Hydrocarbon Solvents Producers Association (HSPA) Proposed Update to the Reciprocal Calculation Procedure following TRGS-900

Background

The Reciprocal Calculation Procedure (RCP) was developed as a framework to provide globally harmonized and consistent occupational exposure limit (OEL) values for complex hydrocarbon solvents in a simple manner and that does not require downstream users/small scale users to generate detailed and expensive compositional information. Therefore, it effectively addressed the problem of accounting for the large number of individual hydrocarbon constituents. The term "individual hydrocarbon constituent" is intended to refer to single molecule hydrocarbon substances with specific structure (aliphatic or aromatic) and carbon number (in the range of C5 – C20), which may be present in a complex hydrocarbon solvent or blend thereof.

It is important to note that the primary goal of the RCP method is not to develop alternative hydrocarbon constituent OELs, but rather to be a framework to ensure that existing national regulatory values for these constituents are not exceeded within the context of the overall occupational advice for complex hydrocarbon solvents.

The RCP method rests on one key principle; that there is a common mode of action for distinct groups of hydrocarbon constituents (additivity principle) and hence, the method cannot be used for non-hydrocarbons (such as ketones, alcohols, less refined petroleum streams) without independent verification of underlying toxicity principles/mode of action. To achieve this, the RCP method uses group guidance values (GGVs) applied to specific groups of hydrocarbons for which there is sufficient data to cover a number of structurally similar constituents with similar physico/chemical properties, similar metabolic profiles[1] and hence similar toxicological properties. The GGV is derived by selecting a value based on a thorough analysis of the available relevant data and existing national regulatory values for these constituents. The data evaluated includes studies of both individual constituents within the hydrocarbon group and complex solvents containing these individual constituents.[2] The GGV is similar to or lower than most national values, to ensure that the individual constituent TLVs are never exceeded when present in a complex solvent.

In addition to the GGVs, the RCP method also takes into account hydrocarbon constituents with unique toxicities and/or those constituents for which national regulatory values are considerably lower. For example, substances like n-hexane and naphthalene (with unique toxicities) are excluded from RCP groupings and are accounted for by using the existing national regulatory values where applicable (referred to as substance-specific values/SSVs). For substances such as cyclohexane and methylcyclohexane (lower national regulatory values than corresponding normal/branched isomers) the levels in complex solvents are usually low enough that exposures are below regulatory values. However, for the small number of

[1] Similarities in metabolic profiles ensure that the potential for interactive effects between individual hydrocarbon constituents in a complex solvent would not be expected to have any toxicological impact. In addition, the toxicological properties of complex mixture of constituents within a GGV are expected and have been shown to be identical to those of the individual constituents.

[2] A detailed review of hydrocarbon solvent toxicology is now published in McKee, R. H., Adenuga, M. D., & Carrillo, J. C. (2015). Characterization of the toxicological hazards of hydrocarbon solvents. *Crit Rev Toxicol, 45*(4), 273-365

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

solvents that contain cyclohexane or methylcyclohexane at relatively high levels, these constituents are excluded from RCP groupings and are accounted for by using the existing national regulatory values where applicable, as SSVs. When these unique hydrocarbon constituents are present at significantly low enough levels in the complex solvent, the SSVs can be ignored in favor of the corresponding GGVs since the individual substance TLVs cannot be exceeded even at maximal exposure to the defined complex solvent OEL.

HSPA Proposal

The RCP method was developed to be adaptable to future changes; i.e. periodic changes to regulatory limit values or the availability of new data that may necessitate changes to existing GGVs or SSVs. Examples of such flexibility is portrayed in the different adaptations of the RCP currently in use by the ACGIH[3], UK HSE[4], and in Germany (TRGS 900)[5]. With respect to the existing TRGS 900 RCP recommendations, updates to the groupings and GGVs proposed by the HSPA are as follows:

Groupings

1. Single group: C5-C8 aliphatics – maintain existing GGV of 1500 mg/m^3
   Considerations – n-hexane, cyclohexane, methylcyclohexane
2. Single group: C9-C15 aliphatics – maintain existing GGV of 600 mg/m^3
   Considerations – decalin
   Single group: C7-C8 aromatics – eliminated
   Considerations – toluene, xylene, ethylbenzene
3. Single group: C9-C15 aromatics – maintain existing GGV of 100 mg/m^3
   Considerations – biphenyl, triethylbenzene, diethylbenzene, naphthalene, methylnaphthalene

