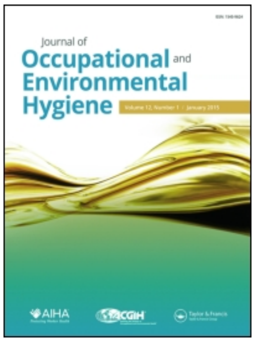

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The reciprocal calculation procedure for setting occupational exposure limits for hydrocarbon solvents: An update

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ABSTRACT

Hydrocarbon solvents are liquid hydrocarbon fractions, often with complex compositions. Due to the potential for human exposure, primarily to the more volatile solvents, substantial effort has been directed toward the development of occupational exposure recommendations. Because of the complex and variable nature of these substances, a proposed approach is to calculate occupational exposure levels (OELs) using an adaptation of the mixture formula developed by the ACGIH® in which "group guidance values" are assigned to similar constituents. This approach is supported by the results of toxicological studies of hydrocarbon solvents and their constituents which have shown that, with a few well-characterized exceptions, these substances have similar toxicological properties and produce additive effects. The objective of the present document is to summarize recommended revisions to the earlier proposals; these recommendations take into account recent toxicological information and changes in regulatory advice. Practical demonstrations on how to use these recommendations to develop occupational exposure advice in different situations (from simple complex solvents to blends of complex solvents) are also provided. Finally, a quantitative ideal gas method is proposed as a means of calculating occupational exposure limits for solvent blends in which, because the blended components have differing vapor pressures, there may be substantial differences between the liquid and vapor phase compositions.

KEYWORDS
Hydrocarbon solvents; occupational exposure limits; reciprocal calculation procedure

Introduction

Hydrocarbon solvents are liquid hydrocarbons derived from crude oil, primarily produced by distillation of petroleum feed-stocks or their synthetic analogs (e.g., Fischer-Tropsch-derived materials), sometimes followed by additional processing steps such as solvent extraction, hydrodesulfurization, or hydrogenation. Hydrocarbon solvents are mostly complex substances composed of molecules containing only hydrogen and carbon with carbon numbers ranging from approximately C5–C20 and having boiling points of approximately 35–370°C; however, most of the hydrocarbon solvents are more narrowly defined and seldom cover more than 3 carbon numbers. The solvent constituents can be of four types, normal paraffins, iso (i.e., branched) paraffins, cycloparaffins (also known as naphthenes), and aromatics. Because of the manufacturing processes, hydrocarbon solvents may contain any or all of these constituent types. Solvents containing more than one type of constituent are referred to as complex. Because of their specific technical requirements, hydrocarbon solvents are normally more highly refined with narrower distillation ranges than the petroleum feed stocks from which they are manufactured and may also have lower levels of more problematic constituents. Because hydrocarbon solvents have wide commercial applications, and some are quite volatile, there has been considerable interest in the development of occupational recommendations to limit workplace exposures.

The development of occupational exposure recommendations for these substances has been complicated by their complex and variable compositions; however, as most of the hydrocarbon solvent constituents have similar toxicological properties, the compositional variability can be managed on a generic basis. Historically, the

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toxicological properties of hydrocarbon solvents were characterized via a representative substance approach, and the results were then verified with studies of specific constituents.[1-17] A key objective of these studies was to provide base data that could be used to set occupational exposure limits. Aside from the finding that hydrocarbon solvents produced minimal systemic effects, three overarching conclusions were drawn from these studies: (1) that the effects of hydrocarbon solvents most relevant to occupational exposure recommendations are upper respiratory tract irritation and acute central nervous system (CNS) depression; (2) that the aromatic and cycloparaffinic constituents are more irritating than the corresponding alkanes; and (3) that these properties are additive.[6]

In 1994, the U.K. Health and Safety Executive (HSE) provided guidance by which hydrocarbon solvent manufacturers could calculate occupational exposure limits (OELs) for their products[18] using compositional information. The method was an adaptation of the American Conference of Governmental Industrial Hygienists (ACGIH®) advice for calculating OELs for mixtures using a reciprocal formula/mixtures formula:

