Electronic Supplementary Information for:

Updating and Expanding GSK's Solvent Sustainability Guide†

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Section 1: Selection of new solvents for assessment

There are a number of solvents which have garnered literature interest in recent years as potentially green options.[1,2,3] The ACS Green Chemistry Institute Pharmaceutical Roundtable (ACS GCIPR)[4] and the EU IMI:CHEM21[5] partnership also have ongoing efforts to produce comprehensive green chemistry solvent selection guides from a collaborative perspective. Any solvents included in the lists for evaluation from these groups which had not previously been part of the GSK solvent guide dataset were incorporated during this update.

The topic of bio-derived chemicals, some of which may serve as solvents, appears quite frequently in the green chemistry literature. Derived from citrus waste biomass, *p*-cymene and its precursor limonene have been shown to have utility as solvents for simple organic reactions.[6] Glycerol, included previously in the GSK guide, is produced as a waste product from biodiesel. Its derivatives glycerol diacetate and glycerol triacetate have been demonstrated as reaction solvents across a range of chemical transformations.[7,8] The bioderived lactic acid has been proposed as an inexpensive and benign alternative to acetic acid and has been demonstrated to have utility as reaction media for multiple transformations.[9] Also derived from biomass and cited for their low toxicity are dimethyl isosorbide,[10] γ-valerolactone,[11] furfural,[12] and tetrahydrofurfuryl alcohol,[13] although not all of these have yet shown wide utility as reaction media in published literature.

Ethers often pose safety risks through their ability to form potentially explosive peroxide byproducts. 1,3-dioxolane is specifically noted to be less toxic than many traditional ether solvents.[14] Dimethoxymethane[15] and diethoxymethane have been mentioned as potentially green solvents based on their low peroxide formation potential, as well as the low water miscibility of diethoxyethane which could facilitate solvent recycling.[16] Diethoxymethane has also been demonstrated as reaction medium on multi-kilogram scale for a pharmaceutical development process.[17] Conclusive literature evidence of low peroxide formation tendency could only be found for diethoxymethane (DEM).[18] Therefore dimethoxymethane (DMM) continues to be scored in our dataset as having a significant peroxide formation rate, similar to commonly used ethers such as 1,4-dioxane and diethyl ether. In addition, the low boiling point and high vapour pressure of DMM raises concern with respect to volatile organic compound (VOC) emissions. Both DEM and DMM are reported to be poorly biodegradable and pose flammability risks due to low flash points.[19] These combined risks result in red evaluations for both of these solvents.

Carbonate solvents[20] have engendered interest within the green chemistry community due to their ready availability, low toxicity, and ease of biodegradation; therefore we expanded on the original dataset which included dimethyl, ethylene, and propylene carbonates to also include diethyl carbonate and butylene carbonate.[21]

Methanesulfonic acid has been mentioned in the literature as a green solvent based on high stability and easy biodegradability.[22] Several additional aliphatic alcohols and esters, both straight-chain and branched, are included in the updated assessments, since they offer EHS and green profiles similar to the alcohol and ester solvents which were recommended in the previous solvent guides. These include: amyl acetate, t-amyl alcohol, diethyl succinate, diisopropyl adipate, dimethyl succinate, 2-ethylhexylacetate, 1-heptanol, 1-hexanol, isoamyl acetate, methyl oleate, methyl propionate, 1-octanol, and 1-pentanol. Additional solvents (methyl formate, formic acid, 1,3-dimethyl-2-imidazolidinone, N-ethylpyrrolidone and tetramethylurea) were added because they have been suggested for evaluation by other groups (as were many of the aliphatic alcohols and esters), or because (2,4,6-collidine,) they were considered to be reasonably common solvents omitted from the 2011 version of the guide even if they were not necessarily expected to be assessed as green options.[23]

Green solvent research is a field that continues to grow and evolve. Recent literature reports suggest that 1,2,3-trimethoxypropane[24] shows utility as a reaction solvent for reduction of small molecules, although this glycerol-derived molecule is not currently commercially available from major vendors. Similarly, we have evaluated the green chemistry properties of dihydrolevoglucosenone, a dipolar aprotic solvent developed by Circa group under the name Cyrene™, although not yet distributed through major suppliers.[25] Given the limited data available for both 1,2,3-trimethoxypropane and dihydrolevoglucosenone, a number of assumptions were required based on chemicals of similar structure. With this combination of experimental and approximated data, the scores for 1,2,3-trimethoxypropane are quite low for human health concerns, while dihydrolevoglucosenone has low to moderate scoring in categories for waste treatment and human health.

A number of other solvents were considered for evaluation, including ones which are manufactured at high volume and frequently employed in other industrial sectors. The scope of this guide, however, is intended to focus on solvents with utility for organic synthesis, therefore solvents for which no such use could be documented were not included.[26]

Other classes of solvents such as ionic liquids,[27] fluorous solvents, supercritical fluids, and polymeric solvents are frequently mentioned in green chemistry references.[2] However, these solvent types are deemed to be beyond the aim of this current work.

Section 2: Details of GSK Solvent Sustainability Guide Methodology

2.1 Assignment of Scores for Properties with a Continuum of Values

Data scores assessed within categories of this guide typically range in value from 1 to 4. For some scores, the correlation of data to discrete score values is done on known risks associated with certain property thresholds. For others, the scoring is a continuum based on the range of known values within the dataset. This process is exemplified for the enthalpy of combustion score, found within the incineration category. The full set of data for the score in question is gathered and sorted in numerical order. With the data thus sorted, a column chart is created to show the range of values:

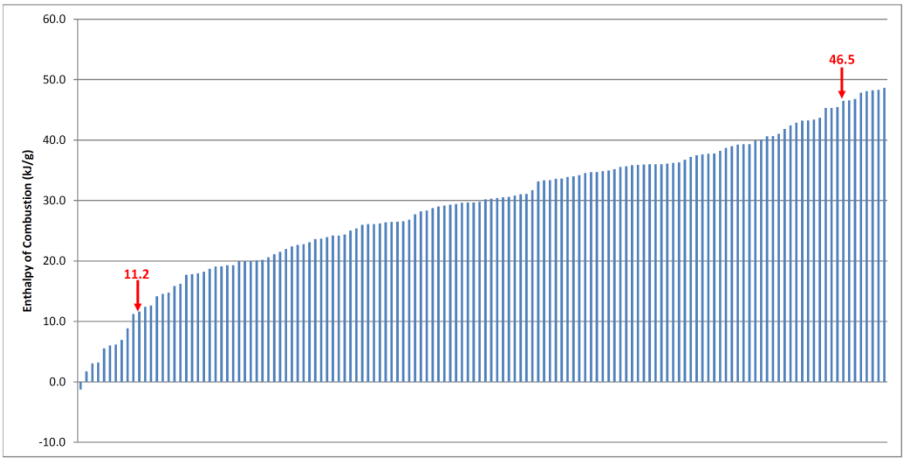


Figure 1: Plot showing range of enthalpy of combustion data and assignment of end limit values

The chart is examined and points are chosen where the ends of the data range show significant inflection from the bulk of the data, as indicated above by the data points with red arrows. These data values are assigned to score values of 1 and 4, which are plotted, and the corresponding equation calculated (Figure 2). This equation is used to calculate score values for the full dataset.

