Brussels, July 2015

HSPA Response to FoBiG proposal (FP372, 2014) to update the Reciprocal Calculation Procedure (RCP) as used in Germany under TRGS 900

Summary

Background

The Reciprocal Calculation Procedure (RCP) was developed as a framework to provide consistent and scientifically sound occupational exposure advice for hydrocarbon solvents. As a basis for the calculation, similar constituents were grouped, and "group guidance values" GGV, based on available data and existing national regulatory values, were recommended for use in the calculation. The toxicology of individual hydrocarbon constituents has been studied in comparison with toxicity studies of complex hydrocarbon solvents, with minimal to no differences observed (summarized in McKee et al, 2015). In other words, the similarities in the physico/chemical, toxicokinetic, and metabolic properties of defined groups of hydrocarbon constituents ensures that the potential for interactive effects having undue influence on the toxicity of complex solvents is of little to no toxicological relevance. Hence, it is possible to characterize the toxicity of a complex hydrocarbon solvent either on the basis of its constituents, or in a more generic way, using data from studies of representative complex solvents.

Substances that can't be accommodated into GGV are excluded from the group and their fraction calculated separately following their own "substance specific values" SSV. The simplicity of GGV and the few SSV has made it easier for manufacturers to provide consistent advice on industrial hygiene practices in the workplace.

In December 2014, Heine et al., (FoBiG, 2014) presented a proposal "FP372" to update the RCP as it currently exists in Germany under TRGS-900. The existing GGVs under TRGS-900 are provided below:

C5-C8 aliphatics = 1500 mg/m^3 C9-C15 aliphatics = 600 mg/m^3
C7-C8 aromatics = 200 mg/m^3 C9-C15 aromatics = 100 mg/m^3

The following two options are proposed in Heine et al., (FoBiG, 2014):

Option A:

C6-C15 aliphatics = 300 mg/m^3
C9-C15 aromatics = 50 mg/m^3

Option B:

C6-C8 aliphatics = 700 mg/m^3
C9-C15 aliphatics = 300 mg/m^3
C9-C15 aromatics = 50 mg/m^3

In addition to the new GGVs proposed by Heine et al., (FoBiG, 2014), the following substances are also proposed to be exempted from the respective groups/GGVs: all pentane isomers, n-hexane, decalin, benzene, toluene, all isomers of xylene, ethylbenzene, naphthalene, tetralin, all diethylbenzene isomers, n-butylbenzenes, all isomers of methylnaphthalene, acenaphthene, acenaphthylene, biphenyl, 1,2,4-triethylbenzene and fluorene.

European Chemical Industry Council
Avenue E. van Nieuwenhuyse 4 B - 1160 Brussels Belgium
Tel: +32 2 676 72 11 Fax: +32 2 676 73 01 mail@cefic.be www.cefic.org

Before a detailed discussion on how to amend the German RCP procedure can take place, it is important to first understand the rationale behind the proposed changes. This understanding helps to evaluate how the existing FoBiG and HSPA proposals address these issues. Following numerous discussions with German stakeholders and downstream users, the European Hydrocarbon Solvents Producers Association (HSPA) understands that there are two critical issues that have prompted the need to revamp the German RCP procedure. These issues (addressed in more detail below) center around a lack of understanding of what substances apply to the RCP and how to calculate RCP-derived OELs for hydrocarbon solvents, particularly those that are a blend of two or more complex hydrocarbon solvents.

1. *Confusion relating to substances covered by the RCP* – An example of this is the assumption that recent attempts to develop MAK values for distillates (CASRN 64742-47-8 and naphtha (CASRN 64742-48-9) may have an impact on the RCP framework. However, as discussed in McKee et al, (2015) the use of CAS numbers to represent hydrocarbon solvents creates confusion. The CAS numbers generally refer to the methods of production of the complex parent feedstocks (which are less well characterized and span wider boiling points) but do not provide an accurate description of the composition of more narrowly refined hydrocarbon solvents. The limitations of the CAS numbering system as it pertains to hydrocarbon solvents led the HSPA to develop a naming convention specific to hydrocarbon solvents (please see *HSPA substance identification and naming convention* document provided separately as part of this package) which provides relatively detailed compositional information. The naming convention forms the basis for the REACH registration of hydrocarbon solvents in Europe and has been fully accepted by ECHA in lieu of the CAS numbering system. **This is an issue that cannot be resolved by merely changing the RCP input values as proposed by Heine and Kalberlah and requires a fundamental understanding of what hydrocarbon solvents are and how they differ from other petroleum streams for which the RCP is not applicable**.