Modifications

As a result of changes in the regulatory values for constituents within the C7-C8 aromatics group, the HSPA proposes to remove the existing TRGS 900 recommended GGV of 200 mg/m^3. Instead, individual constituents within this group will now be accounted for using their existing MAK/TRGS 900 values (as SSVs) as follows: 190 mg/m^3 for toluene, 440 mg/m^3 for all xylene isomers and 88 mg/m^3 for ethylbenzene. This is to ensure that individual TLVs for substances like ethylbenzene (with a TLV that is now more than 2-fold lower than existing TRGS 900 C7-C8 aromatics GGV) is not exceeded within the context of the complex solvent.

Considerations

a) *Pentanes (all isomers, including cyclopentane)* – although the TRGS 900 TLV for pentanes is now 3000 mg/m^3 (double the C5-C8 aliphatics GGV), the HSPA proposes to maintain pentanes as part of the C5-C8 GGV in order to keep the method simple and reduce the number of exclusionary substances that downstream users need to consider.

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[3] American Conference of Industrial Hygienists
[4] UK Health and Safety Executive
[5] Federal Institute for Occupational Safety and Health (BAuA) technical rules for hazardous substances

b) *n-hexane* – due to its unique toxicity, that is not shared by similar aliphatic hydrocarbons, the HSPA recommends that n-hexane remain excluded from the respective groups/GGV and should be accounted for using the existing TRGS 900/MAK value (180 mg/m^3)[6].

c) *Cyclohexane* – as a result of its considerably lower TLV compared to its normal/branched analogues, the HSPA recommends that cyclohexane be excluded from the C5-C8 GGV only if present in the complex solvent at levels greater than 20%. At levels below 20% (which is the case for nearly the entire registered hydrocarbon solvents for which the C5-C8 GGV applies), the TRGS 900 TLV (of 700 mg/m^3) for cyclohexane is never exceeded at ambient temperature (25^{o}C) when the C5-C8 GGV is employed as the complex solvent OEL.

d) *Methylcyclohexane* – Similar to cyclohexane, its TRGS 900 value (of 810 mg/m^3) is approximately half the value of the C5-C8 GGV. The HSPA recommends that methylcyclohexane be excluded from the C5-C8 GGV and its TRGS 900 value employed as a SSV when it is present in the complex solvent at levels greater than 40%. At levels below 40% (which is the case for nearly the entire registered hydrocarbon solvents for which the C5-C8 GGV applies), the TRGS 900 TLV for methylcyclohexane is never exceeded at ambient temperature (25^{o}C) when the C5-C8 GGV is employed as the complex solvent OEL.

e) *Decalin* – The MAK value for decalin is currently 29 mg/m^3, significantly lower than the existing TRGS 900 recommendation of 600 mg/m^3 for C9-C15 aliphatics. However, decalin levels in hydrocarbon solvents are < 2%. As a result, the maximum concentration of decalin in ambient air ranges between 12 – 16 mg/m^3 (approximately half its MAK value) when the C9-C15 GGV of 600 mg/m^3 is observed. As a result, there is no need to revise the RCP to account for decalin.

f) *Benzene* – The worst-case maximum benzene levels in hydrocarbon solvents are <150 ppm (0.015%), and occupational exposure recommendations for benzene are met if the OELs calculated in accordance with the RCP are followed. It is not necessary to separately consider benzene as a hydrocarbon solvent constituent as current manufacturing practices are designed to assure that benzene levels are very low.

g) *Triethylbenzene and diethylbenzenes* –Similar to n-hexane, certain isomeric forms of diethylbenzenes and triethylbenzenes can be metabolized to γ-diketones which cause similar peripheral neurotoxicity in rodents. In view of this unique toxicity and although levels of these constituents are low in complex solvents, HSPA recommends accounting for these substances with available SSVs. A 2013 8-hour TWA of 5 ppm (28 mg/m^3) has been proposed for use with diethylbenzenes by the American Industrial Hygiene Association (AIHA)[7]. HSPA proposes that this value be used as an SSV for all triethylbenzene and diethylbenzene isomers.

