371, EUH071 $H361_{f/d}$, H373, H362 non-toxic gases which may cause asphyxiation	H301, H311, H331, H314, H317, H318 , H335, H370, H373, EUH071	H301, H331, H314, H334, H341, H351, H361f/d, H370, H371, H373, EUH031 (TRGS 907)
1/B	H315, H319 damage to the skin during wet work H304, EUH066, H335, H336 Substances chronically harmful in other ways (no H-statement, but still hazardous)	H302, H312, H332 H371	H302, H332, H318
0/A	substances which experience shows to be harmless (e.g. water, sugar, paraffin etc.)	H303, H304, H305, H313, H315, H316, H319, H320, H333, H336, EUH066 and all H-numbers not otherwise listed	H319, H335, H336, H304 No health hazard H-statements

Figure 4 Differences between HHI grouping schemes in allocating H-statements

3.2.2 Quantitative differences

The 970 substances with a unique HHI/OELV combination are divided over the hazard categories A to E. In Table 5 the numbers per hazard category are displayed showing considerable differences. The differences in the totals are is caused by the differences in including and excluding HHIs in the schemes.

Table 5 The distribution of the 970 HHI/OELV combinations over the hazard categories A to E

HHI grouping scheme (# hazard categories)	PPM					mg/m3					Total #
	A	B	C	D	E	A	B	C	D	E	
EMKG	105	112	122	180	110	13	43	71	68	143	967
Spaltenmodell	2	83	119	246	182	1	9	43	123	162	969
COSHH	68	56	156	225	134	8	31	54	83	148	965

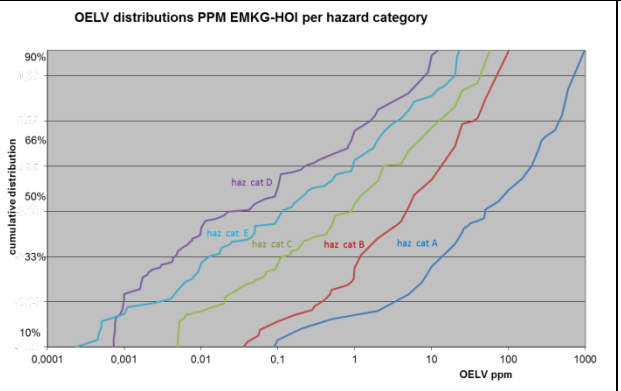
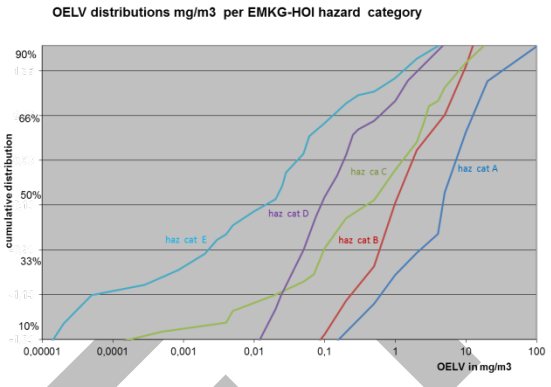
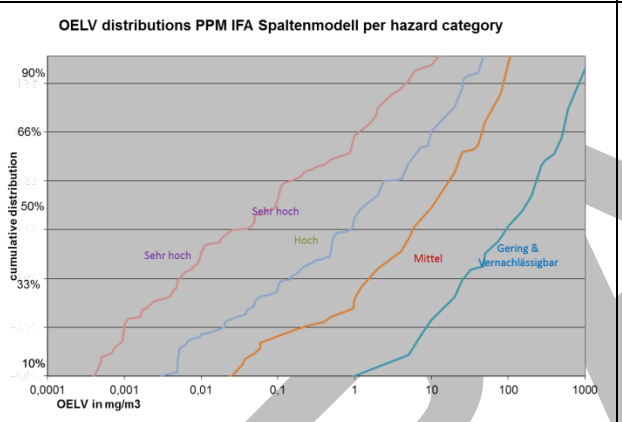
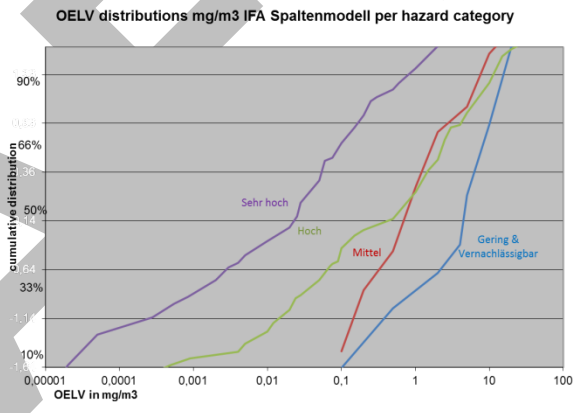
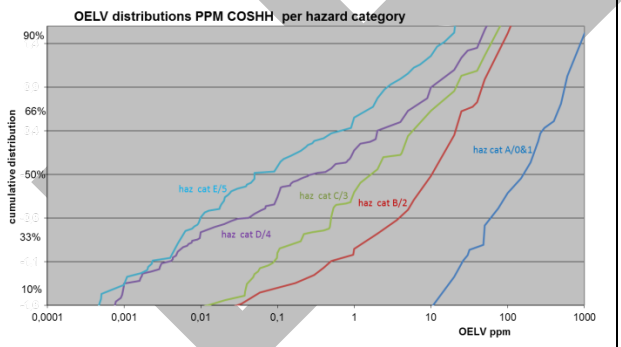
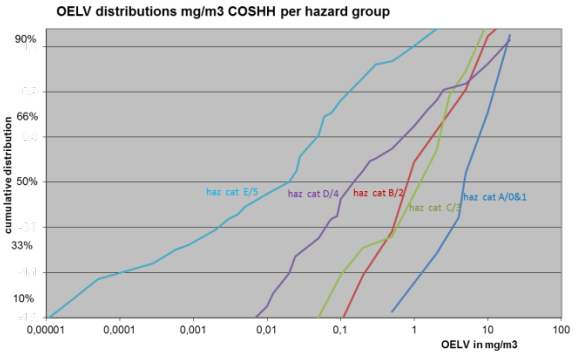
Also the number of substances having a different hazard category between the schemes are counted. Within the group of 970, COSHH and Spaltenmodell (Table 10) differ for 40%. For COSHH and EMKG this is 33%.