2. *Small scale enterprises are unable to calculate RCP-derived OELs for a blend of two or more hydrocarbon solvents* – In many cases, downstream users are unable to calculate RCP-derived OELs for hydrocarbon solvent blends because more often than not, the necessary compositional information to determine what GGVs apply to each blend component is not available in the supplier-provided MSDSs. **This issue cannot be solved by simply changing the GGVs to a different value**. However, as the HSPA will demonstrate at the workshop, an OEL for a hydrocarbon solvent blend can simply be calculated by a similar reciprocal method:

$$\frac{Fa}{OELa} + \frac{Fb}{OELb} + \frac{Fc}{OELc} + \ \ldots = \frac{1}{OELmixture}$$

Where F_a – mole fraction of solvent A in the final blend and OEL_a is the OEL for solvent A provided in the supplier MSDS. In cases where the blend is made up of hydrocarbon solvents with widely varying vapor pressures, the mole fraction in the vapor phase should be used in calculating the final OEL for the blend. HSPA plans to continue providing guidance and additional tools for calculating RCP-derived OELs,

and could also provide training to small scale users on how to apply the RCP, should this be needed.

As noted above, the proposal by Heine et al., (FoBiG, 2014), which essentially keeps the existing TRGS-900 method but revises it by reducing GGVs (which is not toxicologically supported) and introducing more individual constituent exceptions (which is unnecessary and adds more complexity to the RCP), does not address these issues. As we show (please see attached HSPA proposal and background documents), the GGVs are well supported by the toxicology and are consistent with the GGVs as currently exist under the UK HSE and ACGIH adaptations to the RCP. Rather, it appears that a better understanding of what hydrocarbon solvents are and how the RCP can be applied in different scenarios is what is most needed. As an example, although the FoBiG proposal lists certain poly aromatic hydrocarbons (PAHs) as part of the substances to be excluded from the GGV, current manufacturing specifications explicitly exclude this class of substances from hydrocarbon solvents. Other issues that have been highlighted include the discrepancy between the existing TRGS-900 RCP method and the recently derived national regulatory values for individual constituents. Examples of these discrepancies include substances like ethylbenzene and decalin. As the HSPA has consistently indicated, the RCP was designed to be flexible enough to accommodate changes to individual constituents. As a result of this flexibility, these changes can be accommodated without cumbersome, wholesale changes to the entire framework of the RCP. Where it is warranted, substances can either be removed from existing groups (replaced by individual TLVs, where they exist, as SSVs) or by implementing cut-off concentrations for specific constituents, below which occupational exposure limits for the constituents are not exceeded when the current GGV is observed. HSPA recommends that the guidance value for the C7-C8 aromatics category be withdrawn and that the MAK values for these constituents be used as SSVs when appropriate. Recommendations relating to other constituents including cumene and decalin are addressed below. These are also addressed in more detail in the attached HSPA proposal and background documentation provided as separate documents. This document outlines HSPA's general response to the FoBiG proposal below.

C5 aliphatic hydrocarbons

FoBiG: The proposal is to create an extra group for C5 aliphatic hydrocarbons based on the significantly higher regulatory limit values.

HSPA response - The HSPA is in agreement that the available OELs for pentanes are considerably higher (in some cases 2-fold higher) than the recommended GGV of 1500 mg/m^3, as shown in figure 1 below. HSPA understands that this value is conservative by comparison to current regulatory values for pentanes but would prefer to maintain the current value to minimize complexity of the method (i.e. reduce the number of excluded substances to the required minimum). However, if pentanes were to be considered as a separate group, then the GGV should be increased to 3000 mg/m^3 to align it with the current regulatory advice for pentane isomers as reflected in the existing TRGS 900, MAK and ACGIH values.