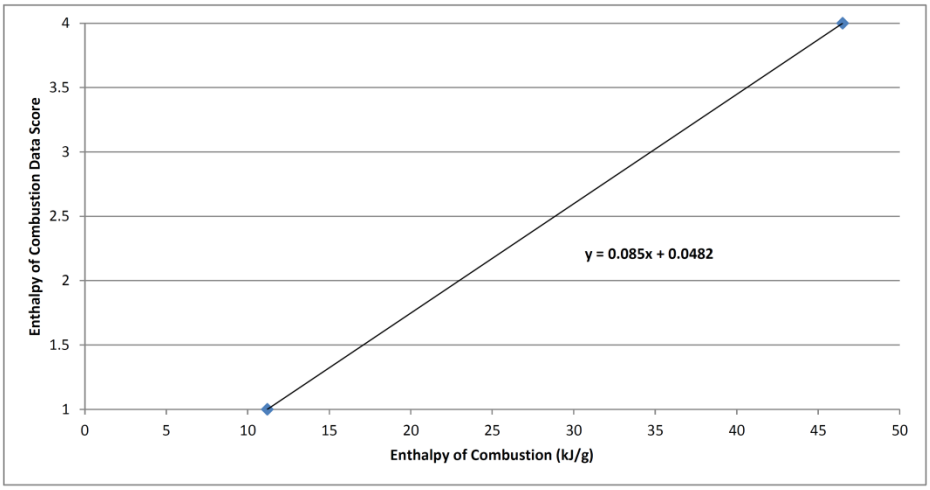


Figure 2: Plot used to determine equation for calculation of enthalpy of combustion data score

This approach is employed for the following data scores:

Category	**Data Score**	**Data Value for Score = 1**	**Data Value for Score = 4**
Incineration	Enthalpy of Combustion	11.2 kJ/g	46.5 kJ/g
Biotreatment	Theoretical Oxygen Demand (ThOD)	3.17 NO_3 eq./kg	1.22 NO_3 eq./kg
Biotreatment	Vapour Pressure	325 mm Hg	0.21 mm Hg
Environmental Impact: Air	Vapour Pressure: Odour Threshold Ratio	22,600 mm Hg/ppm	0.003 mm Hg/ppm

Exposure Potential	Vapour Hazard Ratio	518,400	8.03

Table 1: List of data points for which scores are determined by method shown in Figure 1 and Figure 2.

2.2 Normalisation of Category Scores

For each category, scores are assigned on a scale from 1 to 10, with the intent that the solvent rated the least green in a category has score equal to 1, and that rated the most green has score equal to 10. As shown in Table 2-Table 5, multiple data points are scored within each category. With the exception of the health hazard score, the geometric mean of these data scores is then taken to give a preliminary category score. With each of these data scores ranging from 1 to 4, the preliminary category score would in theory have the same range. For some categories, however, the full range from 1 to 4 is not covered. Therefore, in order to translate these scores to a full 1 to 10 span, the following equation is employed:

$$Score = \left(\frac{Score_{calc} - Min\ Score}{Max\ Score - Min\ Score} \times 9\right) + 1$$

where $Score_{calc}$ is the geometric mean of data scores as calculated for an individual solvent, and Min Score and Max Score are the minimum and maximum values of a particular $Score_{calc}$ across the full dataset.

Incineration	**Recycling**	**Biotreatment**	**VOC Emissions**
Water solubility	Boiling point	Nitrogen content	Boiling point
Emissions to air	Boiling point range	Theoretical oxygen demand	Vapour pressure
Enthalpy of combustion	Ease of drying	Vapour pressure	
	Water solubility	Halogen content	
	Reactivity	Water solubility	
	Flammability		

Table 2: Summary of data points used in calculation of waste category scores

Environment: Aqueous	**Environment: Air**
Acute tox LC_{50}/IC_{50} values for aquatic species (*i.e.* fish, daphnia, and algae)	Photochemical ozone creation potential (POCP)
Partition coefficient (Log K_{OW})	Odour threshold
Biodegradation	Vapour pressure

Table 3: Summary of data points used in calculation of environment category scores

Health Hazard	**Exposure Potential**
GHS Hazard Phrases	Vapour hazard ratio
OEL values	

Table 4: Summary of data points used in calculation of health category scores

Flammability & Explosion	**Reactivity**
Electrical conductivity	NFPA Reactivity Rating
Boiling point	Peroxide formation tendency
Vapour pressure	Self-reactive hazard assessment
Auto ignition temperature	Acidity
Flash point	Special Hazards

Table 5: Summary of data points used in calculation of safety category scores

2.3 Incineration Score

Aqueous solubility is rated by assigning the following discrete values to the integral scores 1-4.

- Score 4: Aqueous solubility = 1 g/L
- Score 3: Aqueous solubility = 5 g/L
- Score 2: Aqueous solubility = 50 g/L
- Score 1: Aqueous solubility ≥ 250 g/L

The solubility of the solvent in water is commonly available in the literature and is used as a surrogate for the less available solubility of water in the solvent.
With these assignments made, a linear graph is obtained by plotting score against log (solubility) to give a plot of:

$$Aqueous\ Solubility\ Score = -1.22 \times \log(solubility) + 3.96$$

where solubility is measured in g/L. This formula is used to convert reported aqueous solubility data to scores between 1 and 4, for 1 g/L < solubility < 250 g/L. Any solubility values outside of this range are given the boundary scores of 1 or 4.

The emissions to air score is based on an ordinal ranking as follows:

- Score 4: If no N, S, or specific unwanted by-products
- Score 2: If solvent contains N or S, therefore NO_X or SO_X can be emitted
- Score 1: If specific unwanted by-products are emitted, specifically: dioxins, phosgene, HCl, or HF

Enthalpy of combustion $\left(\Delta H_c^\circ\right)$ data are sourced at STP conditions. Where published sources disagree, the minimum reported value is utilised. As described in Section 2.1, the range of this data is used to determine the formula:

$$Enthalpy\ of\ Combustion\ Score = 0.085 \times \Delta H_c^\circ + 0.048$$

which is then used to convert reported enthalpies of combustion to values between 1 and 4. In instances where enthalpy of combustion values cannot be sourced, the enthalpy combustion score is set by default to 2.0.
A preliminary incineration score is calculated as the geometric mean of the water solubility, emissions, and enthalpy of combustion scores, followed by normalization to provide the incineration category score.

2.4 Recycling Score

A maximum score of 4 is assigned for a boiling point of $\leq$ 50 °C. A minimum score is assigned of 1 for a boiling point $\geq$ 200 °C. Plotting a graph of boiling point against score gives an equation of:

$$Boiling\ Point\ Score = -0.02 \times boiling\ point + 5.0$$

for 50 °C < boiling point < 200 °C.

