DNELs for workplaces – observations from an inspection of the DGUV DNEL list

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Abstract Derived No-Effect Levels (DNELs) are established by manufacturers and importers in the context of the EU REACH chemical programme and provide new assessment benchmarks for health protection at work. The DNEL list of the German Social Accident Insurance has facilitated virtual access to many DNELs relevant to the workplace. An initial review of the DNEL list has revealed a number of discrepancies and shortcomings, e.g. DNELs for substances without a known toxicological effect threshold or an excessively frequent number of identical DNELs for a substance's systemic and local effects. Such simple evaluations could help to optimise a generally welcome tool for exposure assessment.

DNEL-Werte für Arbeitsplätze – Beobachtungen beim Sichten der DNEL-Liste der DGUV

Zusammenfassung DNEL-Werte (DNEL, Derived No-Effect Levels) werden im Rahmen des EU-Chemikalienprogramms REACH von den Inverkehrbringern aufgestellt und liefern dem Gesundheitsschutz bei der Arbeit neue Beurteilungsmaßstäbe. Mit der DNEL-Liste der Deutschen Gesetzlichen Unfallversicherung wurde der Zugang zu vielen arbeitsplatzrelevanten DNEL-Werten über das Internet erleichtert. Eine erste Sichtung der DNEL-Liste brachte einige Widersprüche und Mängel zutage, z. B. DNEL-Werte für Stoffe ohne bekannte toxikologische Wirkschwelle oder eine überhäufige Anzahl von identischen DNEL-Werten für die systemische und lokale Wirkung eines Stoffes. Solche einfachen Auswertungen könnten dazu beitragen, ein grundsätzlich willkommenes Instrument der Expositionsbewertung zu optimieren[1)].

1 DNELs

The substance-related information demanded in accordance with "REACH" [1], the EU Regulation on chemicals and their safe use, also includes DNELs (Derived No-Effect Levels). For quantities of 10 t or more manufactured or imported per year, manufacturers and importers have to establish these exposure limits for activities with dangerous substances and include them in the Chemical Safety Report and Safety Data Sheet. Although the declaration of DNELs on the website of the European Chemicals Agency (ECHA) is not obligatory, a large number of DNELs are already available there, integrated in the database of registered substances [2]. These are important benchmarks for the assessment of exposure in the absence of binding national limit values for the substance in question. In Germany, for instance, employers are thus still bound by the workplace limit values (AGWs) given in the Technical Rule for Hazardous Substances (TRGS) 900 [3] for the workplace air. However, the DNELs for employees must be taken into consideration in the hazard assessment [4 to 6].

In accordance with the provisions of the REACH Regulation, DNELs have to be derived for the most likely exposure routes (inhalation, dermal and/or oral) for each relevant population (e.g. workers, consumers and humans liable to exposure indirectly via the environment) and possibly for certain vulnerable sub-populations (e.g. children, pregnant women). As assistance with implementation of REACH, ECHA Guidance chapter R.8 [7] names 15 different types of DNELs (the IUCLID software established for registration even provides for 18 types of DNELs), four of which are particularly important for the workplace:

- workers: long-term – inhalation, systemic effects,
- workers: long-term – inhalation, local effects,
- workers: long-term – dermal, systemic effects,
- workers: long-term – dermal, local effects.

2 The DGUV DNEL list

The DNEL database [8] of the GESTIS Hazardous Substances Information System of the German Social Accident Insurance (DGUV) has been available to all interested parties on the Internet since the beginning of 2013. The central element is a list of workplace-relevant DNELs, i.e. those for workers subject to long-term inhalation exposure (local and systemic effects), which were compiled by the German Social Accident Insurance Institution for the Building Trade. The Internet presentation is managed and supervised by a DNEL list work group coordinated by DGUV.