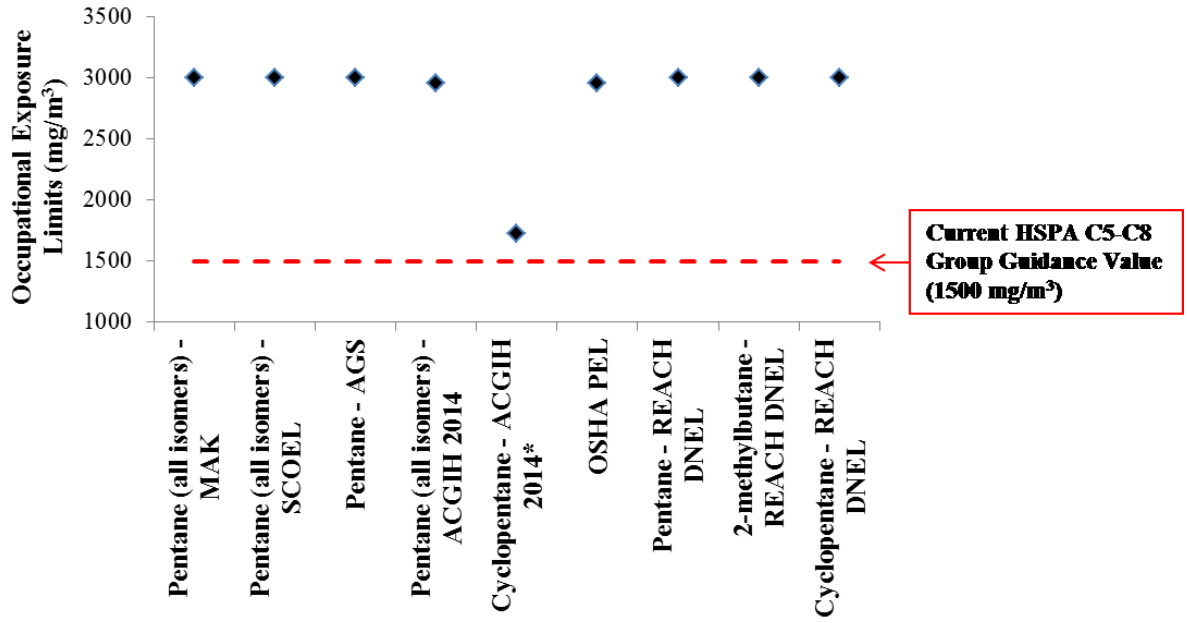

Figure 1: Graphical illustration of existing regulatory values and REACH DNELs for pentanes compared to the with the current HSPA group guidance value for C5-C8 aliphatics. Note the change in ACGIH TLV for pentanes.

C6 aliphatic hydrocarbons

FoBiG: The proposal seeks to create a separate C6-C8 group through the reintegration of cyclohexane into this group in order to propose a representative GGV of 300 or 700 mg/m^3 for all aliphatics within the group. These GGVs are based on the cyclohexane OELs of 350 mg/m^3 (ACGIH) or 700 mg/m^3 (AGW). The advocated reduction in GGV and choice of values would depend on the desired safety.

HSPA response – As stated earlier, the HSPA adaptation of the RCP explicitly excludes substances with unique toxicities such as may drive considerably lower regulatory limit values. The goal is to make sure that the regulatory limits of these substances are not exceeded within the context of RCP-derived complex solvent OELs. However, rather than changing the GGV (which is similar to or lower than the current occupational values for pentanes, hexane isomers other than n-hexane, heptanes and octane isomers, simply to accommodate cyclohexane, the same result can be achieved by ensuring that occupational exposure limits for individual constituents not be exceeded when the overall occupational exposure limits for the complex solvents are observed.

It should be noted that cyclohexane does not have toxicological properties that distinguish it from other aliphatics. Rather, the Indicative Occupational Exposure Limit (IOELV) for cyclohexane was based primarily on human observations (in which there were no objective findings) rather than results of studies in animals which underpin other occupational exposure recommendations.

Nevertheless, if the occupational exposure limits for aliphatic solvents are calculated, following the HSPA recommendations, the IOELV for cyclohexane is not exceeded for most solvents. More specifically, cyclohexane is primarily found in "hexane-range" solvents, and

is typically at levels below 20%, which is low enough that the IOELV for cyclohexane is not exceeded if the RCP-calculated OEL is observed. As an example, consider a hypothetical solvent that contains 80% 2-methylpentane and 20% cyclohexane. If the GGV of 1500 mg/m^3 is applied, the exposure to cyclohexane would be approximately 142 mg/m^3 which is well within its own occupational exposure limit (5-fold lower than AGW value). Thus, as shown, the occupational health objective which is to avoid over-exposure to cyclohexane is compatible with the current HSPA recommendations without further modification.