3.3 The best performing scheme compared to the OELV

3.3.1 OELV distributions per HHI grouping scheme

The OELV distributions per HHI scheme and per state (PPM or mg/m3) are displayed on an electronic version of Lognormal probability paper (see Table 6) .

Table 6 PPM and mg/m^3 OELV distributions per hazard category for 3 H3##-grouping schemes

	PPM	mg/m^3
EMKG		
IFA Spaltenmodell		
		

The following observations are made from the figures in Table 6:

EMGK:

- five hazard categories OELV distributions per physical state (PPM or mg/m^3)
- the PPM OELV distributions are non-parallel. The differences between the D and E distributions are small and cross at the lower side of the OELV distribution.
- The mg/m^3 OELV distributions are non-parallel, specifically the hazard category C distribution. The OELV levels at the lower side of D distribution are higher than the less hazardous C distribution.

IFA Spaltenmodell:

- four hazard categories
- Regular PPM distributions: approximately straight with the exception of B (German “mittel”), parallel, equidistant on ^{10}log-probability scale

- The lower sides of three mg/m^3 OELV distributions (A, C and D) are approximately parallel, hazard category B (German “mittel”) deviates.

COSHH:

- five hazard categories
- the PPM OELV distributions are non-parallel. The differences between the D and E distributions are small.
- The mg/m^3 OELV distributions A to D are parallel in the lower end of the distributions. The differences between the B and C distributions are small and they cross one another several times

Observationally the IFA Spaltenmodell shows the most regular PPM OELV distributions pattern. For mg/m^3 the pattern is less regular for all three grouping schemes. For mg/m^3 the COSHH if the B and C hazard categories are combined.

3.3.2 Goodness-of-fit

Of the transformations (untransformed, logarithmic, square root, squared, exponential Gaussian) tested with HYGINIST [39], the Lognormal distribution shows the best goodness-of-fit. However the most powerful Shapiro omnibus test [43] indicates that even some of the OELV sample distributions of the scheme with the most regular PPM (IFA-Spaltenmodell) or mg/m^3 (COSHH) distribution pattern in Table 6 are rejected to be drawn from a Lognormal distributed population, even if censoring is applied.

3.3.3 Non-parametric

The Kruskal-Wallis (KW) probability that the OELV series per scheme origin from the same unspecified distribution and Page test statistic for trend in the ranks over the hazard categories are displayed in **Fout! Verwijzingsbron niet gevonden.**. Since all Page tests resulted in probabilities <0.000001, the approximate standard normal Z is shown.

Table 7 Non-parametric inference tests on the OELV ranks over the hazard categories for 3 H3## grouping schemes

	PPM		mg/m3	
HHI grouping scheme	P(KW) same population	Z(Page) linear trend	P(KW) same population	Z(Page) linear trend
EMKG	8,30E-45	15,839	5,10E-19	2,878
Spaltenmodell	**3,50E-56**	**17,85**	2,19E-22	12,426
COSHH	7,90E-47	15,839	**2,70E-27**	**12,878**

The IFA Spaltenmodell (**bold**) shows the smallest probability that the PPM OELV series are from the same unspecified population with the highest probability for trend. For mg/m^3 COSHH (**bold**) shows the best performance.

3.3.4 Fraction variance explained and OELV hazard category multiplier.

In Table 8 the fraction of the OELV explained by hazard category and the multiplication factor between the OELV distributions are approximated using single factor (hazard category) ANOVA and linear regression

Table 8 Fraction variance explained and OELV hazard category multiplier

	PPM				mg/m3			
	Fraction variance explained		OELV multiplier over the hazard categories		Fraction variance explained		OELV multiplier over the hazard categories	
HHI grouping scheme (# hazard categories)	fraction	P value	Multiplier, point estimate	Confidence interval 5-95%	fraction	P value	Multiplier, point estimate	Confidence interval 5-95%
EMKG (5)	0,3	7E-46	0,21	0,17-0,26	0,27	2E-21	0,21	0,16-0,28

Spalten-modell (4)	**0,4**	**1E-68**	**0,09**	**0,07-0,12**	0,24	2E-20	0,12	0,07-0,18
COSHH (5)	0,33	8E-47	0,18	0,15-0,22	**0,35**	**1E-29**	**0,16**	**0,12-0,22**

Although the Spaltenmodell has only 4 hazard categories the fraction explained variance for PPM OELV distributions is the highest and the confidence interval of the multiplier is the smallest.
For mg/m3 the COSHH HHI grouping scheme has the highest fraction explained variance and confidence interval of the multiplier is both absolute as relative to the point estimator the smallest

4 Discussion

4.1 The grouping factor

The lack of a common factor in the classification criteria indicates that a objective, scientific, 3 to 6 ordinal HHI grouping scheme combining all HHI's does not exists.
Since there are hardly common factors in the 84 classification criteria, the HHI grouping is performed otherwise. COSHH and the ECHA indicate that the HHI groupings schemes are based on "expert judgment" [6, 38].
Experts have filled out the large in the framework to group and rank the HHIs over the hazard categories, using the guidelines on the classifications of substances [15, 16, 17,18 20, 21, 52] and their professional judgment.