$$\mathrm{Fr_a/OEL_a + Fr_b/OEL_b + \ldots = 1/OEL_{mixture}}$$

in which $\mathrm{Fr_a}$ is the vapor phase mole or liquid mass fraction of component a,[1] $\mathrm{OEL_a}$ is the OEL of component a, etc.[19] For calculation purposes, the HSE grouped similar constituents and assigned “group guidance values” (GGVs) that could be used as OELs in the calculation. n-Hexane and naphthalene were assigned “specific substance values” (SSVs) because of their unique toxicological properties.[20,21] A similar approach, with some modifications, was recommended by the European chemical industry,[22] adopted by the European hydrocarbon solvents producers, and, finally, formally published.[23] The recommendations were adopted with some modifications by the ACGIH[19] and as a national method in Germany in 2007.[24] Since then there have been a number of developments including the completion and publication of a number of toxicology studies of hydrocarbon solvents and their constituents, comprehensive data compilations to provide data supporting the High Production Volume (HPV) initiative and to meet REACH (Registration, Evaluation, and Authorization of Chemicals) registration requirements, and other regulatory developments. In addition, as part of the REACH registration process, a new nomenclature (the naming convention) for hydrocarbon solvents was introduced which provides much more compositional information than is available via the Chemical Abstract Services (CAS) numbering system which had previously been used to meet regulatory requirements. A detailed review of the new naming convention is provided in McKee et al.[17] In light of these more recent developments, it seemed reasonable to revisit the previous advice to determine whether any revisions were needed.

Occupational exposure guidance for complex hydrocarbons

Previously recommended approach and suggested revisions

The reciprocal calculation procedure (RCP) had two principal objectives: the first was to harmonize the approach to setting occupational exposure limits for complex hydrocarbon solvents such that manufacturers could provide consistent advice for compositionally similar products; the second was to assure that existing occupational exposure recommendations for individual constituents would not be exceeded as long as the calculated complex OEL values were respected. To achieve the first objective, it was important that the method be adopted and promoted by the industry. Acceptance by the regulatory community and expert bodies was also important as it increased the credibility of the recommendations. As discussed below, a critical step in gaining acceptance was formal publication of the recommendations and the underlying information.[23] Assurance that occupational exposure recommendations for all constituents do not exceed their respective regulatory limits, where available, was more difficult as there are many national regulatory and/or expert groups with their own internal processes, and so, particular attention was given to the recommendations of the ACGIH® in the United States and the European Scientific Committee for Occupational Exposure Limits (SCOEL) as these groups were considered to be particularly influential. Accordingly, a decision was made to use the occupational exposure recommendations from these groups to develop the GGVs rather than to develop values independently.

As shown in Table 1, the UK HSE divided the constituents into eight groups and assigned guidance values to each of these groups.[18] In a subsequent article, the European chemical industry reduced this to four groups, primarily by removing the differentiation between aliphatic and cycloaliphatic constituents, along with specific substance values for n-hexane and naphthalene.[23] The ACGIH accepted the recommendations of McKee et al.[23] with the separate requirement that the occupational exposure recommendations for individual constituents not be exceeded as long as the overall

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[1] While the mass fraction in the liquid phase is most often used as a surrogate for $\mathrm{Fr_a}$ in most OEL calculations, certain conditions may necessitate the use of the vapor phase mole fraction of the component of a mixture. These varying conditions are discussed further in this publication.

Table 1. Current recommended group guidance/substance-specific values for the RCP calculation.[a]

Constituent Grouping	UK[18] (mg/m^3)	HSPA/ACGIH[19,25] (mg/m^3)	Germany[24] (mg/m^3)
C5–C6 alkanes (excluding n-hexane)	1800	1500	1500
C7–C8 alkanes	1200	1500	1500
C5–C6 cycloalkanes	1800	1500	1500
C7–C8 cycloalkanes	800	1500	1500
C7–C8 aromatics	500	200	200
C9–C15 alkanes	1200	1200	600
C9–C15 cycloalkanes	800	1200	600
C9–C15 aromatics	500	100	100

[a] Current value. Note that national advice requires that exposures to constituents not exceed national recommendations.

recommendation is observed.[19] In Germany, the groupings and most of the recommendations were adopted, but the GGV of 1,200 mg/m^3 recommended by McKee et al.[23] for C9-C15 aliphatic constituents was reduced to 600 mg/m^3.[24] Thus, while there is reasonable agreement that a reciprocal calculation-based approach is appropriate, there have been regional adaptations.

It has been almost 20 years since the GGVs were originally proposed. Over that time there have both been scientific developments and changes in regulatory advice that have implications for the calculated values. In the remainder of this section, revisions to the RCP will be proposed, with more detailed discussion on the scientific developments provided in the Appendix.

Specific GGV/SSV recommendations and proposals for modification

Shown in Table 2 are the constituent hydrocarbon groups, the group guidance, and specific substance values, and, as an example, the ACGIH TLV® values for constituents within the constituent hydrocarbon groups.