There are a few aliphatic solvents that have cyclohexane concentrations > 20%. For these, HSPA advises that cyclohexane be considered "special" and the occupational exposure limit (AGW value of 700 mg/m^3) for cyclohexane introduced into the formula as a SSV. As a more general comment, HSPA considers that it is impractical to change a GGV only unless it is clearly unsuited for the constituents to which it applies. In particular, when the concerns are related to specific constituents that represent minor fractions of the complex solvents, the occupational exposure issues may be more easily addressed in other ways.

As an example that relates to this, the GGV for C5-C8 aliphatics explicitly exclude n-hexane which has a unique toxicity (peripheral axonopathy at high exposures). In this case, the HSPA has always recommended that the existing AGS/MAK value of 180 mg/m^3 be used to account for n-hexane in the complex solvent[1].

C7 aliphatic hydrocarbons

FoBiG: The proposal questions the validity of the current C5-C8 aliphatics GGV of 1500 mg/m^3 to account for toxicity associated to methylcyclohexane (MCH) (and the associated lower German MAK value of 810 mg/m^3), and thus justifying the lowering the GGV to either 300 or 700 mg/m^3 for all heptane isomers.

HSPA response **–** As shown in figure 2, there is no basis for proposing a change to the HSPA GGV of 1500 mg/m^3 for C5-C8 aliphatics with respect to C7 aliphatics, considering this value is lower than the existing German, SCOEL and ACGIH values for n-heptane/heptane isomers. With regard to the lower MAK value for methylcyclohexane (MCH) compared to other heptane isomers, a detailed discussion on the derivation of its current occupational exposure recommendations is included in the *"HSPA Background Documentation in Support of RCP Proposal"* including a discussion on other data providing sufficient evidence that MCH is not toxicologically different from other heptanes.

While the HSPA maintains that MCH is not sufficiently toxic as to warrant a lower OEL than other heptane isomers, it may be possible to address this in exactly the same way as cyclohexane in the example shown above. In other words, HSPA recommends maintaining an SSV (equivalent to the MAK value) that should be taken into account when MCH levels are high enough (> 40%) that the equation requires modification to assure that exposure to MCH does not exceed its own regulatory value. Practically speaking, at levels at or below 40% in a complex solvent, MCH vapor concentration in ambient air is less than 80% of the current MAK value. Hence a need to account for MCH separately, using an SSV in the RCP process,

[1] Note that the 180 mg/m^3 value is recommended for the AGS adaptation of the RCP only. HSPA preferred value for n-hexane, outside of Germany, is the SCOEL TLV of 72 mg/m^3

is not required at MCH levels below 40% (which is the case for nearly all of the registered hydrocarbon solvents).