For boiling point range, a list of 40 commonly used solvents, as determined through consultation with the GSK manufacturing organisation, is consulted. Given the reasonable likelihood of any given solvent appearing together in an organic solvent waste stream with one or more of these common solvents, any similarities in boiling points would tend to significantly increase the difficulty of solvent waste recycling. The boiling point of each solvent in the guide was compared against those of the 40 common solvents. A maximum score of 4 for boiling point range is assigned if none of the 40 common solvents has a boiling point within 10 °C of that of the solvent in question. A minimum score of 1 is assigned if 10 or more solvents are found with a boiling point within 10 °C of the solvent concerned. These data points are plotted to determine the formula:

$$Boiling\ Point\ Range\ Score = -0.30 \times number\ of\ solvents + 4.0$$

for 0 < number of solvents $\leq$ 10.

Ease of drying is rated between 1 and 4 as follows:

- Score 4: Solvent known to form an azeotrope with water.
- Score 3: Not known whether the solvent forms an azeotrope with water and boiling point is not similar to that of water.
- Score 1: Difficult to dry, since boiling point is within 10 °C to that of water or does not form an azeotrope with water.

Azeotrope formation with co-solvents other than water is not considered. The previous methodology penalised solvents for being known to form azeotropes with other solvents within the guide, however similar logic to that described for close boiling solvents applies here in that such data simply is not established for numerous potential combinations of two or more of the 154 solvents within the dataset.

Flammability and explosivity is rated between 1 and 4 using a normalised value (*i.e.* a ranked normalised score taking into account: boiling point, flash point, autoignition temperature, conductivity and vapour pressure, as described further in Section 1.11.[28])

Reactivity is rated between 1 and 4 in a similar manner to flammability and explosivity, normalizing scores described further in Section 2.12 which assess peroxide formation, potential for self-reaction, National Fire Protection Association (NFPA) Reactivity

Ratings, acidity/basicity, and any special hazards.

Aqueous solubility is rated between 1 and 4 as described previously under the assessment of incineration score.

The recycle category score is first calculated as:

$$Recycle\ Score = \sqrt[7]{BP^{1.5} \times BPR \times EoD \times WS \times R \times F}$$

where BP = boiling point score, BPR = boiling point range score, EoD = ease of drying score, WS = water solubility score, R = reactivity score, and F = flammability score.

This is essentially an adjusted variant of the geometric mean approach used for other scores which applies a higher weighting to boiling point, acknowledging the disproportionate impact that this factor has on the ease of recycling. This score, with a theoretical minimum of 1 and a theoretical maximum of 4 is then normalised to give a score between 1 and 10.

2.5 Biotreatment Score

The nitrogen content in solvent score is assigned as 4 if no nitrogen is present and as 2 if nitrogen is present.

The theoretical oxygen demand (ThOD) per kilogram of solvent is calculated as:

$$ThOD = \frac{\#\ of\ O\ atoms}{MW\ of\ solvent} \times 16$$

where 16 represents the molecular weight of oxygen and the number of oxygen atoms required to oxidise one molecule of solvent is calculated from the solvent's molecular formula, based on the values given in Table 6.

# of atoms of [O] required per atom	Atom	Product
2.0	C	CO_2
0.5	H	H_2O
2.5	N	NO_x mixture
3.0	S	SO_3^-
-1.0	O	O_2
0.5	Cl	Cl_2
0.5	F	F_2

Table 6: Assumed fates of elements for calculation of theoretical oxygen demand

Data limits are assigned (see Table 1) and plotted to determine the equation: $Score = -1.54 \times ThOD + 5.88$, and this is used to determine a theoretical oxygen demand score.

A score assessing treatability in aeration tanks is calculated as:

$$Treatability\ in\ Aeration\ Tanks\ Score = \sqrt[2]{ThOD\ Score \times Nitrogen\ Content\ Score}$$

Vapour pressure is used as an indicator of volatility. Data limits for vapour pressure are assigned and plotted to determine the equation:

$$Volatility\ Score = -0.94 \times Vapour\ Pressure + 3.36$$

for 0.20 mm Hg ≤ vapour pressure ≥ 400 mm Hg and this is used to determine a volatility score.

The halogenated score is assigned as follows:

- Score 4: no Cl, F present
- Score 2: F present or only 1 Cl atom present
- Score 1: Cl atoms $\geq$ 2

A score assessing the possibility of releases to air is then calculated as:

$$Release\ to\ Air\ Score = \sqrt[2]{Volatility\ Score \times Halogenated\ Score}$$

The values described in the incineration score for water solubility are used as a potential aqueous burden score for biotreatment. The solubility of the solvent in water is the appropriate measure for this score.

The biotreatment score is first calculated as:

$$Biotreatment\ Score = \sqrt[3]{TiAT \times RtA \times PAB}$$

where TiAT = treatability in aeration tanks score, RtA = release to air score and PAB = potential aqueous burden score.
This score is then normalised to give the biotreatment category score.

2.6 VOC Emissions Score

The vapour pressure score previously described in the biotreatment score section is used.
It should be noted that this data relates to pure solvent at 20 °C and atmospheric pressure, and does not relate to mixtures.

Data limits for boiling point are assigned such that a boiling point of ≤ 40°C correlates to a score of 1 and ≥ 110°C correlates to a score of 4. These points are plotted to determine the equation:

$$Boiling\ Point\ Score = 0.043 \times bp - 0.71$$

where bp = boiling point (in °C). This equation is used to determine boiling point data scores for 40°C < bp < 110°C.

The VOC Emissions score is calculated as:

$$VOC\ Score = \sqrt{VP \times BP}$$

where VP = vapour pressure score and BP = boiling point score, and is then normalised to give the VOC emissions category score.

2.7 Environment– Air Impact Score

A score is assigned to photochemical ozone creation potential (POCP) as follows, where POCP is measured in 100 kg of ethane equivalents:

- Score 4: POCP ≤ 20
- Score 3: 20 > POCP ≤ 40
- Score 2: 40 > POCP ≤ 60
- Score 1: > 60

Where no data is available, the dataset is examined to see if a suitable nearest neighbour value can be utilised. If not, a default value of 2 for POCP is assigned.

Solvent odour is assessed via the ratio of vapour pressure to odour threshold, with odour threshold in units of ppm. Data limits are assigned (see Table 1) to give the equation:

$$Odour\ Score = -0.44 \times log\frac{P_{vap}}{OT} + 2.90$$

where OT = odour threshold (in units of ppm).

If a solvent is assigned GHS hazard phrase H420 (harms public health and the environment by destroying ozone in the upper atmosphere), indicating that it is destructive to ozone in the upper atmosphere, an Environmental Impact-Air score of 1 is automatically assigned.
For all other solvents, the Environment Impact-Air score is calculated as:

$$Environmental\ Impact - Air\ Score = \sqrt{POCP\ Score \times Odour\ Score}$$

which is then normalised to give the Environmental Impact-Air category score.