The vast majority of the DNELs in the DGUV list were taken in mid-2012 from the substance-related registration entries stored on the website of the European Chemicals Agency [2]. Most of these are "high production volume chemicals" that were processed by manufacturers and importers in the first REACH registration period: substances of which at least one company produces or imports at least 1,000 t per year and environmentally hazardous substances from 100 t per year and carcinogenic, mutagenic or reprotoxic substances from 1 t per year were to be registered by 1 December 2010. Roughly 75% of the substances in the DGUV DNEL list belong to the ≥ 1,000 t per year category, roughly 10% ≥ 100 t per year and roughly 5% ≥ 1 t per year. For 7% of the substances, the production volume is confidential and 2% have been registered merely as intermediate products. A very small

[1)] Der vollständige Text in deutscher Sprache steht im Internet zur Verfügung (www.gefahrstoffe.de, Rubrik: Anlagen zu Beiträgen im Heft).

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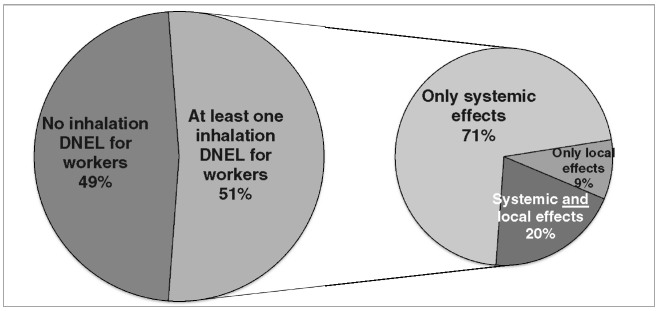

Figure 1. Share of substances fully registered by mid-2012 that have inhalation DNELs for workers – distribution of DNELs according to exposure category.

number of DNELs in the DGUV list came from Safety Data Sheets.

Skin exposure can also undoubtedly play an important role at the workplace. Since only little experience is available for the calculation of limit values for dermal exposure, standardised measuring methods for individual substances are lacking, and only a few reference measured values are available, the DGUV DNEL list is initially confined to workplace-relevant limit values for long-term inhalation.

For 1,781 substance entries, the DGUV DNEL list currently (August 2013) contains at least one workplace-relevant long-term DNEL. For a portion of 1,290 substances having a clear chemical definition, the GESTIS DNEL database contains additional specific information such as synonyms, structural formula, the German workplace limit value (AGW), if available, and a note in case the substance in question is classified as a proven carcinogen. The remaining roughly 500 substances with a DNEL are in many cases reaction mixtures and chemically not clearly identifiable entries from the ECHA website (e.g. "Rosin, fumarated, reaction products with formaldehyde"). Even terms such as "Z-44", "Renewable hydrocarbons (Diesel type fraction)", "Ashes (residues), rice husk" or simply "None available" have been entered as substance names.

In accordance with the REACH Regulation's time-table, chemicals manufactured in EU member states or imported into them in quantities of 100 to 1,000 t per year had to be registered with ECHA by 1 June 2013. According to information from ECHA [9], over 9,000 registrations for about 2,900 substances were submitted in this second phase. Most of these have already been posted on the ECHA website. As during the first period, a disproportionate large number of German companies have participated.

The following is confined to those substances that were submitted for registration by mid-2012. These are roughly 5,300 substances, of which approx. 1,800 have a long-term inhalation DNEL for the workplace, and these currently form the basis of the DGUV DNEL list.

3 Workplace DNELs on the ECHA website

The details from the registration entries of manufacturers and importers, including the substance-related DNELS, are published unchecked by ECHA on its website [10]. However, ECHA's last progress report [11] complains of considerable shortcomings in the dossiers received and particularly with regard to substance identity, exposure determination, risk description and certain toxicological tests. According to an ECHA newsletter [12], over half of the registration dossiers had quality shortcomings. In its dossier evaluations, ECHA itself has the task of checking 5% of the registration dossiers for compliance with requirements (REACH Regulation, Article 41). The examination of a DNEL is possible in this context, but this is not listed in the priorities according to which dossiers are to be selected.