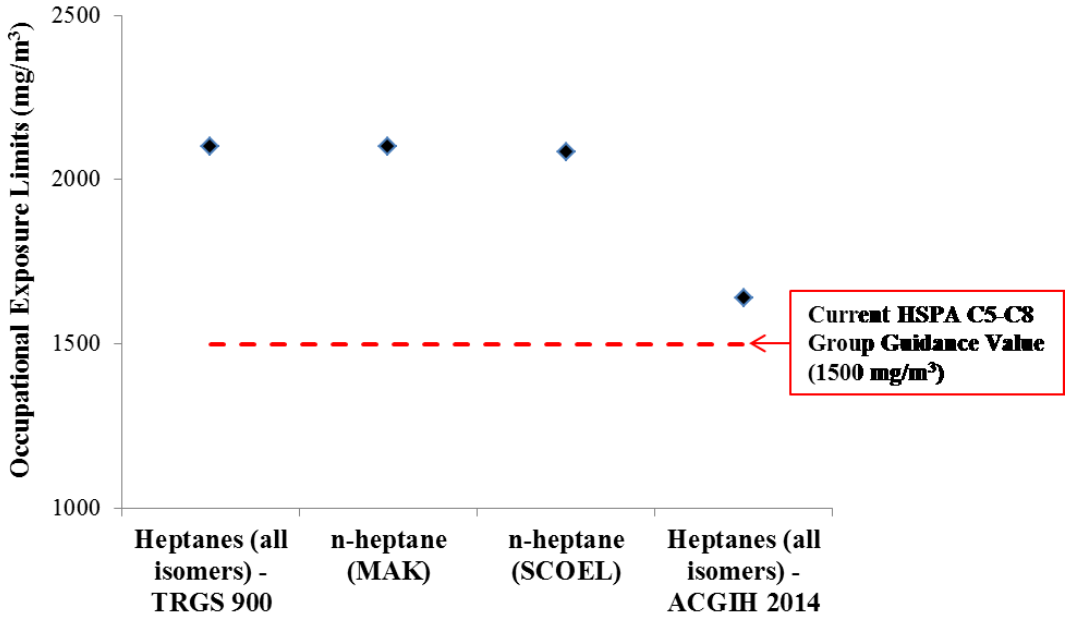

Figure 2: Graphical illustration of existing German regulatory values and ACGIH TLV-TWA for heptane isomers compared to the current HSPA group guidance value for C5-C8 aliphatics. Note that "heptane isomers" may in some cases exclude methylcyclohexane.

C8 aliphatic hydrocarbons

FoBiG: The proposal aims to interpolate C8 aliphatic constituents with C7 and C9 aliphatic data due to a "C8 aliphatics limited data base" and based on a *general trend of increased general toxicity with higher carbon length.*. In addition, it is proposed to tolerate temporary inclusion of trimethylpentanes pending confirmation on the uncertainties around classification for tumor promoting properties. A value of 270 – 840 mg/m^3 is proposed as OEL for C7 constituents and a "low end" of 300 mg/m^3 for C9 aliphatic constituents, as basis to cover C8 constituents.

HSPA response - The toxicological effect referred to in the previous paragraph is acute central nervous system (CNS) depression, a condition that is quickly reversed when exposure is terminated. This was recognized by HSPA as a sensitive indicator of hydrocarbon solvent exposure and was the basis of a research effort to characterize the acute CNS effects of hydrocarbon solvents and their constituents (Hissink et al., 2007; 2009; Lammers et al., 2007; 2009; 2011; McKee et al., 2006; 2010; 2011). Accordingly, the pattern of increased acute CNS effects with increasing carbon number up to C9 is already reflected in the existing HSPA GGVs. For example, the GGV for C9-C14 aliphatics is 1200 mg/m^3 which is lower than the GGV for C5-C8 aliphatics of 1500 mg/m^3. This value is below levels associated with acute CNS effects in animals (Mckee et al. 2011).

As shown in figure 3, with the exclusion of trimethylpentanes, the GGV for C5-C8 aliphatics is more conservative than the AGS and DFG values for n-octane/octane isomers. A detailed evaluation of published literature on the toxicity of octane isomers, particularly trimethylpentanes, is provided in *"HSPA Background Documentation in Support of RCP Proposal"*. Based on the available data, there is no evidence to warrant a change in the occupational exposure recommendations for n-octane and octane isomers.