4.2 Comparing different grouping schemes

If independent experts throughout the world allocate HHI's in exactly the same way than this may be
Like exposure levels and the Lognormal distribution there no theoretical base but
Researchers in Germany, UK and US all found that series independent, well sampled and measured exposure levels in a well-defined work situation are best described by the lognormal distribution.
Combining the results of observational, nonpar and parametric

4.3 The best performing scheme compared to OELV

The unequal distribution of the substances over the hazard categories for the dfferent schemes
Substances with REACH "no Exposure Scenario obligation" cannot be recognized and are therefor not included

4.4 Conversion DSD & REACH to CLP/GHS

See Table 12 R-phrases, REACH categories, EU CLP and GHS and the corresponding Health hazard classification. Toxicity

4.5 Helping SME

The focus of CB tools is more on control than on hazard and exposure and this may have lead to less attention of a correct description and allocation of HHI and a correct shift from R-phrase to H-statement based schemes.
CB are eager to promote control, which is good thing, but should be more careful with the translation of hazard to risk. All CB schemes contain errors in allocation R-phrases and H-statements. As no public comments appear nor corrections this may indicate that there is no serious use of the CBs in practical working conditions control

5 Conclusion

Objective measurable factors that can determine the allocation of Health Hazard Identifiers (HHI) like R-phrases and H-statements in ranked hazard categories as used in Control Band and Exposure Modelling grouping schemes are limited and only exist among some classification criteria endpoints like acute & chronic toxicity (TOX) and carcinogenicity, mutagenicity and reprotoxicity (CMR).

HHI grouping schemes rely therefore heavily on subjective criteria. Different international expert groups are inconsistent in the construction of HHI grouping schemes. This may lead for an individual substance to different hazard categories, different control regimes in CB and different risks in EM. The shift from R-phrases to H-statements results in less HHIs and introduces other classification cut-off points for which no visible correction is made. The current days OELVs distributions per HHI category indicate that the CB least stringent control exposure ranges are for PPM insufficient to protect workers' health. These conclusions undermine the credibility of a worldwide use of the CB and EM tools in Small and Medium Enterprises.

Despite these flaws and limitation, the three schemes analysed show a strong relation between HHI grouping and current days, health based OELVs of which DGUV_IFA GHS-Spaltenmodell performs best for PPM and COSHH performs best for mg/m^3.

6 Recommendations

CB are eager to promote control, which is good thing, but should be more careful with the translation of hazard to risk. The least stringent controls for PPM in COSHH should be upgraded as they do not comply with current day OELVs. The current schemes must be replaced by one international accepted, harmonized and optimized HHI grouping scheme. This scheme must have an optimized number of HHI groups, with the best fitting HHI allocations and must account for the shift from R-phrases to H-statements. It should be based on the smallest most distinguished Lognormal OELV distributions. This should lead to more effective, consistent and appreciated Control Banding and Exposure modelling. This work should be done under the umbrella of an international body like e.g. WHO, ILO or the International Occupational Hygiene Association (IOHA).

Supplementary data

Supplementary data can be found on www.dohsbase.com

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Table 9 Seven R-phrases based HHI groupings

Hazard group	TRGS440 [51] & TRGS600 [8] [1]	COSHH_R 2009 [27]	COSHH 1999 [6,9, 26] [2]	ECHA Hazard Bands Table_E3-1 [3]	ILO CCT[28]	SOMS [47]	ECETOC [22]
4/E	26, 27, 28, 32 45, 49 (AGS Car 1,2) 46 (AGS Mut 1,2) 48/23,24,25 [4]	42, 45, 46, 49 68	42, 45, 46, 49 40 (Mut. Cat. 3; old)	42, 45, 49 46, 68 35 26, 27, 28 43, 42 39/23,24,25 39/26,27,28	42, 45, 46, 49 68		
3/D	23, 24, 25 29, 31, 33, 35 40 (AGS Car 3) 42, 43 (Sa, Sh) 48/20,21,22 60,61 (AGS Rep 1,2) 68 (AGS Mut 3)	26, 27, 28 39/26,27,28 40 48/23,24,25 60, 61, 62, 63, 64	26, 27, 28 40 (Carc. Cat. 3; old) 48/23, 24, 25 60, 61, 62, 63	40, 34 23, 24, 25 68/20, 21, 22 36,37 & 38 [5] 43, 41	26,27,28 39/26,27,28 40 48/23, 24, 25 60, 61, 62, 63, 64	26,27,28, 40 45 , 46,49 48/23,24,25 60,61 68	26,27,28 42 48/23, 24, 25
2/C	20, 21, 22, 34, 41, 62, 63, 64 (AGS Rep 3) non-toxic gases which may cause asphyxiation	23, 24, 25 34, 35, 37 48/20, 21, 22 39/23, 24, 25 68/23, 24, 25 41, 43	23, 24, 25 34, 35 [6], 37 48/20, 21, 22 41, 43		23, 24, 25 34, 35, 37 48/20, 21, 22 39/23, 24, 25 41,43	23,24,25, 29,31, 32,34,35, 40 Carc .cat 3, 42,43, 62,63,64,67	23, 24, 25 34, 35 39, 40, 68 41,43 48/20, 21, 22 62,63
1/B	36,37,38, 65,66,67 damage to the skin during wet work. Substances chron-ically harmful in other ways (no R phrase, but still hazardous)	20, 21, 22 and 68/20, 21, 22	20, 21, 22 40	36, 37, 38	20,21,22 R68/20/21/22 [7] 33, 67	20,21,22, 41, 65	20,21,22 36,37,38 65,66,67
0/A	substances which experience shows to be harmless (e.g. water, sugar, paraffin etc.)	R36, R38 and all R-numbers not otherwise listed (65, 66, 67)	R36, R38 All dusts and vapors not allocated to another band		36,38 65,66 No R-phrases in higher categories (=hazard group)	36,37,38, 66	
Exemp-tions							45,46,49 60,61