Under the Rolling Action Plan [13], the EU member states are to conduct substance evaluations for problematical substances. In their selection, priority is given to persistent, bioaccumulative and ecotoxic substances and to those with carcinogenic, mutagenic, reprotoxic (CMR) or sensitising properties. The purpose of substance evaluation is to thoroughly examine the submitted risk assessment, request missing data and if necessary propose restrictions or authorisation obligations. DNEL corrections can be demanded [14].

It can be assumed that most DNELs have not so far undergone an independent quality control. Documents describing the derivation method are not accessible to the scientific community. In several cases an "overall assessment factor" is disclosed with which the DNEL was calculated; here the maximum dose or concentration with no observed adverse effect level (NOAEL) on health is the starting point in most cases.

The DGUV DNEL list work group is not in a position to scientifically check the DNELs either. However, even a cursory review of the DNEL list reveals certain discrepancies which will be presented in greater detail here. Since copying mistakes cannot be excluded during the compilation of the DNEL list by DGUV, the following may contain numeric inaccuracies or omissions, but this has no effect on the trends described:

1. A total number of about 5,300 substances were registered with ECHA by mid-2012. About 3,500 of these substances were fully registered, i.e. not with a limited set of data, as is permitted for isolated intermediates, for instance. Of these 3,500, only about 1,800 substances had registration entries containing at least one long-term inhalation DNEL for workers. **Figure 1** shows that these are mainly long-term inhalation DNELs for systemic effects. 9% of the substances have a DNEL exclusively for the local effect. 20% have DNELs for both systemic and local long-term effects.
2. In 211 registration entries, amounting to 12% of all substances in the DGUV DNEL list and to over 55% of all substances having a DNEL for both the local and systemic effects, the DNELs for the two categories were identical.
3. For only 43 substances (2% of all substances in the DGUV DNEL list) there are several registration entries with differing workplace DNELs for the local and/or systemic effects (long-term inhalation). Concerning petroleum-based mixtures and fractions, the divergences are in some cases considerable (up to a factor of 60). But even for chemically clearly definable individual substances like sodium chlorate (entry A: DNEL systemic 5 mg/m³; entry B: DNEL systemic 0,51 mg/m³) or triethylene glycol monobutyl ether (entry A: DNEL local 30,5 mg/m³, systemic 24 mg/m³; entry B: DNEL local –; systemic 195 mg/m³), the range can be considerable. For xylene, one registrant's systemic DNEL of 77 mg/m³ for the isomer mixture is lower than the local and systemic DNELs of the individual isomers from other registrations (221 mg/m³). The DGUV DNEL list work group will report such discrepancies to ECHA and the German Committee on Hazardous Substances (AGS).
4. Of the substances listed on the ECHA website with DNELs, 43 (2% of all substances in the DGUV DNEL list) are classi-

fied in Annex VI of the CLP Regulation [15] or by the manufacturer as H350/R45 or H350i/R49 as a proven carcinogen (registration data) or listed in the German Technical Rule 905 (directory of substances that are carcinogenic, mutagenic or toxic to reproduction [16]) in cancer category 1 or 2 (i.e. 1A or 1B according to the CLP system). In the GESTIS DNEL database, such DNELs continue to be named, but appear with a clear warning.

5. The substances listed in **Table 1** are not classified as harmful, but have astonishingly low DNELs (< 1 mg/m³).

Table 1. Substances with very low DNELs not classified as harmful.

Substance	CAS number	DNEL in mg/m³	
		local	systemic
Benzoin	119-53-9		0.1
Potassium iodide	7681-11-0		0.7081
	7681-11-0		0.07
Aluminium fluoride	7784-18-1		0.047
Dodecane-12-lactam	947-04-6		0.88

4 DNELs and occupational exposure limit values in Germany and Europe

In Germany, the workplace limit values (AGWs) of TRGS 900 [3] are to be complied with. They are largely based on the MAK (maximum workplace concentrations) of the Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area of the German Research Foundation (DFG) [17]. It is therefore of some interest to compare the existing AGW and MAK values with the DNELs from the point of view of German occupational safety and health.