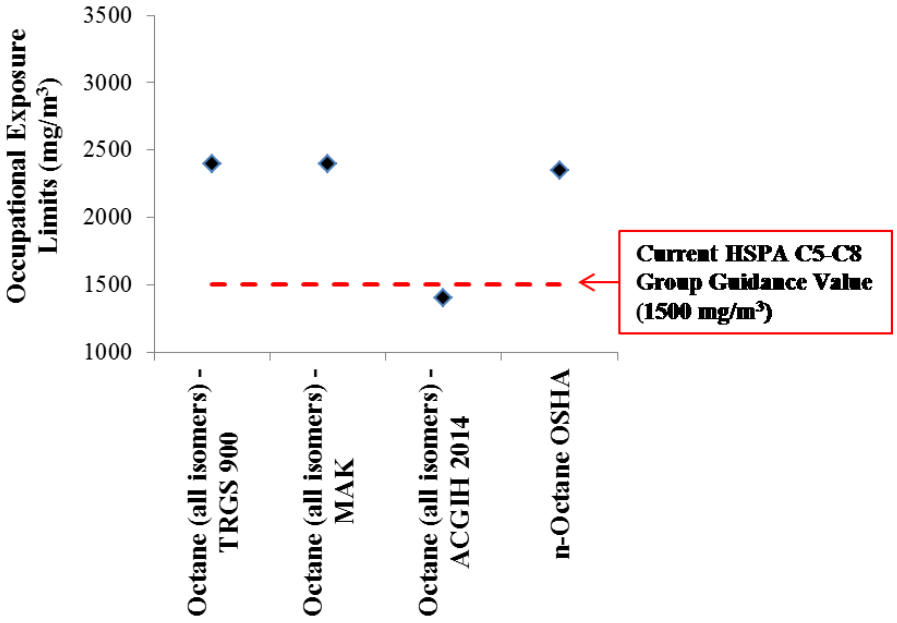

Figure 3: Graphical comparisons of existing German and US OELs for octane and its isomers with the current HSPA group guidance value for C5-C8 aliphatics. Note that AGS and MAK values explicitly exclude all isomers of trimethylpentane. Trimethylpentanes are classified as 3A for carcinogenicity by the DFG.

C9 aliphatic hydrocarbons

FoBiG: The proposal is to lower the current GGV of 600 mg/m^3 to 300 mg/m^3, justified by increasing toxicity with higher carbon length (although C8 isomers do not follow this pattern), and supportive information from a study on C9-C11 isoparaffin and other data including n-nonane.

HSPA response - There are no MAK, TRGS 900 or SCOEL values for n-nonane and nonane isomers. According to the TRGS 900 RCP method, a 600 mg/m^3 GGV for C9-C15 aliphatics is provided to cover the C9 aliphatics (the most volatile member of the group and hence the most toxicologically relevant from the standpoint of acute CNS effects). It must be noted that this GGV is different from the HSPA recommended GGV for the C9-C15 aliphatics which is 1200 mg/m^3 and is consistent with the UK HSE GGV for aliphatics >C7, the ACGIH GGV for C9-C15 alkanes (excluding n-nonane which has a TLV-TWA value of 1048 mg/m^3) and the OEL values of 1050 – 1200 mg/m^3 for 13 other countries on the GESTIS database including Australia, Belgium, Canada, France, Switzerland and Denmark. This value is also consistent with human evidence showing that CNS effects and potential sensory irritation are not observed at lower concentrations (Pedersen and Cohr, 1984; Ernstgard et al., 2009). The basis for the ACGIH and other regulatory values for nonane are discussed elsewhere (see

HSPA Background Documentation in Support of RCP Proposal). However it should be noted that the ACGIH has proposed an 8 hour time weighted average of 1050 mg/m^3 exclusively for n-nonane. For other isomers of nonane, a GGV value of 1200 mg/m^3 for C9-C15 alkanes under the ACGIH adaptation of the RCP is recommended. This value is consistent with the available data showing acute CNS effects (the critical adverse effect associated with nonane exposure) occur at considerably higher concentrations as shown by McKee et al, (2011). On this basis, the HSPA believes that the C9-C14 aliphatics GGV of 600 mg/m^3, as proposed in TRGS 900, is below levels that cause irritation and/or acute CNS effects and is also protective of other possible adverse effects.

In addition, although we agree with FoBiG that increasing carbon chain length is directly proportional to increasing acute CNS toxicity for aliphatic constituents; cycloparaffinic constituents do not follow this pattern. NOECs for normal- and isoparaffinic constituents decrease with increasing chain length (correlating with a similar pattern of increased brain/blood ratios) from C6-C10. In the case of cycloparaffinic constituents, peak brain/blood ratios occur around C8 (correlating with lowest NOEC) and then increase up to C10, where no effects are found with exposure to up to 5000 mg/m^3. Beyond C11, no acute CNS effects are observed for aliphatic constituents.

C10 aliphatic hydrocarbons

FoBiG: Proposal is to lower OEL for group to 300 mg/m^3 and exclude decalin from the group based on low decalin OEL by the DFG and low REACH DNEL. Neurotoxicity observed with n-decane and C9-C11 isoparaffin would support this reduction, as well as liver hypertrophic effects.

HSPA response - The current HSPA GGV recommendation of 1200 mg/m^3 for C9-C20 aliphatics is consistent with the UK HSE GGV for aliphatics >C7, the ACGIH GGV for C9-C15 alkanes (excluding n-nonane which has a TLV-TWA value of 1048 mg/m^3) and the OEL values of 1050 – 1200 mg/m^3 for 13 other countries on the GESTIS database including Australia, Belgium, Canada, France, Switzerland and Denmark. This value is also consistent with available data showing that CNS effects and potential sensory irritation are not likely at lower concentrations. On this basis, the HSPA believes that the C9-C14 aliphatics GGV of 600 mg/m^3, as proposed in TRGS 900, is sufficiently protective of possible adverse effects.