[1] Combination phrases – where these are not listed in column TRGS – must be regarded as a compilation of individual R phrases, e.g. R39/26 as R39 and R26. R68 is only referred to for an assessment if it does not appear in a combination phrase.
[2] Note: the R-phrase combinations with R68 and R39 are omitted from the column COSHH_R 1999. R68 combined with R20, 21 or 22, R39 combined with R23, 24 or 25, enter R23 en R39 combined with R26, 27 or 28, enter R26.
[3] The R-phrases 60, 61 (reproduction toxicity) 20, 21, 22 (acute toxicity), H372 & H373 (repeated dose toxicity 1&2), H362 (lactation), H336 (drowsiness) and all EUH statements (029, 031, 032, 066, 070 & 071) are not included in the hazard groups.
[4] R phrases 20, 21, 22, 23, 24 and 25 arise in combination with the R phrase 48 one group up
[5] Only if the 3 R-phrases are attributed to the substance simultaneously, “moderate hazard” (3/D) is assigned, otherwise “low hazard” is assumed (2/C).
[6] Red : skin and eye contact
[7] ILO toolkit [28] uses the non existing R-phrase combination R40 with R20/21/22 where probably R68/20/21/22 is meant

Table 10 Four H-statements based HHI groupings

HHHI group	DGUV IFA spaltenmodel TRGS 600 [45]	COSHH [27]	BAUA.EMKG Inhalation [24]. Einfaches Maßnahmenkonzept[8].	ECHA Hazard Bands Table_E3-1[14][9]
4/E	H300, H310, H330, EU032 H340 (AGS Mut 1AB) H350, H350i (AGS K1/2 & TRGS 906)	H334, H340, H341, H350, H350i EU70	H340, H350, H350i, H360F (TRGS 905 & 906)	H300, H310, H330 H340, H341 H350, H350i Skn Corr 1A H314, Skn sens 1 or 1A H317, H334 H370
3/D	H301, H311, H331 EUH070, EUH029, EUH031 H370, H317 (Sh), H334 (Sa), H318 $H360_{xy}$ (AGS R_{EF}1/2) H351 (AGS K3), H341 (AGS M3), H372	H300, H310, H330 H351, $H360_{xy}$, H361, H362, H372	H300, H330, H360D, H372, EUH032	H301, H311, H331 H351, H360xy, H361, H362, H371 Corr 1BC H314 H315,319 & 335[10] Skn sens 1B H317 Eye Dam 1 H318
2/C	H302, H312, H332 H314 (pH ≥ 11,5, pH ≤ 2), H371, EUH071 $H361_{f/d}$, H373, H362 non-toxic gases which may cause asphyxiation	H301, H311, H331 H314, H317, H318 , H335 H370, H373 EUH071	H301, H331, H314 H334, H341, H351, H361f/d, H370, H371, H373, EUH031 (TRGS 907)	
1/B	H315, H319 damage to the skin during wet work H304, EUH066, H335, H336 Substances chronically harmful in other ways (no H-statement, but still hazardous)	H302, H312, H332 H371	H302, H332, H318	H315, H319, H335
0/A	substances which experience shows to be harmless (e.g. water, sugar, paraffin etc.)	H303, H304, H305, H313, H315, H316, H319, H320, H333, H336, EUH066 and all H-numbers not otherwise listed[11]	H319, H335, H336, H304 No health hazard H-statements	

[8] The H-statements H362 (lactation), the EUH statements 029, 066, 070 & 071 and the skin related H-statements H312**; H315, H317, H371*; H373*, H311; H314 (Hautätz. 1B, 1C); H341*; H351*; H361*; H370*; H372*, H310; H314 (Hautätz. 1A); H340*; H350*, H360* are not included in the EMKG CB scheme for inhalation.

[9] The H-statements 360, 361 (reproduction toxicity) H302, H312, H332 (acute toxicity 4), H372 & H373 (repeated dose toxicity 1&2), H362 (lactation), H336 (drowsiness) and all EUH statements (029, 031, 032, 066, 070 & 071) are not included in the ECHA hazard bands.

[10] Only if the 3 irritation hazard statements are attributed to the substance simultaneously, “moderate hazard” (3/D) is assigned in the ECHA CB scheme , otherwise “low hazard” is assumed (1/B).