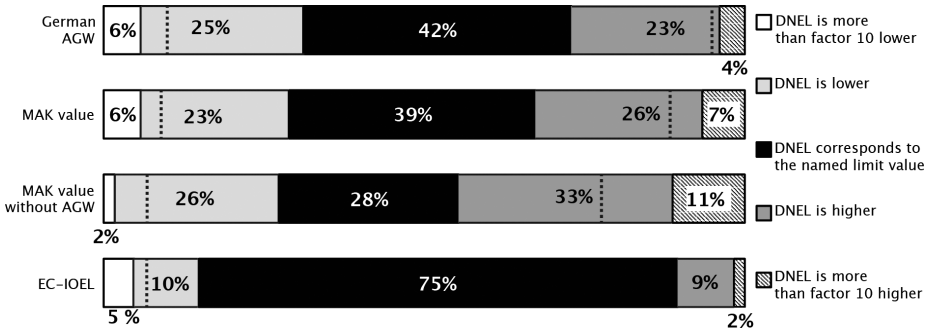

Figure 2. Degree of match between DNELs and German AGW or MAK values of the DFG (for all MAK substances or MAK substances without AGW) or the IOELs of the European Commission. The subdivision of the areas "DNEL is lower" (left) and "DNEL is higher" (right) marked with broken lines refers to deviation by a factor of 5 rather than 10.

4.1 AGW values

Of the 1,781 substances contained in the DNEL list, 309 substances (17%) have a German workplace limit value (AGW). 54 of these fall within the scope of the group AGWs for hydrocarbon mixtures. A comparison of the DNELs of the remaining 255 substances with their AGWs (see **Figure 2**, line 1) shows that 42% of all DNELs concur with the AGWs. A quarter of the DNELs are in each case up to a factor of 10 higher or lower than the German AGWs. However, for 4% of the substances, the DNEL value is more than a factor of 10 larger than the German AGWs and for 6% of substances more than a factor of 10 smaller (**Table 2**). Particularly worthy of note are naphthalene, trimellitic acid anhydride and diphenyl ether with DNELs 35 to 400 times as high as the German AGWs. **Table 3** shows the other extreme: the DNELs of these substances are a factor of 10 to 86 smaller than their German AGWs.

4.2 MAK values

A comparison of the DNELs with the MAK values of the German Research Foundation reveals discrepancies of a similar magnitude (Figure 2, line 2). This is not surprising since many AGWs are based on proposals from the MAK Commission. However, among the 261 substances that have a DNEL and a MAK value, there are 64 substances with a DNEL value for which no AGW exists. If these DNELs are compared to the MAK values, only 28% of the DNELs comply with the recommendations of the MAK Commission. 33% are up to a factor of 10 higher than the MAK value and 11% of these DNELs are even higher. 26% are up to a factor of 10 lower than the MAK values and 2% of the DNELs are lower still (Figure 2, line 3). Of the 11% of the DNELs that are much higher than the MAK values, half relate to zinc compounds with the MAK value of 0,1 mg/m³. 3-Chloro-1,2-propanediol and three lithium compounds (13 times higher), formaldehyde (24 times higher) and two organo-tin compounds (almost 200 times higher) also have DNELs that are much higher than the MAK values.

Table 2. Substances with DNELs more than a factor of 10 higher than the German AGW.

Substance	CAS number	DNEL in mg/m³		AGW	DNEL/AGW	
		local	systemic	in mg/m³	local	systemic
Boric acid	10043-35-3		8.3	0.5		16.6
Diphenyl ether	101-84-8	*9.68**	245.8	7.1	*1.4**	34.6
Disodium octaborate	12008-41-2		6.9	0.5		13.8
Disodium tetraborate	1330-43-4	11.7	6.7	0.5	23.4	13.4
Ethanethiol	75-08-1	18.6	14.5	1.3	14.3	11.2
Naphthalene	91-20-3	25	25	0.5	50.0	50.0
Silver oxide	20667-12-3		0.107	0.01		10.7
Sulfur hexafluoride	2551-62-4	77,900	77,900	6,100	12.8	12.8
Trimellitic anhydride	552-30-7		17.5	0.04		437.5
Zinc selenite	13597-46-1		1.7	0.05		34.0

* Figures in italics represent further DNEL values of the substance which do not meet the criterion "more than a factor of 10 higher than the AGW".