In particular it should be noted that the effects of n-decane and C9-C11 isoparaffinic hydrocarbon solvent constituents are acute and reversible with predicted human no effect levels of 1500 mg/m^3 (Lammers et al., 2011; McKee et al., 2011, based on pharmacokinetic data from Hissink et al., 2007). Human studies provide evidence that these substances do not produce acute CNS effects at levels up to at least 1200 mg/m^3 (Pedersen and Cohr, 1984). In addition, decalin is present at such small levels in hydrocarbon solvents that its MAK value is never exceeded in the context of the 600 mg/m^3 GC for C9-C15 aliphatics. A more detailed explanation on this is provided in *"HSPA Background Documentation in Support of RCP Proposal"*.

>C11 aliphatic hydrocarbons

FoBiG: Proposal aims to consider C11 equivalent to findings related to C9-C11 isoparaffins, although it is recognized that at this and higher carbon number uptake will be limited. By using the studies by McKee et al. 2011/Lammers et al., 2011 (C9-C11-isoparaffines) as a conservative benchmark for this group, which, would take into account other studies on aliphatic hydrocarbons ≥ C11 a group reference value 300 mg/m³ is proposed.

HSPA response – This proposal is not necessary and is an overly conservative approach that is neither supported by the data nor consistent with the RCP approaches adopted by other regulatory authorities. In particular it should be noted that Nilsen et al. (1988) have shown that aliphatic hydrocarbons with carbon numbers > C9 do not produce acute CNS effects in rodent studies. This is in part due to the lower vapor pressures of these higher molecular weight constituents, but may also be due to inhibition of uptake of these molecules into the central nervous system as demonstrated by the reductions in the brain/air partition coefficients for the higher molecular weight constituents.

Aside from the fact that the McKee et al. 2011/Lammers et al. 2011 studies on C9-C11 isoparaffins provide evidence for much higher limit values, RCP adaptations by the UK HSE and ACGIH support a GGV of 1200 mg/m^3 for >C7 aliphatics and C9-C15 alkanes respectively. These recommendations are consistent with the HSPA GGV for C9-C20 aliphatic substances of 1200 mg/m^3. As cited by FoBiG, many studies are available to provide support for the current HSPA GGV. However, a common problem with extrapolating or deriving DNELs/OELs from many of these studies is that the NOAECs are often merely the highest attainable vapor concentrations for the substances tested in the respective studies, and, thus, largely dependent on experimental constraints. For example, with the exception of undecane (C11) and dodecane (C12), maximum vapor concentrations of all alkanes ≥ C13 are less than half the HSPA GGV at 25 °C. Although the vast majority of the inhalation studies show relatively little to no adverse effects outside the male rat kidney effects, the use of the highest dose tested (more often than not the highest concentration experimentally achievable) as the point of departure for the derivation of DNELs/OELs tends to yield much smaller values than for more volatile aliphatic hydrocarbons where data on much higher test concentrations are possible. In essence, the low DNEL/OEL values calculated by FoBiG are a consequence of the relative vapor pressures of these molecules rather than evidence of an increase in systemic toxicity.

Based on the available data and practical constraints of aliphatics in this group, it is recommended that the HSPA GGV of 1200 mg/m^3, consistent with the ACGIH and UK HSE RCP adaptations, or the 600 mg/m^3 value under the German AGS adaptation, be maintained in the absence of any other data to suggest otherwise. This value is mainly protective of the most volatile ends of the range (C9-C10) and is supported by validation studies in humans showing no evidence for CNS effects at 1200 mg/m^3 for the dearomatized white spirits and 600 mg/m^3 for the regular white spirits. Beyond C11, a sufficient vapor concentration to cause acute CNS effects would not be expected.

C7-C8 aromatic hydrocarbons

FoBiG: The proposal is to assess C7-C8 aromatic hydrocarbons through their individual SSV, thus effectively eliminating the aromatic RCP GGV for this group to single substances

HSPA proposal **–** Agree. Based on the inconsistencies in regulatory values for individual constituents in the C7-C8 aromatics category, the HSPA recommends the withdrawal of the former GGV of 200 mg/m^3 for C7-C8 aromatics. The HSPA is recommending that for substances containing individual C7-C8 aromatics at levels > 1%, the current occupational exposure limits for the individual constituents should be used as specific substance values (SSVs).