C5–C8 aliphatic constituents

This grouping covers all aliphatic substances (normal paraffins, iso-paraffins, and cyclo-paraffins) within the C5-C8 carbon range, excluding n-hexane (unique metabolite/toxicity) and cyclohexane. It is apparent that the original group guidance value of 1,500 mg/m^3 is below the current ACGIH TLV recommendations for the majority of the C5–C8 aliphatic constituents; nevertheless, to more fully harmonize the guidance with the ACGIH, it is proposed to reduce the guidance value for this group of constituents from 1,500 mg/m^3 to 1,400 mg/m^3, the current ACGIH TLV for octanes. The cyclohexane value of 350 mg/m^3 was adopted after the development of the group guidance values (GGV); however, most of the complex aliphatic solvents contain $< 20\%$ cyclohexane. Assuming strict proportionality, this means that exposure to cyclohexane is unlikely to exceed 300 mg/m^3 as long as the overall guidance value of 1,400 mg/m^3 for C5–C8 aliphatic constituents is respected, meeting the ACGIH requirement that single constituent TLV recommendations are not exceeded.

Table 2. Proposed group guidance/substance-specific recommendations for the RCP calculation.

Hydrocarbon Solvent Constituent Group	Proposed Group Guidance/Substance Specific Value (mg/m^3)	Constituents with ACGIH TLVs (mg/m^3)
C5–C8 Aliphatics	1400	Pentane (all isomers) – 2950 Hexane (all isomers)[a] – 1760 Heptane (all isomers) – 1640 Octane (all isomers) – 1401 Cyclopentane – 1720 Cyclohexane – 350 Methylcyclohexane – 1610
C9–C15 Aliphatics[b]	1050	Nonane – 1050
C7–C8 Aromatics[c]	NA	Toluene – 75 Xylene (all isomers) – 434 Ethylbenzene – 87
C9–C15 Aromatics[d]	100	Trimethylbenzene isomers – 123 Cumene – 246 Indene – 24 Biphenyl – 1.3
Substances with Substance Specific Values		
n-hexane Naphthalene Diethyl/Triethyl benzene	176 50 28	176 50 No value

[a] Except n-hexane.

[b] Because of their very low vapor pressures, constituents with carbon numbers $>$ C15 do not contribute significantly to overall vapor exposure. However, the potential for aerosol exposure must be considered.

[c] Group eliminated in favor of adopting existing national regulatory values as SSVs.

[d] Because of their higher boiling points, aromatics with more than two rings are not commonly found at more than trace levels in hydrocarbon solvents.

Accordingly, it is recommended that the current GGV of 1,500 mg/m^3 for C5–C8 aliphatic hydrocarbon solvent constituents be reduced to 1,400 mg/m^3 and that the specific constituent TLV of 350 mg/m^3 be used in situations in which cyclohexane is used as a mono-constituent solvent or used as an SSV in the reciprocal calculation formula for complex solvents or blends in which the cyclohexane content is greater than 20%.

It should be noted that occupational exposure limits for pentanes are substantially higher than the proposed GGV in some regions. For example, the recommended occupational exposure limit for pentanes (all isomers) is 1,000 ppm ($\sim$ 3,000 mg/m^3) in the U.S. (ACGIH and OSHA), Germany (TRGS 900 and MAK), Spain, and Ireland. Nevertheless, pentanes are included in this group to reduce complexity in the calculations.

C9–C15 aliphatic hydrocarbon constituents

This grouping covers all aliphatic constituents within the C9–C15 carbon range. The only aliphatic constituent with an ACGIH TLV is nonane (1,050 mg/m^3). As discussed in more detail in the Appendix, the only known toxicological hazards of these constituents are acute CNS effects and upper respiratory tract irritation. Experimental evidence indicates that hydrocarbons with carbon numbers >C10 have such low vapor pressures that acute CNS effects are unlikely.[25–27] There were no acute effects in studies in which volunteers were exposed to a complex aliphatic solvent at levels up to 1,200 mg/m^3, either for one day or for five consecutive days.[28,29] To harmonize the GGVs with the ACGIH, it is recommended that the current guidance value of 1,200 mg/m^3 for C9–C15 aliphatic hydrocarbon solvent constituents be reduced to 1,050 mg/m^3.