[11] HSE confirmed that there is an error on page 5 of The Technical Basis for COSHH Essentials and that H318 should only be mentioned in group C. The document is due to be revised and this error will be amended (email HSE 2014 Jan 16).

Table 11 Steps to construct the substance database with mutually independent OELV- HHI combinations for gas/vapour (PPM) and aerosols (mg/m3)

step	Description
0	The records from the DOHSBase NL-Extend 14-01 OELV table (dohsgrsw.dbf) with a workplace air OELV>0 TWA 8 hours or more, excluding DNELs, nano reference values, Kickoff levels, or with a CMR classification or REACH annex IV
1	OELV records with the following units of measurements are removed: • Empty unit of measurement • fibres/cm3 or /ml • CMU/m3 • EU/m3 • particles/cm3 • glicine units/m3 • fibrils/ml
2	Records with a Dutch Health Council OELV advice of 0,1 mg/m3 for mineral oils substances with different ID# and CAS-numbers 6474#-##-# are removed, with the exception of Petrolatum (8009-03-8) which HHI-OWLV combination is considered to be representative of the whole group.
3	Lacking HHIs are added to the following substances: • Magnesium sodium fluoride silicate • Rosin • Refractory Ceramic Fibres, Special Purpose • Ttrialkylborates • Hexylacetate{sec-} • Trimethyltin compounds • Piperazine anhydraat • Piperazine [liquid]
4	The respirable dust OELV for a substance is removed if an inhalable dust OELV exist for the same substance which is established by the same limit setting organization.
5	The records with a carcinogenicity, mutagenicity or reprotoxicity (CRM) classification of IARC, Dutch Health Council and ACGIH are copied to a separate table if a health based OELV for the same CAS# exists. The CRM HHI property is linked to the OELV record(s) later on (see 0).
6	The records with the REACH ANNEX IV property “Considered to cause minimum risk” are copied to a separate table, if a health based OELV for the same CAS# exists. This property is linked to the OELV record(s) later on (see step 0).
7	OELVs with the following units of measurements are recalculated to mg/m3: • “ug/m3” is divided by 1000 • “ng/m3” is divided by 1000000 • “pg/m3” is divided by 1000000000
8	Low Hierarchy regulatory OELVs are removed if one or more high hierarchy health based OELV are available. The remaining database table contains substances with at least one health based OELV or one regulatory OELV.
9	The physico/chemical information on the state (vapour, liquid, gas) or to establish the physical state by which the substance exceeds the OELV is linked to the OELV records using the CAS#. The saturation concentration and the ratio OELV/saturation concentration are calculated.
10	The ID# harmonized R-phrases and H-statements are linked to the OELV records using the CAS#. For multiply or group Harmonized HHIs with equal multiple or group OELV (like the xylenes) only one CAS# is linked per limit setting organisation.
11	Substances without clear information on the physical state at OELV exceedance are removed.
12	The physical state at OELV exceedance at 25 C and 1 bar is established using the ratio OELV/saturation concentration: • If OELV>10*C_{sat}: then the OELV exceedance concentration will contain more 90% aerosol and the state is indicated as ”aerosol” • If C_{sat}<OELV <=10* C_{sat} then the OELV exceedance concentration will contain at most 90% aerosol and the state is indicated as ”vapor and/or aerosol” • If OELV< C_{sat} then the OELV exceedance concentration will contain no or a limited amount of aerosol and the state is indicated as ”vapor”
13	For a limited number of substances with unpublished information on their physical state, the state is entered or removed based on professional judgement.
14	The DSD R-phrases and the CLP H-statements on Carcinogenicity and Mutagenicity for Benzene, Butadiene and/or Pitch containing impurities above 0,1% are removed, since health based OELV are based on the substance and not on the impurities.

15 The REACH ANNEX IV property “Considered to cause minimum risk” is linked to the OELV record using the CAS# and used for HHI grouping if possible.
16 The EMKG, IFA_Spaltenmodell and COSHH hazard groups are established based on the substance H- and EUH hazard phrases.
17 EMKG, IFA_Spaltenmodell and COSHH hazard groups are increased if motivated by the classification of IARC, DECOS or ACGIH.
18 If OELV and the HHI are for a different components in the substance (like BeF2 with HHI for Be and the OELV for F^-) then the record is removed
19 Recalculate mg/m3 to PPM and vice versa if the OELV lacks the unit of measurement for the OELV exceedance state.

Table 12 R-phrases, REACH categories, EU CLP and GHS and the corresponding Health hazard classification. Toxicity.