C9-C15 aromatics

FoBiG: The current GGV = 100 mg/m^3 for C9 aromatics is not in line with the newly derived value for iso-propylbenzene (Cumene), which is 50 mg/m^3. The data on tri-methyl-benzene (TMB) is supportive of such reduction. One neurotoxicity study with a C9 "mixture" supports this lower value.

Regarding constituents which are encompassed in the C10 and higher aromatic carbon numbers, such as tetralin, di- and tri-ethylbenzenes , biphenyl which have a different toxicity profile and add uncertainty to the group, the lower GGV = 50 mg/m^3 is justified.

HSPA response - The HSPA recommended GGV for C9-C15 aromatics of 100 mg/m^3 is based on existing TLV and IOELVs for trimethylbenzene isomers and cumene (isopropylbenzene). With the exception of the MAK value for cumene of 50 mg/m^3, all other regulatory values available (including ACGIH RCP GGV for C9-C15 aromatics) through the GESTIS database (including ACGIH 2014 and SCOEL IOELv values) for trimethylbenzene and cumene range from 100-125 mg/m^3 and 100 – 246 mg/m^3 respectively.

The proposal to drop the GGV on the basis of CNS effects in rats is not scientifically justified as it ignores adequate data in human exposure studies showing no evidence for CNS effects at the existing GGV. The human data are published and reviewed in the "*HSPA Background Documentation in Support of RCP Proposal*". With specific reference to the FoBiG proposal, it should be noted that Douglas et al. (1993) showed that a complex substance comprised of C9 aromatics (isomers of trimethylbenzene and ethyltoluene) did not produce persistent neurological effects. With regard to cumene, it is conservatively found in levels below 10% in C9 aromatic solvents. Based on Raoult's law calculations, worst-case ambient air concentrations of cumene is less than half its MAK value when present in a complex C9 aromatic solvent at 10% (if the C9-C15 aromatic GGV of 100 mg/m^3 is applied).

Special consideration should be given to substances with unique toxicities such as diethylbenzene (worst case level <5%) and triethylbenzene (worst case level <5%) which are known to generate chromogenic γ-diketone metabolites that cause similar peripheral nervous system effects as observed with n-hexane. HSPA recommends that these substances be accounted for using an SSV. In the absence of existing European regulatory values, HSPA proposes the use of American Industrial Hygiene Association (AIHA) 8-hour TWA of 28 mg/m^3. For biphenyl which has a low ACGIH TLV of 1.5 mg/m^3, this value can be used as a SSV. However, due to its low vapor pressure and the fact that HSPA has adopted a 1.5%

content limit on biphenyl in complex solvents, ambient air vapor concentrations are not expected to exceed its TLV even if the 100 mg/m^3 GGV was applied. In that case, for biphenyl levels <1.5%, no SSV is required.

Unlike other alkylated benzenes and alkylated naphthalenes, naphthalene is metabolized primarily through ring oxidation, which may introduce metabolites with unique toxicological properties. In the absence of a definitive regulatory value for naphthalene, HSPA proposes to continue using the 50 mg/m^3 historical OEL (based on human observations) as an SSV pending the completion of ongoing human observational studies in Germany. HSPA supports the replacement of this value with the final regulatory value as determined by the AGS. Methylnaphthalene is metabolized through side chain oxidation (80%) and ring oxidation (20%). In light of the small metabolic difference (compared to alkylated benzenes), it is proposed that a 50 mg/m^3 SSV be considered for this substance in the absence of SCOEL, TRGS 900 or MAK values. In the alternative, an exposure validation program should be considered to ensure validity of existing 100 mg/m- GGV.

There is no new data supporting a need to change the 100 mg/m^3 GGV for C9-C15 aromatic hydrocarbons. HSPA recommends that other aromatic substances with unique toxicology (diethylbenzene as an example) and metabolic differences that may influence toxicity (naphthalene) should be accounted for separately using SSVs. In the case of biphenyl the low vapor pressure and low level in complex solvents suggests that its presence is accommodated in the context of the C9-C15 aromatics GGV.

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Jose A. Ruiz
Chairman, Hydrocarbon Solvents Producers Association (HSPA)

Antoine Brossier
Director General European Solvents Industry Group (ESIG)