C7–C8 aromatic constituents

When the GGV recommendations were initially developed, the C7–C8 aromatic constituent with the lowest TLV was toluene (188 mg/m^3), and it seemed unlikely that exposures to any of the C7–C8 aromatics (toluene, ethylbenzene and xylene) could exceed its own occupational exposure limits in the context of an overall guidance value of 200 mg/m^3. However, as TLV values for toluene and ethylbenzene have been substantially reduced, it now seems that the best strategy is to remove the guidance value in favor of substance specific values if any of the constituents is present at a level high enough to exceed its own TLV. In most cases, these constituents would not be found in hydrocarbon solvents at levels exceeding a few percent and are unlikely to have a substantial impact on the calculated values.

C9–C15 aromatic constituents

This grouping, with a GGV of 100 mg/m^3, covers all aromatic constituents within the C9–C15 carbon range, with the exception of certain C9+ constituents with lower recommended occupational exposure limits and/or unique toxicities. These constituent exceptions are biphenyl, triethylbenzene, diethylbenzene,[30,31] indene, naphthalene, and methylnaphthalene isomers. The original group guidance recommendation (100 mg/m^3) was based on the SCOEL Indicative Occupational Exposure Limit Value (IOELV) of 100 mg/m^3 for trimethylbenzenes, and was, therefore, lower than the corresponding ACGIH TLV of 123 mg/m^3. This value was applied to all aromatics with the exception of naphthalene, for which the TLV® of 50 mg/m^3 was recommended as a substance specific value. There is now more information on these constituents, particularly chronic studies of naphthalene in which respiratory tract tumors have been observed.[32,33] The relevance of these data to humans is controversial,[34,35] but there does seem to be a consensus that exposure levels should be set to avoid upper respiratory tract irritation (see the Appendix). In light of these developments it is now recommended that the guidance value of 100 mg/m^3 be maintained for alkylated benzenes with 9 or more carbons, but that the 50 mg/m^3 TLV® for naphthalene be also applied to alkylated naphthalenes. Other aromatic constituents including cumene, indene, and biphenyl are at levels that are low enough that their own occupational exposure limits would not be exceeded as long as the group guidance value of 100 mg/m^3 is observed.

Other recommendations

As above, it is recommended that 50 mg/m^3 be maintained as a specific substance value for naphthalene (although this value could be reduced if the guidance changes) and that the same value be used for other alkylated naphthalenes as well. It is recommended that the SSV for n-hexane be maintained at 176 mg/m^3 to align with the ACGIH recommendation.[19] Finally, it is recommended that an occupational exposure limit for diethyl- and triethylbenzenes be adopted separately, due to the neurotoxic properties of some of the isomers. In the absence of any other recommendations, it seems reasonable to adopt the Workplace Environmental Exposure Level (WEEL) of 28 mg/m^3[36] for diethyl- and triethylbenzenes as a group.

OEL calculations for complex hydrocarbon solvents

Complex solvents

The RCP procedure is designed to be simple to use and should not require downstream users to generate detailed and expensive compositional information. As indicated earlier, the vapor phase mole or liquid mass fraction of a constituent in a mixture can be used as a surrogate for Fr_a in the RCP formula. For highly refined complex solvents which are compositionally defined by the presence of aliphatic and/or aromatic constituents with narrow boiling ranges (i.e., seldom varying by more than three carbon numbers), the liquid mass fraction is most often preferred since this is readily available. More importantly, the narrow boiling range for these solvents ensures that each individual constituent is present in the liquid phase at approximately similar ratios as would be expected in the vapor phase. Two practical examples of RCP-derived OELs for complex solvents are provided below:

Calculate the RCP-derived OEL for a regular white spirit (stoddard solvent)

In this example, regular white spirit is identified as a hydrocarbon solvent within the C9–C12 aliphatic carbon range, containing ~21% aromatics. Since this substance has a relatively narrow boiling range, substantial differences in constituent vapor pressures are not expected and mass fractions can be used in the RCP equation. Individual carbon range/constituents of the regular white spirit in this example, including appropriate GGVs and/or SSVs for each constituent or carbon range, are indicated in Table 3.

Based on calculations shown in Table 3, $1/\mathrm{OEL}_{\mathrm{complex}} = 1/0.003243$

$$\mathrm{OEL}_{\mathrm{complex}} = 308.4\ \mathrm{mg/m^3}.$$

The $\mathrm{OEL}_{\mathrm{complex}}$ of 308.4 $\mathrm{mg/m^3}$ is rounded down to 300 $\mathrm{mg/m^3}$ based on the ACGIH rounding rules (Appendix H). According to the rules, calculated values $<100\ \mathrm{mg/m^3}$ can be rounded up to the nearest 25, calculated values between 100 and 600 $\mathrm{mg/m^3}$ are rounded to the nearest 50 and values $>600\ \mathrm{mg/m^3}$ are rounded to the nearest 200. For this calculation, unique substances such as naphthalene and diethylbenzene were accounted for using existing ACGIH® and AIHA recommendations. As a result of the elimination of the C7–C8 aromatic RCP group, toluene and xylene were accounted for using current ACGIH TLV® values as recommended SSVs (see Table 2). Liquid mass fractions were indicated as the percentage of each constituent in the complex solvent, such that the sum total is equal to 1 (100%). The appropriateness of the calculated OEL for this substance is validated by studies in human volunteers showing no adverse effects during or after exposure to 100 or 300 $\mathrm{mg/m^3}$ of a regular white spirit, similar to that profiled in Table 3.[37]