2.8 Environment– Aquatic Impact Score

Acute Toxicity

The literature was searched for LC_{50} values against various aquatic species (including minnow, other fish, algae and daphnia). A maximum acute toxicity score of 4 is assigned to a worst case LC_{50} of 1000 mg/L, and a minimum score of 1.0 is assigned for a worst case LC_{50} of 1 mg/L. For all solvents except γ-valerolactone, such data was available on at least one aquatic species. In this single case, an estimate is made based on nearest neighbour. In addition, if the GHS hazard phrases for any solvent include H400 (very toxic to aquatic life), the acute toxicity score is set automatically to 1.0 and for H401 (toxic to aquatic life), this score is set automatically to 1.5. A GHS phrase of H402 (harmful to aquatic life) would correlate to an acute toxicity score of 2.0, although no solvents in the current data set are listed with this risk phrase.

For those solvents not listed with one of these GHS H&P phrases, plotting a graph of score against log (worst case LC_{50}) gives the following equation for 1 mg/L < LC_{50} < 1000 mg/L:

$$Acute\ Toxicity\ Score = \log(worst\ case\ LC_{50}) + 1$$

Chronic Toxicity

The partition coefficient (log K_{ow}) is used to indicate the lipophilicity of a solvent, which in turn correlates to its likelihood of posing chronic toxicity issues in the aquatic environment. A log $K_{OW} \geq 4.0$ is associated with a high risk of bioaccumulation,[29] therefore this value is assigned to a chronic toxicity score of 1.0 and a low log K_{OW} of 2.5 is assigned to a score of 4.0. These points are plotted to determine the equation:

$$log\ K_{OW}\ Score = -2 \times logK_{OW} + 9$$

Also considered in the chronic toxicity score is whether any of H410 (very toxic to aquatic life with long-lasting effects), H411 (toxic to aquatic life with long-lasting effects), H412 (harmful to aquatic life with long-lasting effects), or H413 (may cause long-lasting harmful effects to aquatic life) is included in a solvent's GHS hazard phrase listing. The relationship between these hazard phrases and the chronic toxicity score has been set as follows:

GHS Hazard Phrase	Chronic Toxicity Score
H410	1.0
H411	1.33
H412	1.66
H413	2.0
None of above phrases	log K_{ow} Score

Table 7: Environmental GHS Hazard Phrase correlations to Chronic Toxicity Score

The chronic toxicity score is determined as the worst of either the K_{ow} score or the scores shown in Table 7.

A score is assigned to Biodegradation as follows:

- Score 4: Readily biodegradable (biodegradability > 60%) or biochemical oxygen demand (BOD) > 50.
- Score 3: BOD = 20-30 or stated to be inherently biodegradable.
- Score 2: Slow to very slow rate of biodegradation.
- Score 1: Recalcitrant, or data suggests a serious biodegradation issue.

Where no biodegradation data is available, a score is assigned based on nearest neighbour.

The Environmental Impact–Aqueous score is first calculated as:

$$Environmental\ Impact - Aqueous\ Score = \sqrt[3]{AT \times CT \times BD}$$

where AT = acute toxicity score, CT = chronic toxicity score, and BD = biodegradability score, which is then normalised to give the Environmental Impact-Aqueous category score.

2.9 Exposure Potential Score:

The Vapour Hazard Ratio (VHR) is calculated as:

$$VHR = \frac{SC}{OEL}$$

Where:

- Saturation Concentration (SC) is a measure of the concentration (in ppm) of solvent vapour in the gas phase. Saturation concentration is calculated by converting vapour pressure values (in mm Hg) to ppm, via the formula:

$$SC = VP \times \frac{1\times10^6\ ppm}{760\ mm\ Hg}$$

- Occupational Exposure Limit (OEL) is the minimum value of regulated occupational exposure levels found by comparing data from multiple sources.[30]

If no data for OEL can be found, the solvent is assigned a default value of 2.5 ppm, chosen with an understanding that a lack of data does not necessarily correlate to lack of risk.[31]

Data limits are assigned and plotted to determine the equation:

$$VHR\ Score = -0.62 \times \log(VHR) + 4.56$$

and this is used to determine a vapour hazard ratio score. This score is then normalised to give the exposure potential category score.

2.10 Health Hazard Score:

The main drivers for the health hazard score are regulatory OEL values and GHS H&P phrases. For each solvent, the process described in Figure 3 is followed to determine the appropriate GHS phrases to utilise.[32] With the GHS phrases thus determined, the procedure detailed in Figure 4 is used to assign the health hazard score. In cases where Figure 3 states that OEL value should be employed to set the health hazard score, this assignment is made using the correlations in Table 8.

For those solvents which are not harmonized via GHS and also do not have an OEL value assigned by one of the major regulatory agencies consulted in this work, our team examined the available data[33] and determined on an individual solvent basis whether sufficient toxicological testing results are available to support that the GHS phrases listed on the vendor MSDS are comprehensive. The annual level of production for each solvent is here included (Table 9), because REACH guidelines require more stringent toxicological testing for all chemicals produced above 1,000 tons per year.[34] If the annual production falls below this level, a precautionary health hazard score of 4 is applied.