Table 3. Substances with DNELs more than a factor of 10 lower than the German AGW.

Substance	CAS number	DNEL in mg/m³		AGW	DNEL/AGW	
		local	systemic	in mg/m³	local	systemic
1,3-Dioxolane	646-06-0		19	310		0.061
1-Chlorobutane	109-69-3		8.5	95.5		0.089
1-Nitropropane	108-03-2	3.6	7.1	92	0.039	0.077
2-Diethylaminoethanol	100-37-8	1.07	*7.34**	24	0.045	*0.306**
2-Phenoxyethanol	122-99-6	8.07	8.07	110	0.074	0.074
4-tert-Butylbenzoic acid	98-73-7		0.067	2		0.033
Aluminium fluoride	7784-18-1		0.047	1		0.047
But-2-yne-1,4-diol	110-65-6	0.02	0.02	0.36	0.056	0.056
Dimethoxymethane	109-87-5		132	3,200		0.041
Disulfiram	97-77-8		0.146	2		0.073
Hydrogen fluoride/hydrofluoric acid	7664-39-3	0.0015	*1.5**	0.83	0.002	*1.807**
Methylamine	74-89-5		0.9	13		0.069
Nitrobenzene	98-95-3		0.07	1		0.07
N-Methylaniline	100-61-8		0.0495	2.2		0.023
Tetraethyllead	78-00-2		0.00058	0.05		0.012
Vinyl toluene (isomers)	25013-15-4	37	37	490		0.076

* Figures in italics represent further DNEL values of the substance, which do not meet the criterion "more than a factor of 10 lower than the AGW".

4.3 IOEL values

Finally, the DNELs of the DGUV list were compared to the Indicative Occupational Exposure Limit Values (IOELs) of the European Commission. For substances with IOELs, the EU member states are obligated to establish a national limit value based on the IOEL. 95 of the substances contained in the GESTIS DNEL database have such an IOEL. As can be seen from Figure 2 (line 4), the IOELs show much closer concurrence with the DNELs reported to ECHA than with the German AGWs or MAK values. A remarkable 75% of the IOELs match the DNELs. Only about 10% of the DNELs are in each case up to a factor of 10 higher or lower than the IOELs. The local DNELs for hydrogen fluoride (by a factor of 1,000!) and potassium aluminium fluoride (factor of 18) and the systemic DNELs for aluminium fluoride (factor of 53) and nitrobenzene (factor of 14) deviate downwards by more than a factor of 10.

5 DNELs in Safety Data Sheets

Despite the continuing criticism of their quality and completeness [18], Safety Data Sheets (SDSs) under REACH are key information dissemination tools for companies (see BekGS 409 [6]). The German Hazardous Substances Ordinance (Article 6(2) [19]) lists SDSs as a basis for the hazard assessment. The GHS Column Model [20], the Easy-to-use Workplace Control Scheme for Hazardous Substances (EMKG) [21], the Stoffenmanager [22] and GISBAU [23], for example, also derive their basic data from the SDSs.

In Germany, a DNEL given in an SDS is, according to the Hazardous Substances Ordinance, an important information source for the hazard assessment at the workplace to which the employer can refer. As a result of these formal consequences, the giving of a DNEL in an SDS is interpreted legal confirmation of this DNEL.

To check the congruence between the DNELs on the ECHA website and in the SDSs, the DNEL details from SDSs of the ISi database (Information System for Safety Data Sheets [24]) of the Association of the German Chemical Industry (VCI) and IFA were compared to the information supplied by registrants to ECHA. For this, a random sample of 94 substances was taken from the DNEL list, and for these the ISi database was searched for SDSs.