Calculate the RCP-derived OEL for varnish makers and paints (VM&P) naphtha reported in Carpenter et al.[12]

This example was selected to demonstrate some of the considerations that go into calculating OELs for complex substances when detailed compositional data is not readily available. In this example, no additional information was provided beyond the carbon number range and constituent structures (Table 4). However, the most critical aspect is to first consider the potential for constituents with unique toxicities and/or low regulatory TLVs. According to Table 2 of Carpenter et al.,[12] VM&P naphtha is predominantly a C7–C10 "white spirit"-type substance. Levels of C6 paraffins and monocycloparaffins were approximately 0.3 and 0.5%, respectively. Hence, n-hexane and cyclohexane, if present, would occur only at trace levels (particularly n-hexane) and do not need to be taken into account. In other words, all aliphatics in the solvent are represented by the GGVs for the C5–C8 and C9–C15 aliphatic hydrocarbon groups.

With respect to the aromatic constituents, no GGV is available for alkylbenzenes in the C7–C8 aromatic group. The only possible C7 alkylbenzene is toluene. Although C8 alkylbenzenes could include ethylbenzene and isomers of xylene, the most likely constituents are xylene isomers as ethylbenzene is typically found only at low levels in white spirits of this type. For C9 alkylbenzenes, present at 3.7%, the only unique substance that could be present is indene which, if present, is normally at low levels. Further, as a result of its low vapor pressure, its impact on the OEL would be negligible. C10 alkylbenzenes are present

Table 3. RCP OEL calculation for regular white spirit.

Constituent	RCP Hydrocarbon Group	GGV or SSV ($\mathrm{mg/m^3}$)	Liquid Mass Fraction (Fr_a)[a]	Reciprocal Calculation[b]
C8 aliphatics	C5-C8 aliphatics	1400	0.02	1.43×10^{-5}
C9 aliphatics	C9-C15 aliphatics	1050	0.14	0.00013
C10–C15 aliphatics	C9-C15 aliphatics	1050	0.652	0.00062
Toluene	NA	75	0.001	1.333×10^{-5}
Xylene	NA	434	0.006	1.383×10^{-5}
C9 trimethylbenzene isomers	C9-C15 aromatics	100	0.18	0.0018
Naphthalene	NA	52	0.006	0.0001154
Diethylbenzenes	NA	28	0.015	0.000536
Sum				0.003243

[a] Mass fraction in liquid phase divided by 100%. NA = not available

[b] Fr_a/GGV or Fr_a/SSV

Table 4. Composition/RCP OEL calculation of VM&P Naphtha.[12]

Constituent	Weight (%)	RCP Hydrocarbon Group	GGV or SSV (mg/m^3)	Reciprocal Calculation[a]
C5–C8 alkanes	26.0	C5–C8 aliphatics	1400	0.000186
C5–C8 cycloalkanes	21.2	C5–C8 aliphatics	1400	0.000151
C9–C11 alkanes	29.4	C9–C15 aliphatics	1050	0.00028
C9 cycloalkanes	7.8	C9–C15 aliphatics	1050	7.43×10^{-5}
C10 cycloalkanes	3.3	C9–C15 aliphatics	1050	3.14×10^{-5}
C11 cycloalkanes	0.4	C9–C15 aliphatics	1050	3.81×10^{-6}
C7 alkylbenzenes	1.6	Toluene	75	0.000213
C8 alkylbenzenes	5.9	Xylene	434	0.000136
C9–C10 alkylbenzenes	4.2	C9–C15 aromatics	100	0.00042
Sum				0.001496

[a] Fr_a/GGV or Fr_a/SSV

at 0.5% and are expected to have a negligible impact on the overall OEL of the naphtha solvent. As a result, all C9/C10 alkylbenzenes were represented by the 100 mg/m^3 GGV for C9–C15 aromatics.