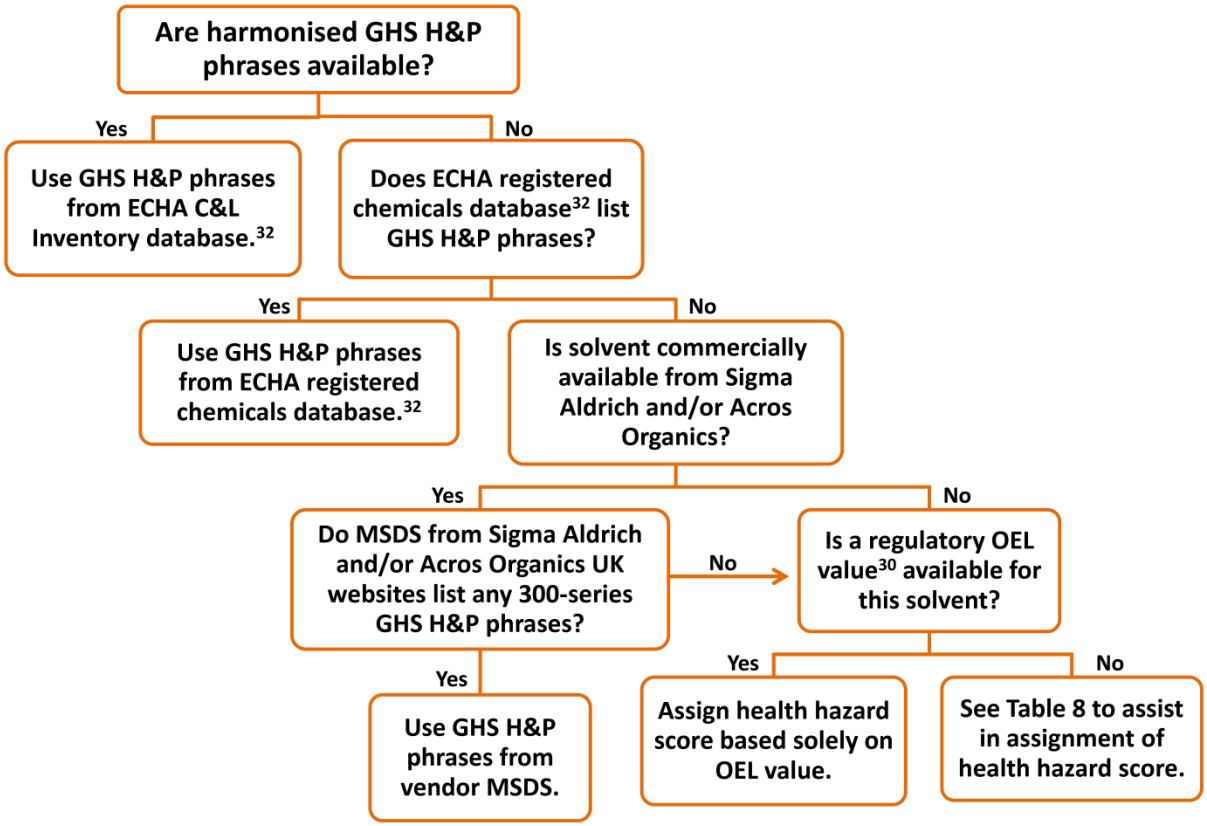


Figure 3: Decision tree detailing process for determination of GHS phrases for a given solvent.

OEL (ppm)	Health Hazard Score
< 0.5	1
≤ 5	4
≤ 50	7
> 50	10

Table 8: OEL value correlations to Health Hazard Score

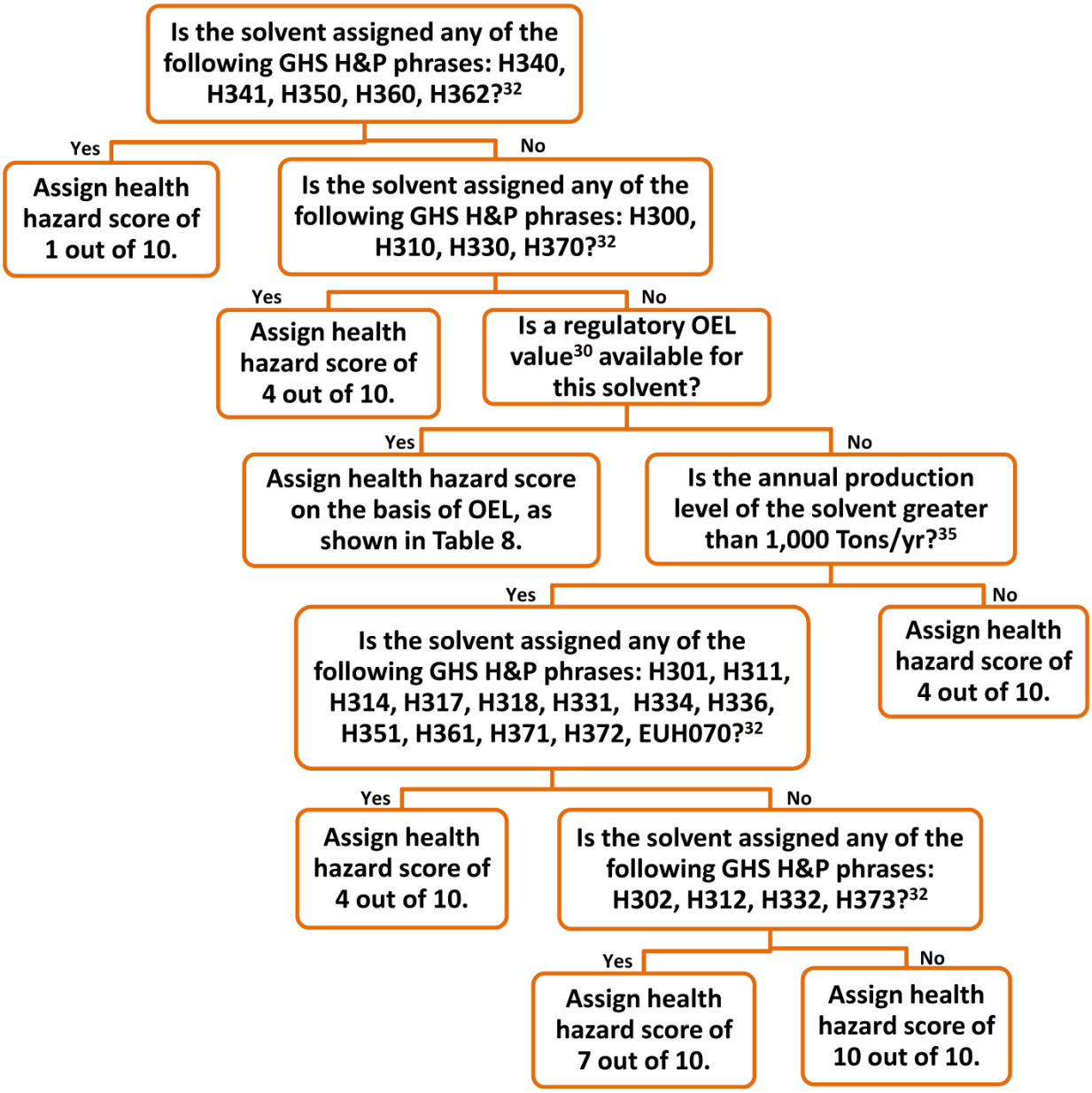


Figure 4: Decision tree showing process for assigning health hazard score.

Solvent	GHS Phrases	GHS Phrases Source	Annual Production Level (tons/yr)[35]	Precautionary 4 out of 10 Score?
Butylene carbonate	No MSDS available		Unknown	Yes
Cyclopentyl methyl ether	H225, H302, H315, H319, H412	ECHA	10-100	Yes
p-Cymene	H226, H315, H319, H304, H335	ECHA	Classified in US as High Production Volume (HPV) chemical	No – approved by FDA for use in human foodstuffs.
Diethoxymethane	H225	ECHA	100-1,000	Yes
Diethyl carbonate	H226	ECHA	100-1,000	Yes
Diethyl succinate	H227	Sigma Aldrich	Unknown	Yes
Dihydrolevoglucosenone	H319	Circa Group	Unknown	Yes
Diisopropyl adipate	H315	Sigma Aldrich	100-1,000	Yes
1,3-Dimethyl-2-imidazolidinone	H302, H318, H361, H373	ECHA	10-100	Yes
Dimethyl isosorbide	No GHS phrases listed		Unknown	Yes
Ethoxybenzene	H226	ECHA	0-10	Yes
Ethylene carbonate	H302, H319, H373	ECHA	1,000+	No
2-Ethylhexyl acetate	H315	ECHA	1,000+	No
Fluorobenzene	H225, H318, H401, H411	ECHA	Unknown	Yes
Glycerol triacetate	No GHS phrases listed		10,000-100,000	No
Glycerol diacetate	H227, H315, H319, H335, H412	Sigma Aldrich	1,000-10,000	No
1-Heptanol	H319	ECHA	1,000-10,000	No
2-Methyltetrahydrofuran	H225, H302, H315, H318	ECHA	100-1,000	Yes
n-Octyl acetate	No GHS phrases listed		Unknown	Yes
Perfluorocyclic ether	No MSDS available		Unknown	Yes
Perfluorocyclohexane	No MSDS available		Unknown	Yes
Perfluorohexane	H315, H319, H335, H413	Sigma Aldrich & Acros Organics	Unknown	Yes
Perfluorotoluene	H225, H302, H315, H319, H331	Sigma Aldrich	Unknown	Yes
1,3-Propanediol	None listed		1,000-10,000	No
Tetramethylurea	H227, H302, H360	Sigma Aldrich	Unknown	No –GHS phrase H360 correlates to a score of 1.
1,2,3-Trimethoxypropane	No MSDS available		Unknown	Yes
γ-Valerolactone	H227	Sigma Aldrich	Unknown	Yes

Table 9: Health data analysis for non-harmonized solvents which lack OEL values.