Classification criteria for the choice of the health hazard indicators (HHI) R-phrase, H-statement and GHS hazard				EU DSD[17,18], CLP [20] and REACH[19] categories			UNECE [52]
nature: toxicity	operator	level		DSD R-phrase/ REACH	CLP Health hazard class and category code	CLP H-State ment	GHS Hazard class, category and statement
		Quantity	Units				
Acute lethal - oral (LD50)	≤	5	mg/kg	28	Acute Tox 1	300	Acute Tox 1 H300
	=	5-25	mg/kg	28	Acute Tox 2	300	Acute Tox 2 H300
	=	25-50	mg/kg	25	Acute Tox 2	300	Acute Tox 2 H300
	=	50-200	mg/kg	25	Acute Tox 3	301	Acute Tox 3 H301
	=	200-300	mg/kg	22	Acute Tox 3	301	Acute Tox 3 H301
	=	300-2000	mg/kg	22	Acute Tox 4	302	Acute Tox 4 H302
	=	2000-5000	mg/kg	no REACH registration Exposure Scenario Obligation			Acute Tox 5 H303
Acute lethal - oral (LD0)	>	5000	mg/kg	Considered to cause minimum risk REACH Annex IV			
Acute lethal - dermal (rat/rabbit) (LD50)	≤	50	mg/kg	27	Acute Tox 1	310	Acute Tox 1 H310
	=	50-200	mg/kg	24	Acute Tox 2	310	Acute Tox 2 H310
	=	200-400	mg/kg	24	Acute Tox 3	311	Acute Tox 3 H311
	=	400-1000	mg/kg	21	Acute Tox 3	311	Acute Tox 3 H311
	=	1000-2000	mg/kg	21	Acute Tox 4	312	Acute Tox 4 H312
	=	2000-5000	mg/kg	no REACH registration Exposure Scenario Obligation			Acute Tox 5 H313
Acute lethal - dermal (LD0)	>	5000	mg/kg	Considered to cause minimum risk REACH Annex IV			
Acute lethal - inhalation aerosol (Dust/mist CLP) (LC50)	≤	50	mg/m3/4hr	26	Acute Tox 1	330	Acute Tox 1 H330
	=	50-250	mg/m3/4hr	26	Acute Tox 2	330	Acute Tox 2 H330
	=	250-500	mg/m3/4hr	23	Acute Tox 2	330	Acute Tox 2 H330
	=	500-1000	mg/m3/4hr	23	Acute Tox 3	331	Acute Tox 3 H331
	=	1000-5000	mg/m3/4hr	20	Acute Tox 4	332	Acute Tox 4 H332
	=	5000-12500	mg/m3/4hr	no REACH registration Exposure Scenario Obligation			Acute Tox 5 H333
Acute lethal - inhalation aerosols or particulates (LC0)	>	12500 (LC0)	mg/m3/4hr	Considered to cause minimum risk REACH Annex IV			
Acute lethal - inhalation vapor (& gas DSD) (LC50)	≤	500	mg/m3/4hr	26	Acute Tox 1	330	Acute Tox 1 H330
	=	500-2000	mg/m3/4hr	23	Acute Tox 2	330	Acute Tox 2 H330
	=	2000-10000	mg/m3/4hr	20	Acute Tox 3	331	Acute Tox 3 H331
	=	10000-20000	mg/m3/4hr	20	Acute Tox 4	332	Acute Tox 4 H332
	=	20000-50000	mg/m3/4hr	no REACH registration Exposure Scenario Obligation			Acute Tox 5 H333
Acute lethal - inhalation vapor & gas (LC0)	>	50000	mg/m3/4hr	Considered to cause minimum risk REACH Annex IV			
Acute lethal - inhalation gas only (CLP)	≤	100	PPM/4hr	n. a.	Acute Tox 1	330	Acute Tox 1 H330
	=	100-500	PPM/4hr	n. a.	Acute Tox 2	330	Acute Tox 2 H330
	=	500-2500	PPM/4hr	n. a.	Acute Tox 3	331	Acute Tox 3 H331
	=	2500-20000	PPM/4hr	n. a.	Acute Tox 4	332	Acute Tox 4 H332
Acute, Specific organ, non lethal - oral	≤	25	mg/kg	39/28	STOT SE 1	370	STOT SE 1. H370
	=	25-200	mg/kg	39/25	STOT SE 1	370	STOT SE 1. H370
	=	200-300	mg/kg	68/22	STOT SE 1	370	STOT SE 1. H370
	=	300-2000	mg/kg	68/22	STOT SE 2	371	STOT SE. 2 H371
	>	2000 (NOEL)	mg/kg	Considered to cause minimum risk REACH Annex IV			
Acute, Specific organ, non lethal - dermal (rat/rabbit)	≤	50	mg/kg	39/27	STOT SE 1	370	STOT SE 1. H370
	=	50-400	mg/kg	39/24	STOT SE 1	370	STOT SE 1. H370
	=	400-1000	mg/kg	68/21	STOT SE 1	370	STOT SE 1. H370
	=	1000-2000	mg/kg	68/21	STOT SE 2	371	STOT SE. 2 H371