Based on calculations in Table 4,

$$1/\mathrm{OEL}_{\mathrm{complex}} = 0.001496$$
$$\mathrm{OEL}_{\mathrm{complex}} = 700\,\mathrm{mg/m^3}.$$

Carpenter et al.[12] proposed an OEL of 2,000 mg/m^3 for VM&P naphtha, based on repeated-exposure responses in rats, dogs, and human volunteers. The calculated OEL value of 700 mg/m^3 thus underscores the conservative nature of the RCP method, as it is well below the no effect level in the volunteer study. Additional practical examples of RCP-derived OELs for a dearomatized white spirit and high flash aromatic naphtha are provided in detail in the Appendix.

Solvent blends

A blend solvent may be defined as a mixture of two or more individual complex solvents, two or more individual hydrocarbon constituents or a mixture of individual hydrocarbon constituents and/or complex solvents. The key distinction is that blends are intentional mixtures whereas complex solvents are products of the manufacturing process. In certain cases, oxygenated substances may also be included in the blend mixture. Thus, similar to the considerations for complex solvents, it is important that each component of the blend be verified for compliance with the additivity principle on which the RCP formula is based. Oftentimes, a detailed composition of each complex solvent in the blend is not required, and the RCP-derived OEL for the blend can be calculated if the OEL for each complex solvent is available (using the ACGIH mixtures rule).

Practical considerations for calculating RCP-derived OELs for hydrocarbon solvent blends

Most regional adaptations of the RCP procedure recommend the use of the liquid mass fraction of the individual constituents of a complex solvent, in the RCP equation. In other words, for a substance containing 20% n-hexane, 40% n-octane and 40% n-nonane, the mass fractions (Fr_a) used in the RCP equation would be 0.2 for n-hexane, 0.4 for octane isomers and 0.4 for nonane. However, this recommendation comes with certain limitations. For example, the Ontario Ministry of Labor (Canada) specifies that the RCP should be "restricted to applications where the boiling points of the solvents in the mixture are relatively narrow", i.e., within a range of less than 45°C and with vapor pressures within approximately one order of magnitude. The same restriction is indicated in the ACGIH adaptation. Furthermore, the ACGIH adaptation recommends that if the above conditions cannot be met, the liquid mass fraction (F_r) should be substituted with the mole fraction for each constituent in the vapor phase (see Appendix H of ACGIH TLV recommendation). The implication of the boiling range restriction is that for substances such as blend solvents, which may contain components with a wider vapor pressure range, the mass fraction of each component in the liquid phase may not be representative of the true fraction of each component in the vapor phase. In other words, a highly volatile substance which may be present at low levels in the liquid phase of a low vapor pressure blend solvent may be over-represented in the vapor phase of a blended solvent. An illustrative example of this situation is provided below.

Assume that blend solvent A consists of 20% n-hexane, 40% n-octane and 40% n-nonane. Using the liquid mass fraction in the RCP equation, the OEL for the solvent A is calculated as follows (see Table 2 for GGVs and SSVs utilized):

$$1/\mathrm{OEL}_{\mathrm{blend}} = 0.2/176 + 0.4/1400 + 0.4/1050 = 0.0018$$
$$\mathrm{OEL}_{\mathrm{blend}} = 550\,\mathrm{mg/m^3}.$$

The vapor pressure for n-hexane (19.68 kPa at 25°C) is much higher than that of n-nonane (0.653 kPa at 25°C). Therefore, the ambient air vapor concentration of n-hexane in blend solvent A is likely to be substantially greater than 20%, and the n-hexane TLV could be exceeded. In order to take into account the differences in vapor pressure, we need to calculate the vapor phase mole fraction for each component using a combination of Raoult's law and Dalton's law of partial pressures.

According to Raoult's law, the partial vapor pressure of a component in a mixture (PP_A) is equal to the vapor pressure of the pure component (P_A) at that temperature multiplied by its mole fraction in the mixture (M_A) (in this case, the mass fraction of the constituent in the liquid mixture is used as a surrogate for the mole fraction). On the other hand, Dalton's law of partial pressures states that the total pressure exerted by a mixture of gases (P_{tot}) is equal to the sum of the partial pressure ($PP_A \ldots PP_\infty$) of each individual gas (i.e. $P_{tot} = PP_A + \ldots + PP_\infty$). Using both laws, we can determine the mole fraction of components of a blend solvent in the vapor phase by first determining the partial pressure of each component. Using the example for n-hexane above:

Partial pressure of n-hexane in blend solvent A = mass fraction in blend × vapor pressure of n-hexane at 25°C:

$$\text{Partial pressure} = 0.2 \times 19.68\,\text{kPa} = 3.94\,\text{kPa}.$$

Applying the same equation, partial pressures for n-octane (vapor pressure = 1.97 kPa at 25°C) and n-nonane are determined to be 0.79 and 0.26 kPa, respectively.