2.11 Flammability & Explosivity Score:

The boiling point score is assigned as described previously in the VOC Emissions section 2.6.

The flash point score is assigned as follows:[36]

- Score 4: Flash point > 50 °C
- Score 3: 20 °C ≤ Flash point ≤ 50 °C
- Score 2: 0 °C ≤ Flash point < 20 °C
- Score 1: Flash point < 0 °C

The Autoignition Temperature score is assigned as follows:

- Score 4: > 300 °C
- Score 3: 135-300 °C
- Score 2: 85-135 °C
- Score 1: < 85 °C

The Conductivity score is assigned based on electrical conductivity or resistivity data as follows:

- Score 4: > 10,000 pS/m (Resistivity < $1x10^9$ Ω m)
- Score 3: 50 < Conductivity ≤ 10,000 pS/m (Resistivity: 1 $x10^9$ - $2x10^{10}$ Ω m)
- Score 2: 1 < Conductivity ≤ 50 pS/m (Resistivity: $2x10^{10}$ - $1x10^{12}$Ω m)
- Score 1: ≤ 1 pS/m (Resistivity >$1x10^{12}$ Ω m)

For solvents without conductivity data, a solvent is assigned a High, Medium, Low or Very Low ranking based on its class as follows:

Solvent Class	Default Value
Alcohol	High
Aromatic	Very Low
Carbonate	High
Dipolar Aprotic	High
Ester	Medium (The data shows a mixture of high and medium. Applying a precautionary principle, the more stringent grouping is therefore applied.)
Hydrocarbon	Very Low
Ketone	High

Table 10: Solvent class-based default values for electrical conductivity

For ethers and halogenated solvents the experimental data showed no clear trend and manual assignments are made on a nearest neighbour basis. The vapour pressure score is assigned as previously described under Biotreatment in section 2.5.

The flammability and explosion potential score is first calculated as the following geometric mean:

$$Flammability\ \&\ Explosion\ Potential\ Score = \sqrt[5]{BP \times FP \times AIT \times EC \times VP}$$

where BP = boiling point score, FP = flash point score, AIT = autoignition temperature score, EC = electrical conductivity score, and VP = vapour pressure score. This geometric mean is then normalised to give the flammability and explosion potential category score.

2.12 Reactivity Score:

The peroxide formation score is assigned as follows:

- Score 4: No evidence of peroxide formation.
- Score 3: Peroxide formation known under certain conditions.
- Score 2: No data available, yet chemical structure suggests the possibility of peroxide formation.
- Score 1: Peroxide formation known to occur readily.

The potential for self-reaction score is assigned as follows:

- Score 4: None known
- Score 3: Some self-reaction known
- Score 2: Strong tendency for self-reaction
- Score 1: Very strong tendency for self-reaction

The NFPA score for the GSK guide is assigned based on NFPA reactivity hazard ratings, one of three NFPA rating values typically found on the MSDS for chemicals sold in the United States. For the two non-commercially available solvents (dihydrolevoglucosenone and 1,2,3-trimethoxypropane), a default NFPA Guide Score of 4 is assigned, as there are no known reasons to expect either of these chemicals to exhibit the types of reactivity hazards covered by these ratings.

NFPA Score for GSK Guide	NFPA Reactivity Hazard Rating	Description of Rating Class
4	0	Stable when exposed to heat, pressure or water.
3	1-2	May become unstable at elevated temperatures and pressures or when mixed with water.
2	3	Violent chemical changes possible at normal or elevated temperatures and pressures. Potentially violent or explosive reaction when mixed with water.
1	4	Readily capable of detonation or explosion at normal temperatures and pressures.

Table 11: Guidelines for assignment of NFPA Reactivity Hazard Score

The acidity/basicity score is assigned as follows:

- Score 4: No acidity
- Score 3: Mild acid/base
- Score 2: Moderate acid/base
- Score 1: Strong acid/base

The special hazards score is assigned as follows:

- Score 4: No special hazard
- Score 2: Risk of explosion on industrial process scale
- Score 1: Significant issues are known, *e.g.* pyrophoricity, shock sensitivity, severe known explosion risk, or demonstrating extreme stench

The reactivity potential score is first calculated as:

$$Reactivity\ Potential\ Score = \sqrt[5]{PF \times SR \times NFPA \times SH \times A}$$

where PF = peroxide formation score, SR = self reactive hazard score, NFPA = NFPA score, SH = special hazard score, and A = acidity score. This score is then normalised to give the Reactivity category score.