Classification criteria for the choice of the health hazard indicators (HHI) R-phrase, H-statement and GHS hazard				EU DSD[17,18], CLP [20] and REACH[19] categories			UNECE [52]
nature: toxicity	operator	level		DSD R-phrase/ REACH	CLP Health hazard class and catego-ry code	CLP H-State ment	GHS Hazard class, category and statement
		Quantity	Units				
Acute, Specific organ, non lethal - dermal	>	2000 (NOEL)	mg/kg	Considered to cause minimum risk REACH Annex IV			
Acute, Specific organ, non lethal - inhalation aerosol (Dust/mist CLP)	≤	250	mg/m3/4hr	39/26	STOT SE 1	370	STOT SE 1. H370
	=	250-1000	mg/m3/4hr	39/23	STOT SE 1	370	STOT SE 1. H370
	=	1000-5000	mg/m3/4hr	68/20	STOT SE 2	371	STOT SE. 2 H371
Acute, Specific organ, non lethal - inhalation aerosols or particu-lates	>	5000 (NOEL)	mg/m3/4hr	Considered to cause minimum risk REACH Annex IV			
Acute, Specific organ, non lethal - inhalation vapour (& gas DSD)	≤	500	mg/m3/4hr	39/26	STOT SE 1	370	STOT SE 1. H370
	=	500-2000	mg/m3/4hr	39/23	STOT SE 1	370	STOT SE 1. H370
	=	2000-10000	mg/m3/4hr	68/20	STOT SE 1	370	STOT SE 1. H370
	=	10000-20000	mg/m3/4hr	68/20	STOT SE 2	371	STOT SE. 2 H371
Acute, Specific organ, non lethal - inhalation gas only (CLP)	≤	2500	PPM/4hr	n. a.	STOT SE 1	370	STOT SE 1. H370
	=	2500-20000	PPM/4hr	n. a.	STOT SE 2	371	STOT SE. 2 H371
Acute, Specific organ, non lethal - inhalation vapor & gas	>	20000 (NOEL)	mg/m3/4hr	Considered to cause minimum risk REACH Annex IV			
Repeated dose - oral	≤	5	mg/kg/d	48/25	STOT RE 1	372	STOT RE 1. H372
	=	5-10	mg/kg/d	48/25	STOT RE 1	372	STOT RE 1. H372
	=	10-50	mg/kg/d	48/22	STOT RE 2	373	STOT RE 2. H373
	=	50 -100	mg/kg/d	n. a.	STOT RE 2	373	STOT RE 2. H373
	=	100-500	mg/kg/d	no REACH registration Expo-sure Scenario Obligation			
	>	500 (NOEL)	mg/kg/90d	Considered to cause minimum risk REACH Annex IV			
Repeated dose - dermal (rat/rabbit)	≤	10	mg/kg/d	48/24	STOT RE 1	372	STOT RE 1. H372
	=	10 - 20	mg/kg/d	48/21	STOT RE 1	372	STOT RE 1. H372
	=	20-100	mg/kg/d	48/21	STOT RE 2	373	STOT RE 2. H373
	=	100 -200	mg/kg/d	n. a.	STOT RE 2	373	STOT RE 2. H373
	=	200-1000	mg/kg/d	no REACH registration Expo-sure Scenario Obligation			
	>	1000 (NOEL)	mg/kg/90d	Considered to cause minimum risk REACH Annex IV			
Repeated dose - inhalation aerosol (Dust/mist CLP)	≤	0,02	mg/l/6hr/d	48/23	STOT RE 1	372	STOT RE 1. H372
	=	0,02- 0,025	mg/l/6hr/d	48/23	STOT RE 2	373	STOT RE 2. H373
	=	0,025 - 0,2	mg/l/6hr/d	48/20	STOT RE 2	373	STOT RE 2. H373
	=	0,2 - 0,25	mg/l/6hr/d	48/20	n. a.		
Repeated dose - inhalation vapour	≤	0,025	mg/l/6hr/d	48/23	STOT RE 1	372	STOT RE 1. H372
	=	0,025- 0,2	mg/l/6hr/d	48/20	STOT RE 1	372	STOT RE 1. H372
	=	0,2 - 0,25	mg/l/6hr/d	48/20	STOT RE 2	373	STOT RE 2. H373
Repeated dose- inhalation gas DSD	≤	0,025	mg/l/6hr/d	48/23			
	=	0,025 - 0,25	mg/l/6hr/d	48/20			
Repeated dose - inhalation gas CLP	≤	50	PPM/6hr/d	n. a.	STOT RE 1	372	STOT RE 1. H372
	=	50-250	PPM/6hr/d	n. a.	STOT RE 2	373	STOT RE 2. H373
Repeated dose –non lethal	accumulation in the human body is likely and may cause some con-cern which, however, is not suffi-cient to justify the use of R48.			33	STOT RE 2	373	STOT RE 2. H373
Repeated dose - inhalation vapour & gas	=	0,25- 2,5	mg/l/6hr/d	no REACH registration Expo-sure Scenario Obligation			
Repeated dose - inhalation vapour, gas & aerosol	>	2,5 (NOEL)	mg/l/6hr/90d	Considered to cause minimum risk REACH Annex IV			

Table 13 R-phrases, REACH categories, EU CLP and GHS for corrosion, irritation & sensitization and their corresponding Health hazard classifications.

Classification criteria for the choice of the health hazard indicators (HHI) R-phrase, H-statement and GHS hazard				EU DSD[17,18], CLP [20] and REACH[19] categories			UNECE [52]
Nature: corrosion, irritation, sensitization	operator	exposure duration		DSD R-phrase/ REACH	CLP Health hazard class and catego-ry code	CLP H-State ment	GHS Hazard class, category and statement
		Quantity	Untis				
Causes severe skin burns and eye damage - animal skin		3-60	minutes	34	Skin corr. 1B	314	Skin Corr. 1B. H314
Causes severe skin burns and eye damage - animal skin		60-240	minutes	34	Skin corr. 1C	314	Skin Corr. 1C. H314
Causes severe skin burns and eye damage - animal skin	≤	3	minutes	35	Skin corr. 1A	314	Skin Corr. 1A. H314
Corrosive to the respiratory tract (acute inhalation toxicity)						euh071	n. a.
Significant inflamation for > 24 hours (but reversible 14 days) dermal: for erythema/eschar ≥ 2.3 -≤4.0 - exposure duration	≤	4	hours	38	Skin irrit. 2	315	Skin irrit. 2. H315
Significant inflamation for > 24 hours (but reversible 14 days) dermal: for erythema/eschar ≥ 2.0 -<2.3 - exposure duration	≤	4	hours	38	n. a.	n. a.	Skin irrit. 3. H316
Significant inflamation for > 24 hours (but reversible 14 days) dermal: for erythema/eschar ≥ 1.5 -<2.0 - exposure duration	≤	4	hours		n. a.	n. a.	Skin irrit. 3. H316
Causes serious eye damage - High Ocular lesion values				41	Serious eye dam. 1	318	Eye dam. 1 H318
Causes serious eye irritation - Low Ocular lesion values				36	Eye irrit. 2	319	Eye irrit. 2A H319
Causes serious eye irritation - Low Ocular lesion values				36	Eye irrit. 2	319	Eye irrt. 2B H320
May cause respiratory irritation. Single exposure				37	STOT SE 3	335	STOT SE 3. H335
May cause an allergic skin reaction				43	Skin Sens. 1 or 1A	317	Skin Sens. 1 or 1A. H317
May cause an allergic skin reaction				n. a.	Skin Sens. 1B	317	Skin Sens. 1B H317
Inhalation sensitisation				42	Respir. Sens. 1 or 1A	334	Respir. Sens 1 or 1A. H334
May cause allergy or asthma symptoms or breathing difficul-ties if inhaled				n. a.	Respir. Sens. 1B	334	Respir. Sens 1B H334
No sensitisation, eye irritation, skin irritation, harm to breastfed babies, narcotic effects, danger of cumulative effects				Considered to cause minimum risk REACH Annex IV			