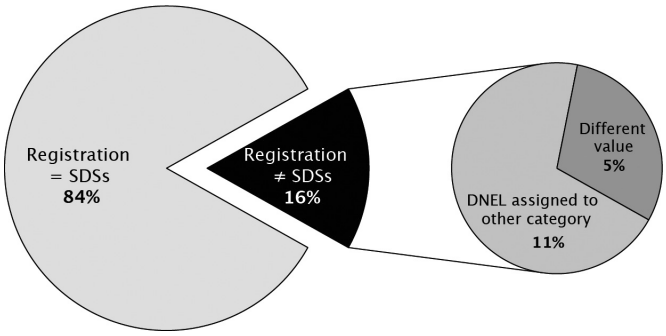

Figure 3. Degree of match between the DNELs found in a random sample of 94 Safety Data Sheets and the DNELs registered with ECHA for the same substances.

Figure 3 shows the portion of DNELs in SDSs that concur with the registration compared to DNELs deviating from these. In over 80% of cases, the DNELs from the registration entries with ECHA are the same as those on the SDSs. 16% of the DNELs found in SDSs deviate from the data registered with ECHA. However, of these, two thirds are attributable to an assignment of the DNELs listed with ECHA to the other exposure category (i.e. "local" instead of "systemic" or vice versa). Only 5% of all DNELs in the SDS sample otherwise differ from the values in the ECHA registration entries.

6 Discussion

6.1 Completeness of information

On the ECHA website workplace DNELs are listed for only about half of the "fully" registered substances. Even if one assumes that some of these substances without DNELs are not classified as harmful and therefore do not require a DNEL, it can be assumed that manufacturers and importers of numerous relevant high production volume substances have not established worker DNELs for chronic intake via the respiratory organs or at least have not entered them in

the desired template. On the other hand, DNELs are often given for substances that do not require classification as harmful, e.g. barium sulfate, sodium chloride, acetylene, ammonium acetate, sodium sulfate, sodium acetate, cyclopentane, 1,1,1-trifluoroethane, sulfur hexafluoride and potassium sodium tartrate.

Some registrants have evidently exploited the fact that the giving of DNELs is not obligatory under the REACH Regulation (Article 10). Consequently, the registration software IUCLID (International Uniform Chemical Information Database) does not program the DNELs as obligatory fields. As a result, some DNELs are probably not available on the ECHA website although they may be contained in the (not publicly accessible) complete registration dossier [25]. To fill this gap that runs against the requirement of the Internet accessibility of all DNEL values (REACH Article 119), ECHA endeavours to motivate registrants to enter DNELs with recommendations [26].

The evaluation of the raw data collected for the DNEL list revealed that for about 100 substances the phrase "Exposure based waiving" has been entered for long-term inhalation exposure at the workplace instead of a DNEL. However, this waiving of human toxicity data is only permissible if the exposure of persons, in this case workers, is excluded. It is therefore incomprehensible that the waiving statement also appears for a number of widespread substances like boric acid, 2-ethylhexyl methacrylate, 1,1-dichloroethene and maleic acid. It is totally implausible that the declaration of such data is "waived" for the local effects of about 50 substances, although the DNEL is given for the systemic effects and vice versa.

6.2 Origin and derivation of DNELs

For 2% of the substances in the DNEL list one can find several, in some cases considerably divergent, DNEL entries for the same exposure category. According to REACH there is no obligation to harmonise DNELs for registration [27].

Some registrants have possibly preferred to register the occupational exposure limit values applicable in their own countries as the DNELs. The Guidance R.8 ([7] Appendix R.8–13) makes the posting of a national limit value as a DNEL contingent on the following conditions: The derivation of the national limit value must be evaluated as to its scientific correctness and currency and any differences from the approach for deriving DNELs are to be taken into account.