[6] Note that the HSPA preferred value for n-hexane is the SCOEL TLV of 72 mg/m^3
[7] https://www.aiha.org/get-involved/AIHAGuidelineFoundation/WEELs/Documents/2011WEELValues.pdf

h) *Biphenyl* – biphenyl has a low vapor pressure and is present at significantly low levels in complex solvents. Thus, it is not anticipated to be present in ambient air to any appreciable degree. In the absence of any other European regulatory values for biphenyl, the HSPA has proposed adopting the 1.5 mg/m^3 ACGIH TLV as a SSV. In addition, the HSPA has also adopted a 1.5% limit on biphenyl content in complex solvents. At levels ≤ 1.5%, ambient air concentrations of biphenyl cannot exceed the ACGIH TLV should the 100 mg/m^3 GGV for C9-C15 aromatics be applied. Below the proposed HSPA limit, accounting for biphenyl in complex solvent is not necessary.

i) *Naphthalene* – Unlike other alkylated benzenes and alkylated naphthalenes, naphthalene is metabolized primarily through ring oxidation, which may introduce metabolites with more 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.

j) *Methylnaphthalene* – Methylnaphthalene is metabolized through side chain oxidation (80%) and ring oxidation (20%) similar to naphthalene. 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^3 GGV

k) *All others* – Although available data is limited on the higher alkyl benzenes, they are not expected to differ significantly from lower molecular weight forms in terms of toxicity responses, and hence are covered under the existing GGV of 100 mg/m^3 for C9-C15 aromatics. For example, a hazard assessment of n-butylbenzene has been conducted, showing no evidence for unique toxicity[8]. A more recent 2-generation reproductive toxicity study in the rat showed no effects on reproduction and the fetus with oral treatment up to 300 mg/kg/day[9]. Due to manufacturing specifications, polycyclic aromatic hydrocarbons (PAHs), i.e., aromatic molecules containing 3 or more rings are excluded from hydrocarbon solvents and are not accounted for in the RCP method.

Summary and conclusions

In summary, the RCP method remains a useful tool in the sense that it provides a sound occupational safety tool for complex hydrocarbon solvents that is aligned and simplifies compliance with national regulatory values, is globally consistent and simple to apply by downstream users and small-scale enterprises. With the exception of a few cases, the regulatory values for most hydrocarbon constituents are similar across the US, UK and Germany. Not surprisingly, the RCP GGV adaptations (which are essentially based on individual constituent TLVs) by the ACGIH, UK HSE and AGS (TRGS 900) are similar. It is

[8] http://www.meti.go.jp/english/report/downloadfiles/gED0303e.pdf

[9] Izumi, H., Kimura, E., Ota, T., & Shimazu, S. (2005). A two-generation reproductive toxicity study of n-butylbenzene in rats. *J Toxicol Sci, 30 Spec No.*, 21-38.

important to reiterate that the RCP is not intended to introduce alternative hydrocarbon constituent OELs, but rather to ensure that in the context of hydrocarbon solvent exposures, existing constituent values which are already in place are not exceeded.

A fundamental restructuring of the RCP adaptation by the AGS leads to the added risk of completely dissimilar OELs for the same complex substance across different regions, a problem the RCP was originally designed to eliminate. In keeping with the goal of maintaining the simplicity of the RCP, the HSPA recommends limiting the list of excluded constituents to the necessary minimum. For example, key excluded constituents should be limited to those with unique toxicities such as n-hexane, naphthalene, triethylbenzene and diethylbenzene. For cyclohexane, methylcyclohexane, decalin and biphenyl, these can be ignored in favor of the respective GGVs as long as they are below the stated concentration limits indicated above.

Overall, the goal of the RCP method, as envisioned by the HSPA, is that any individual should be able to calculate an OEL for any complex hydrocarbon solvent or blend of complex hydrocarbon solvents without the need for developing a detailed and expensive compositional analysis of the product. In the case of solvent blends for example, all that may be needed to calculate an OEL for the blend may be the OEL provided in the supplier MSDS for each blend component as shown below:

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

Where F_i = mole fraction of each blend component and OEL_i is the supplied OEL for each blend component.

The HSPA is currently developing a simple-to-use excel application that will be made available to customers willing to calculate OELs either for complex hydrocarbon solvents or blends.

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

Antoine Brossier
Director General European Solvents Industry Group (ESIG)