Table 14 R-phrases, REACH categories, EU CLP and GHS for Carcinogenicity, Mutagenicity & Reprotoxicity and their corresponding Health hazard classifications

Classification criteria for the choice of the health hazard indicators (HHI) R-phrase, H-statement and GHS hazard				EU DSD[17,18], CLP [20] and REACH[19] categories			UNECE [52]
Nature: Carcinogenicity, Mutagenicity, Reprotoxicity		Weight of evidence		DSD R-phrase/ REACH	CLP Health hazard class and category code	CLP H-State ment	GHS Hazard class, category and statement
Known human carcinogen,		Largely based on human evidence	Carc cat 1	45	Carc 1A	350	Carc 1. H350
Known human carcinogen, lung			Carc cat 1	49	Carc 1A	350i	Carc 1. H350
Presumed human carcinogen,		Largely based on animal evidence	Carc cat 2	45	Carc 1B	350	Carc 1. H350
Presumed human carcinogen, lung			Carc cat 2	49	Carc 1B	350i	Carc 1. H350
Suspected human carcinogens			Carc cat 3	40	Carc 2	351	Carc 2. H351
no evidence of carcinogenic potential				Considered to cause minimum risk REACH Annex IV			
Known human mutagen, germ cell.		Epidemiological evidence	Muta cat 1	46	Muta 1A	340	Muta 1. H340
Regarded as human mutagen, germ cell.		Other evidence	Muta cat 2	46	Muta 1B	340	Muta 1. H340
Suspected human mutagen			Muta cat 3	68	Muta 2	341	Muta 2. H341
no evidence of mutagenic potential				Considered to cause minimum risk REACH Annex IV			
Known human reproductive toxicant. Sexual function and fertility.		Largely based on human evidence	Repr cat 1	60	Repr 1A	360F	Repr 1. H360
Known human reproductive toxicant. Development.			Repr cat 1	61	Repr 1A	360D	Repr 1. H360
Presumed human reproductive toxicant. Sexual function and fertility		Largely based on animal evidence	Repr cat 2	60	Repr 1B	360F	Repr 1. H360
Presumed human reproductive toxicant. Development.			Repr cat 2	61	Repr 1B	360D	Repr 1. H360
Suspected human reproductive toxicant. Sexual function and fertility.			Repr cat 3	62	Repr 2	361f	Repr 2. H361
Suspected human reproductive toxicant. Development			Repr cat 3	63	Repr 2	361d	Repr 2. H361
Lactation effect				64	Lact	362	H362
		Quantity	Units				
no evidence of reproductive toxicity: oral route	>	1000 (NOEL)	mg/kg/d	Considered to cause minimum risk REACH Annex IV			
no evidence of reproductive toxicity: dermal route	>	2000 (NOEL)	mg/kg/d				
no evidence of reproductive toxicity: inhalation route	>	20 (NOEL)	mg/l/6h/d				

Table 15 R-phrases, REACH categories, EU CLP and GHS and their corresponding Health hazard classifications

Classification criteria for the choice of the health hazard indicators (HHI) R-phrase, H-statement and GHS hazard		EU DSD[17,18], CLP [20] and REACH[19] categories			UNECE [52]
Other endpoints		DSD R-phrase/ REACH	CLP Health hazard class and catego-ry code	CLP H-State ment	GHS Hazard class, category and statement
Lung damage if swallowed (Xn)				304	Asp. cat 1. H304
Lung damage if swallowed		n. a.	n. a.	n. a.	Asp. cat 2. H305
Repeated exposure may cause skin dryness or cracking		66	n.a.	euh066	n. a.
May cause drowsiness or dizzi-ness. Single exposure		67	STOT SE 3	336	STOT SE. 3 H336
Liquid contact gas release with Water: toxic gas		29	n.a.	euh029	n. a.
Liquid contact gas release with Acid: toxic gas		31	n.a.	euh031	n. a.
Liquid contact gas release with Acid: very toxic gas		32	n.a.	euh032	n. a.
Toxic by eye contact		39-41	n.a.	euh070	n. a.
No endocrine activity		Considered to cause minimum risk REACH Annex IV			
No PBT nor vPvB					
Not listed in Annex II or Annex III of the Cosmetic Directive 76/768/EEC.					