Equally, European IOELs can also be adopted. The cited Appendix of the ECHA Guidance states: *"A registrant is allowed to use an IOEL as a DNEL for the same exposure route and duration, unless new scientific information that he has obtained in fulfilling his obligations under REACH does not support the use of the IOEL for this purpose".* It is worth noting that for almost all substances with which ECETOC (see below) attempted and published an exemplary and guidance-compliant DNEL derivation [28], the registrants finally chose the IOEL.

In cases where for a certain chemical a workplace DNEL has been posted both for local and systemic long-term inhalation exposure, these two substance-related values are identical surprisingly often. This is hardly plausible toxicologically, as in most cases the most sensitive health effect after inhalation of a substance is manifested either in the respiratory organs (usually irritation) or in a distant organ, but rarely both locally and systemically for the same exposure level. Merely in the case of substances of very low toxicity is it sometimes the case that even at the highest tested dose or concentration no negative effects on health whatsoever are observed. In the context of DNEL derivation, such a body of data does not of course permit a differentiation between "systemic" and "local". The European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) [28] which is organised by companies concerned with the production and use of chemicals has demonstrated this with the example of pentanes.

Well-designed studies usually yield two decisive parameters: the maximum dose/concentration at which no adverse effect was observed (No Observed Adverse Effect Level or NOAEL) and the lowest dose/concentration at which the first effects were diagnosed (Lowest Observed Adverse Effect Level or LOAEL). The point of departure for the calculation of DNELs is usually the NOAEL. This can be divided by one or more extrapolation factors in order to fill gaps in the data. If, for example, a 90-day feeding experiment on rats is identified as the key study for deriving a long-term workplace inhalation DNEL, these divisors known as "assessment factors" must be used for making the leap from the animal to humans, from oral to inhalation route and from short-term to long-term exposure. Guidance R.8 for the implementation of REACH [7] puts forward standard extrapolation factors, the application of which tends to yield relatively low limit values.

Given sufficient data, these divisors can be reduced for specific substances. The German AGW strategy defined in BekGS 901 [29] makes use of extrapolation factors very similar to those in the ECHA Guidance. When fully exploited, these result in AGWs that in certain circumstances are slightly higher than the DNELs derived in accordance with the ECHA Guidance as long as the calculations proceed from the same point of departure. The German MAK Commission and the Scientific Committee on Occupational Exposure Limits (SCOEL) of the European Commission perform extrapolations on less formal principles.

Making full use of the standard extrapolation factors in ECHA Guidance R.8 [7], ECETOC [28] derived workplace DNELs for 25 substances and showed that all DNELs are much lower than the IOELs. A substance-related and scientifically justified adaptation of the standard factors yielded values that were higher but usually still below the corresponding IOELs. In similar manner, *Schenk* and *Johanson* [30] compared 88 SCOEL air limit values to DNELs for the same substances that the authors themselves derived on the principles of EU guidelines. Here again, the DNELs were lower on average, albeit with pronounced variation.

In the EU Commission's view, when national limit values and DNELs differ, the lower one should always apply [31]. For the sake of simplicity it is assumed here that the registrant sets a lower DNEL on the basis of recent scientific findings because the higher national limit value no longer provides sufficient protection. The position of the EU Commission is to be interpreted for the time being as a preliminary expression of opinion. As already mentioned, the AGWs are legally binding in Germany. However, according to BekGS 409 (Question 4.2) [6], the hazard assessment is to be updated if the protective measures at the workplace do not ensure compliance with a DNEL lower than the AGW.

6.3 DNEL magnitude

Our comparison of DNEL entries with AGWs and MAK values for the same substances shows that DNELs tend not to be inappropriately high. 70% of the DNELs with AGWs are the same as the AGW or lower. On the other hand, however, 4% (compared to the AGW) and 11% (compared to the MAK value) of the investigated DNELs exceed the German occupational exposure limit values more than tenfold. Similar findings were also yielded by an evaluation by the Federal Institute for Occupational Safety and Health (BAuA) which was based on a smaller body of data [25].