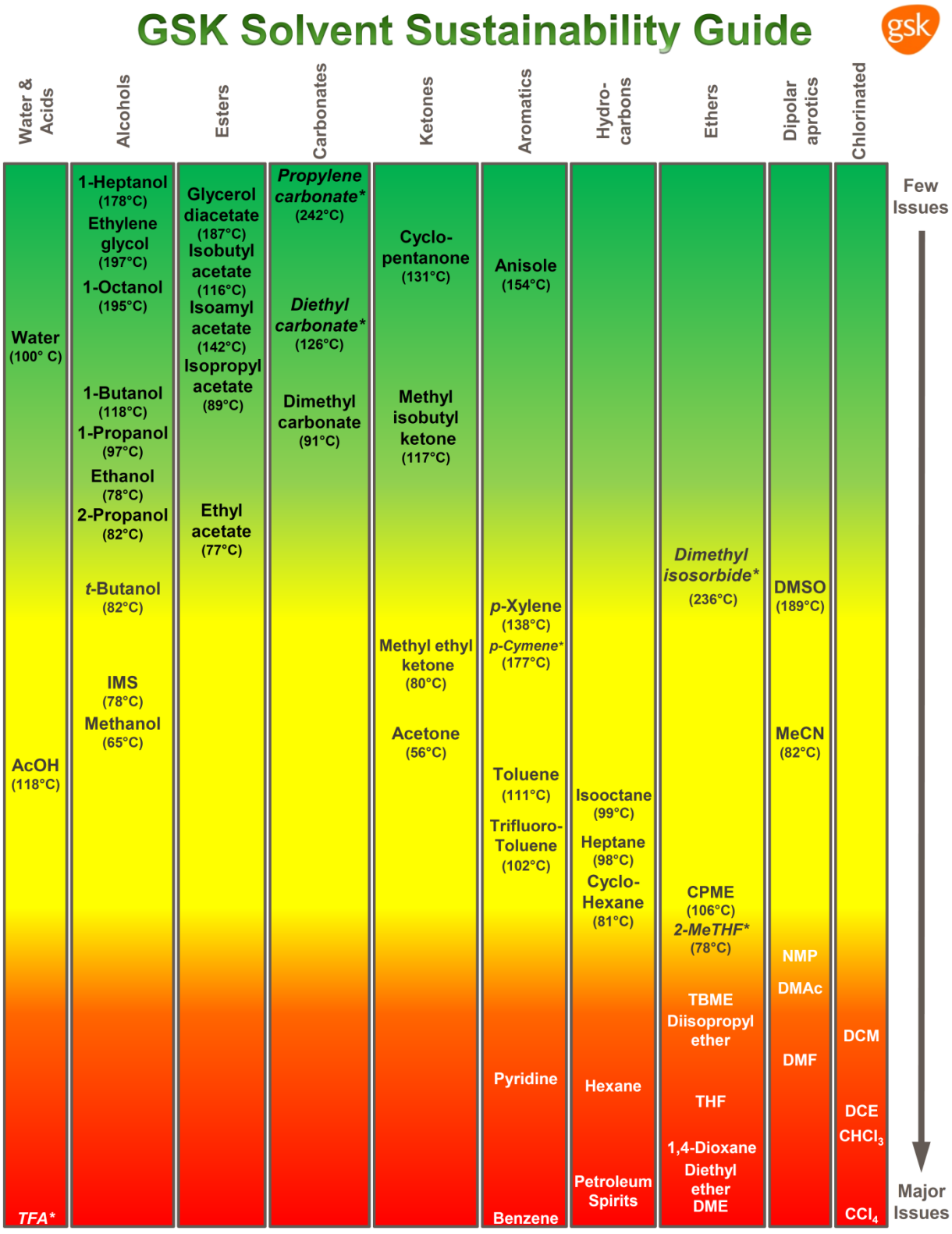
Section 3: Chart showing scoring outcomes for full 154 solvent dataset, sorted by chemical class

Classification	Solvent Name	CAS Number	Composite Colour	Boiling Point (°C)	Incineration	Recycling	Biotreatment	VOC Emissions	Aquatic Impact	Air Impact	Health Hazard	Exposure potential	Flammability & Explosion	Reactivity & Stability
	Water	7732-18-5		100	4	2	4	6	10	8	10	9	8	10
	Lactic acid	50-21-5		122	3	6	5	10	9	6	4	9	10	8
	Propionic acid	79-09-4		141	4	6	4	8	8	5	7	7	9	6
	Methanesulfonic acid	75-75-2		167	2	5	5	10	6	6	4	10	9	6
	Formic acid	64-18-6		101	5	4	8	6	8	8	4	4	7	7
	Acetic acid (glacial)	64-19-7		118	3	5	4	7	8	4	7	5	8	6
Alcohols	1,3-Propanediol	504-63-2		214	4	5	5	10	10	6	10	9	10	10
	1-Pentanol	71-41-0		137	7	8	8	9	9	4	10	9	9	10
	2-Ethyl hexanol	104-76-7		185	9	8	8	10	7	5	7	10	9	9
	1-Heptanol	111-70-6		178	9	8	10	9	8	4	10	7	9	10
	Ethylene glycol	107-21-1		197	4	5	5	10	10	8	7	10	10	10
	Di(ethylene glycol)	111-46-6		246	4	5	5	10	10	8	7	10	10	9
	Tri(ethylene glycol)	112-27-6		285	4	5	5	10	9	6	10	10	10	9
	1,2-Propanediol	57-55-6		188	4	5	5	10	10	6	7	10	10	10
	Benzyl alcohol	100-51-6		205	7	6	6	10	8	6	7	9	10	8
	Isoamyl alcohol	123-51-3		131	7	8	6	8	9	3	10	9	9	9
	1-Octanol	111-87-5		195	9	7	8	10	5	4	7	10	9	10
	Glycerol	56-81-5		290	4	5	5	10	10	8	4	10	10	10
	1,4-butanediol	110-63-4		235	4	5	4	9	10	6	7	9	10	10
	Cyclohexanol	108-93-0		161	7	7	6	9	8	5	7	9	9	9
	Isobutanol	78-83-1		108	6	3	5	7	10	6	7	7	8	9
	2-Pentanol	6032-29-7		119	7	8	5	8	9	4	7	7	8	9
	1-Hexanol	111-27-3		157	5	6	3	9	8	5	7	9	9	10
	1-Butanol	71-36-3		118	6	7	5	8	9	3	7	7	8	9
	1-Propanol	71-23-8		97	5	3	3	6	10	4	10	7	8	10
	Ethanol	64-17-5		78	5	5	3	4	9	5	10	8	6	10
	2-Butanol	78-92-2		100	5	3	3	6	10	4	10	7	8	9
	2-Propanol	67-63-0		82	5	5	3	5	8	7	10	6	6	8
	t-Amyl alcohol	75-85-4		102	6	3	4	7	9	5	7	6	8	10
	1,2-Isopropylidene glycerol	100-79-8		192	6	5	5	10	4	6	4	8	10	10
	t-Butanol	75-65-0		82	5	5	3	5	9	7	7	5	6	10
	IMS (ethanol, denatured)	64-17-5		78	5	5	3	5	9	5	4	7	6	10
	Methanol	67-56-1		65	4	7	3	3	10	7	4	6	5	10
	Tetrahydrofurfuryl alcohol	97-99-4		178	4	4	4	8	9	6	1	5	9	6
	2-Methoxyethanol	109-86-4		124	4	5	4	7	10	5	1	2	8	6
Esters	Glycerol triacetate	102-76-1		259	5	5	7	10	9	10	10	10	9	10
	Glycerol diacetate	111-55-7		187	5	6	6	10	6	8	10	8	10	10
	Isobutyl acetate	110-19-0		116	7	9	8	6	9	6	10	6	8	10
	Amyl acetate	628-63-7		146	7	8	8	8	9	5	7	8	8	10
	2-Ethylhexyl acetate	103-09-3		199	9	7	9	10	4	6	10	7	9	10
	Butyl acetate	123-86-4		126	8	9	7	8	8	3	10	8	8	10
	Methyl oleate	112-62-9		218	9	6	8	10	5	8	4	10	7	10
	Isoamyl acetate	123-92-2		142	9	9	8	8	4	6	7	8	8	10
	Isopropyl acetate	108-21-4		89	6	7	5	5	9	5	10	6	6	10
	Propyl acetate	109-60-4		102	6	4	6	6	9	5	10	7	7	10
	Dimethyl succinate	106-65-0		200	4	5	6	10	9	7	4	7	9	10
	n-Octyl acetate	112-14-1		210	9	7	9	10	3	8	4	7	8	10
	Ethyl acetate	141-78-6		77	5	6	5	4	9	5	10	7	5	10
	Ethyl lactate	97-64-3		154	4	6	4	8	9	6	4	6	8	10
	Diethyl succinate	123-25-1		218	7	7	9	10	9	8	4	8	9	10
	Dimethyl adipate	627-93-0		110	8	5	10	10	8	8	4	8	9	10
	γ-Valerolactone	108-29-2		207	8	7	10	9	10	6	4	7	9	10
	Diisopropyl adipate	6938-94-9		136	5	7	6	10	7	8	4	10	9	10
	Methyl lactate	547-64-8		144	4	6	4	8	9	6	10	6	8	9
	t-Butyl acetate	540-88-5		95	7	4	6	6	6	5	7	6	6	10
	Ethyl formate	109-94-4		54	5	8	4	2	8	7	10	5	4	10
	Methyl acetate	79-20-9		57	4	7	3	2	9	6	10	6	4	10
	Methyl propionate	554-12-1		79	5	5	5	4	10	6	7	3	4	10
	Ethyl propionate	105-37-3		99	7	3	6	6	6	6	4	4	7	6
	Methyl formate	107-31-3		33	3	7	3	1	9	9	7	4	3	9
Carbonates	Propylene carbonate	108-32-7		242	4	5	6	10	10	10	10	10	10	10
	Ethylene carbonate	96-49-1		248	3	5	5	10	10	10	7	10	10	9
	Diethyl carbonate	105-58-8		126	7	9	9	7	9	8	4	5	8	10
	Dimethyl carbonate	616-38-6		91	4	3	5	5	9	7	10	6	6	10
	Butylene carbonate	4437-85-8		250	5	5	7	10	9	9	4	9	9	10