Using Dalton's law of partial pressures, we can calculate the vapor phase mole fraction for each constituent by dividing the sum of the partial pressures for all blend constituent by the total vapor pressure of the solvent blend, i.e., vapor phase mole fraction for n-hexane = 3.94 / (3.94 + 0.79 + 0.26) = 3.94 / 4.99 = 0.79.

Based on the calculations above, while n-hexane only comprised 20% of blend solvent A in the liquid phase, it actually comprises 79% of the total hydrocarbon in the vapor phase. In contrast, vapor phase proportions of n-octane and n-nonane were determined to be 15.8 and 5.2%, respectively. Using these values, we can recalculate the OEL for solvent blend A:

$$1/\text{OEL}_{\text{blend}} = 0.79/176 + 0.158/1400 + 0.052/1050$$
$$= 0.00465\ \text{OEL}_{\text{blend}} = 200\,\text{mg/m}^3.$$

The OEL calculated using the vapor phase mole fraction is approximately 3-fold lower than the OEL calculated using mass fraction in the liquid phase. This OEL would be considered to be more appropriate as it reflects actual ambient air concentrations for each constituent in the solvent blend.

Implications of vapor phase calculations

Since one goal of the RCP is to ensure that the individual TLVs for constituents (especially for constituents with unique toxicological properties) are not exceeded within the context of the OEL for the total blend mixture, it is important to make sure that ambient air exposures to n-hexane do not exceed its TLV of 176 mg/m^3 in the example discussed above. If we assumed that blend solvent A has an OEL of 550 mg/m^3 and that it contains about 20% n-hexane, what would the anticipated concentration of n-hexane in the vapor phase be at this OEL?

Note that the partial pressure for n-hexane was already determined to be 3.94 kPa and total pressure of blend solvent A was determined to be 4.99 kPa (see above). Assuming ideal gas situation, the saturated vapor concentration of n-hexane at 25°C can be calculated, as shown below:

$$\left(3.94\,\text{kPa} \times 1,000,000\,\text{ppm}\right)/101.3\,\text{kPa}$$
$$= 38{,}894\,\text{ppm n}-\text{hexane}.$$

To calculate the saturated vapor concentration of solvent blend A at 25°C:

$$\left(4.99\,\text{kPa} \times 1,000,000\,\text{ppm}\right)/101.3\,\text{kPa}$$
$$= 49{,}260\,\text{ppm solvent blendA}.$$

The concentration of n-hexane that would be present in the vapor phase, using an exposure limit of 550 mg/m^3 for solvent blend A would be:

$$\left(38{,}894\,\text{ppm}/49{,}260\text{ppm}\right) \times 550\text{mg/ m}^3 = 434.3\,\text{mg/ m}^3.$$

As shown above, observing an OEL of 550 mg/m^3 for blend solvent A yields exposures to n-hexane that are approximately 2.5-fold higher than its TLV. On the other hand, by substituting an OEL of 200 mg/m^3 in the above equation (in place of 550 mg/m^3), maximum exposure to n-hexane at 25°C is 160 mg/m^3. In this case, with a recommended OEL of 200 mg/m^3, ambient air exposures to n-hexane are controlled to levels below its individual TLV® of 176 mg/m^3. This simple calculation is a useful means of checking whether a recommended OEL is appropriate, especially in cases involving a substance with unique toxicity or with an unusually low national occupational exposure recommendation. As shown above, it would have been more appropriate to use the vapor phase mole fraction than the mass fraction in the liquid phase to account for the large difference in vapor pressures. Two additional examples of RCP-derived OEL calculations for blend solvents are provided in the Appendix.

OEL calculations for hydrocarbon solvent blends with non-hydrocarbon organic solvents

With the recent trend to replace volatile constituents of hydrocarbon solvents (such as toluene and xylene) for certain applications (consumer paints and thinners, etc.), formulators are starting to develop replacement solvent blends that include a combination of aliphatic hydrocarbons and oxygenated solvents. As stated earlier, the RCP method requires a common mode of action for hydrocarbon solvent constituents (additivity principle). While a great deal of information is available to indicate that complex hydrocarbon solvent constituents (within the range C5–C20) adhere to this principle,[17] the same cannot always be said for non-hydrocarbon constituents of certain blend solvents. In other words, the RCP method cannot simply be extended to blends of hydrocarbon solvents with other organic solvents such as ketones, alcohols, or other wider boiling potentially less refined hydrocarbons such as petroleum/naphtha streams or petroleum fuels (which may contain benzene which is excluded from the method) without independent verification of underlying toxicity principles/mode of action. In cases where the toxicological properties of the non-hydrocarbon component of the solvent blend are shown to be similar to those of hydrocarbon solvents, the RCP method or the mixtures rule (when relatively limited data is available) can be applied in calculating the OEL of the blend.