It must be stressed that the comparison of national lists of limit values also sometimes reveals marked discrepancies (see GESTIS International Limit Values database [32]), and even within Germany, for various reasons, the MAK values of the DFG do not always concur with the AGW values in TRGS 900.

6.4 Carcinogenic substances

DNELs are defined as health-based limit values, and literally as *"derive[d] levels of exposure to the substance above which humans should not be exposed"* (Annex I, No. 1.0.1 of the REACH Regulation [1]). This definition is based on the concept of a threshold for the critical toxicological effect. However, on the basis of current knowledge, such a threshold cannot be derived for many carcinogenic substances. For the bulk of the carcinogenic substances for which registrants give "DNELs", including numerous metal compounds, it must therefore be assumed that compliance with the published "Derived No Effect Level" does not provide protection from cancer. The single-substance documents issued by the GESTIS DNEL database are therefore accompanied by a corresponding warning.

In Guidance R.8 for the REACH Regulation – though not in the regulation itself – so-called Derived Minimum Effect Levels (DMELs) have been recommended as limit values for carcinogenic and mutagenic substances without known toxicological effect thresholds. Since no quantification of risk is usually made for these DMELs – in contrast to the exposure-risk relationship according to the German BekGS 910 [33] – they are not dealt with further here. The problems associated with the DMEL values have been investigated in detail by *Püringer* [34; 35].

6.5 Quality assurance

As yet, the REACH system does not have an effective tool for correcting a registered DNEL whose derivation proves to be flawed or obsolete. The substance evaluation, in the context of which DNELs play at best a subordinate role, is only stipulated for substances that satisfy the priority criteria; substance evaluation is usually a process taking several years [36] and in practice restricted to relatively few substances (2012: approximately 30 substances). ECHA is currently urging the EU member states to conduct 100 evaluations per year.

Our finding that more than 80% of the SDSs take the DNELs from the registration with ECHA confirms our expectations. Even in small and medium-sized enterprises, individuals whose task is to prepare SDSs obviously make use of the DNELs that they can find on the ECHA website. The fact that in a further tenth of the SDSs the endpoints "systemic" and "local" have been interchanged does not speak for the quality of the SDSs.

Observations as facilitated by the DNEL list for substances with low DNELs but without classification for health hazards (Table 3) could aid the detection of possible classification errors.

7 Conclusions and outlook

REACH supplies an abundance of new information that ought to be of use for health protection at work. The process is still only a few years old and it is therefore hardly surprising that the initial phase has revealed flaws.

Even a superficial review of the workplace-relevant long-term inhalation DNELs uncovers certain shortcomings. The above presentation of a number of inconsistencies is by no means intended as a blanket rejection of the DNEL approach. In the generation of so many data, mistakes and misunderstandings can occur. Insufficient knowledge of the complex REACH procedures may be a factor in this. National limit values are not always free of flaws either. Worth remembering is that in 2005 about a quarter of all German workplace limit values were withdrawn because they failed to satisfy the strict criteria for health-based exposure limits.

We should generally welcome the fact that REACH makes available occupational exposure limit values in the form of DNELs for a far larger number of substances than would be possible in the foreseeable future through the – in most cased voluntary – activities of national or pan-European regulatory expert bodies. For health protection at the workplace they supply additional assessment benchmarks. In the construction sector, for example, the number of substances with an assessment benchmark in the form of DNELs has been raised from 37 to 60% [37; 38]

The DNEL list work group wishes to help reveal and identify possible shortcomings in order to accelerate the necessary process of improvement. It will approach manufacturers with striking DNEL discrepancies and request clarification. It would be desirable if a workplace DNEL (long-term exposure) were to be published for all chemicals registered with ECHA, at least with regard to their critical health effect. The disclosure of the derivation processes of the individual DNELs should be urgently demanded in order to permit an independent subsequent revision.

As its next step, the DGUV DNEL list work group will read out the workplace DNELs added during the most recent registration phase and integrate them in DGUV's DNEL list. A module containing practical examples of applications is in preparation.

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