As an illustration, a hypothetical manufacturer has requested for the calculation of an RCP OEL for an aerosol coating formulation (containing 20% acetone, 30% toluene, and 30% xylene). This solvent blend contains a mixture of hydrocarbons (toluene and xylene), for which the RCP method applies, and a non-hydrocarbon substance, in this case, a ketone. Acetone is a well-studied substance and its toxicological properties are generally limited to mucosal irritation and acute CNS effects with high exposures.[38] Since these properties are not different from those already described for hydrocarbon solvents, the RCP method is considered to be appropriate to use in calculating an OEL for this product. However, the vapor pressures for all three product components vary by up to 38-fold (24.44, 2.98, and 0.652 kPa at 20°C for acetone, toluene, and xylene, respectively). Hence, vapor phase mole fractions (rather than mass fractions in the liquid phase) would be a more appropriate parameter to use in the RCP equation. Using Raoult's and Dalton's law equations previously discussed, the vapor phase mole fractions for each component of the product were determined to be 82, 15, and 3% for acetone, toluene, and xylene, respectively. For toluene and xylene, SSVs of 75 and 434 mg/m^3 were employed in the OEL calculation (see Table 2). For acetone, the ACGIH® 8-hr TLV-TWA of 594 mg/m^3 was used as a surrogate SSV.

OEL calculation

$$\begin{aligned}1/\mathrm{OEL}_{\mathrm{blend}} &= 0.82/594 + 0.15/75 + 0.03/434\\ 1/\mathrm{OEL}_{\mathrm{blend}} &= 0.00345\\ \text{Proposed OEL}_{\mathrm{blend}} &= 289.9\ \mathrm{mg/m^3}\ \text{or}\ 300\ \mathrm{mg/\ m^3}\end{aligned}$$

Considering the relatively low ACGIH TLV for toluene, it is important that we consider whether the ambient air concentrations at the calculated OEL do not exceed this value. Using the Raoult's law and Dalton's law equations, maximum ambient air concentration of toluene at the 300 mg/m^3 OEL for the blend is approximately 45 mg/m^3. Since this value is lower than the ACGIH® TLV of 75 mg/m^3, the blend OEL calculated is considered protective of exposures to its individual components.

Summary

The RCP method was developed as a means to provide occupational exposure recommendations for complex, relatively narrow boiling, and highly refined hydrocarbon solvents which may contain a large number of constituents for which toxicology data may not be readily available. The method also reduces the need for an industrial hygienist to independently monitor a large number of constituents when emphasis can be placed on a small number of uniquely toxic substances, when present. The RCP methodology presented relies on the use of GGVs (for a host of hydrocarbon constituents within a narrow range and for which common metabolic and toxicological profiles have been established) and SSVs for unique substances which need to be accounted for separately. The small number of substances with SSVs also eliminates the need for extensive compositional information. As long as it can be established that the toxic properties of non-hydrocarbon constituents are additive with those of hydrocarbon substances, it is possible to extend the RCP methodology beyond the current scope.

With the exception of minor considerations, the RCP is not only applicable to complex solvents or blends of two or three mono-constituent hydrocarbons; it can also be used to provide OEL recommendations for blends of two or more complex solvents. In calculating the RCP-derived OEL, it is imperative that potential vapor pressure differences between individual constituents and the complex solvent or blend be considered in determining whether the mass fraction in the liquid phase or mole fraction in the vapor phase is the most appropriate parameter to use in the equation, as the mass fraction may not always be reflective of actual vapor phase contributions of each constituent.

Overall, the RCP method remains the most viable method to developing occupational exposure values for complex hydrocarbon solvents. The ease and flexibility of the method provides opportunities for regular updates when changes to the toxicological database and/or regulatory limit values occur.

Conflict of interest statement

Two of the authors (MDA, JCC) are employed by companies that manufacture hydrocarbon solvents. The first author (RHM) is retired from but retains an emeritus relationship with ExxonMobil Biomedical Sciences, Inc. The article was written as part of their normal employment.

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