Classification	Solvent Name	CAS Number	Composite Colour	Boiling Point (°C)	Incineration	Recycling	Biotreatment	VOC Emissions	Aquatic Impact	Air Impact	Health Hazard	Exposure potential	Flammability & Explosion	Reactivity & Stability
Ketones	Cyclopentanone	120-92-3		131	8	9	6	7	10	5	7	6	8	10
	Cyclohexanone	108-94-1		155	7	8	6	8	8	6	7	6	8	9
	3-Pentanone	96-22-0		102	7	3	5	6	10	4	10	7	7	9
	Methylisobutyl ketone	108-10-1		117	7	8	5	7	9	3	7	6	7	9
	2-Pentanone	107-87-9		102	7	3	5	6	9	3	10	7	6	10
	Methylethyl ketone	78-93-3		80	5	5	3	4	8	4	10	6	5	9
	Acetone	67-64-1		56	5	6	2	2	10	6	10	6	4	9
Aromatics	2,4,6-Collidine	108-75-8		171	7	9	6	8	10	5	7	8	9	9
	Anisole	100-66-3		154	8	8	8	8	7	6	7	8	7	9
	Ethoxybenzene	103-73-1		170	9	9	8	9	9	5	4	6	9	10
	p-Xylene	106-42-3		138	10	9	6	7	5	2	7	7	5	10
	Mesitylene	108-67-8		165	10	8	7	8	3	3	7	8	6	10
	p-Cymene	99-87-6		177	10	8	7	9	3	2	10	6	6	9
	Cumene	98-82-8		152	10	8	7	8	3	4	7	7	6	6
	Toluene	108-88-3		111	10	7	6	7	7	2	7	6	5	10
	Trifluorotoluene	98-08-8		102	4	4	5	6	3	8	10	4	4	10
	Pyridine	110-86-1		115	3	6	2	7	7	3	4	4	8	9
	Benzene	71-43-2		80	9	6	6	4	7	5	1	1	3	10
Hydrocarbons	Isooctane	540-84-1		99	10	4	5	6	2	5	10	7	3	10
	cis-Decalin	493-01-6		196	10	7	6	9	2	5	4	5	7	9
	Heptane	142-82-5		98	10	4	5	6	3	5	10	6	3	10
	L-Limonene	5989-54-8		175	10	8	7	9	3	3	4	6	5	10
	Cyclohexane	110-82-7		81	10	6	5	4	3	5	10	6	2	10
	D-Limonene	5989-27-5		175	10	8	7	9	3	3	4	7	5	10
	Methyl cyclohexane	108-87-2		101	10	4	5	6	1	5	10	7	3	10
	Methylcyclopentane	96-37-7		72	10	7	5	3	6	3	10	7	2	9
	Pentane	109-66-0		36	10	10	4	1	3	6	10	5	2	10
	2-Methylpentane	107-83-5		60	10	9	4	2	3	3	10	7	2	10
	Hexane	110-54-3		69	10	8	4	3	3	5	7	4	2	10
	Petroleum spirit	8032-32-4		55	8	9	4	2	5	5	1	6	2	10
Ethers	Diethylene glycol monobutyl ether	112-34-5		231	4	4	4	10	9	8	7	10	9	6
	Dimethyl isosorbide	5306-85-4		236	4	4	5	10	9	6	4	9	9	8
	Dibutyl ether	142-96-1		140	10	8	7	8	4	4	10	5	7	6
	t-Amyl methyl ether	994-05-8		86	7	6	5	5	9	4	7	5	5	9
	1,2,3-trimethoxypropane	20637-49-4		143	4	5	4	8	7	7	4	5	8	9
	Diphenyl ether	101-84-8		258	9	7	9	10	3	3	4	9	9	6
	t-Butyl ethyl ether	637-92-3		70	8	7	5	3	8	3	7	4	4	9
	1,3-Dioxolane	646-06-0		75	4	4	3	4	7	5	7	5	2	9
	Cyclopentyl methyl ether	5614-37-9		106	8	4	5	6	4	3	4	4	6	9
	Diethoxymethane	462-95-3		88	6	5	4	4	5	7	4	3	4	8
	2-Methyltetrahydrofuran	96-47-9		78	6	5	3	4	7	4	4	3	4	6
	t-Butylmethyl ether	1634-04-4		55	7	8	4	2	7	5	7	4	3	9
	Diisopropyl ether	108-20-3		68	9	7	6	3	5	4	10	6	4	3
	Dimethoxymethane	109-87-5		42	5	6	3	1	6	6	10	7	3	5
	Tetrahydrofuran	109-99-9		65	5	5	2	3	9	3	7	5	4	6
	Bis(2-methoxyethyl) ether	111-96-6		162	4	5	4	8	9	5	1	4	6	6
	1,4-Dioxane	123-91-1		102	4	1	3	6	8	4	4	3	4	6
	Diethyl ether	60-29-7		35	7	7	3	1	5	3	10	4	2	6
	1,2-Dimethoxyethane	110-71-4		85	4	4	3	5	8	7	1	4	4	6
	Dimethyl ether	115-10-6		-25	6	1	4	1	7	7	10	4	2	5
Dipolar Aprotics	Dimethylpropylene urea	7226-23-5		247	5	7	6	10	5	6	4	10	9	9
	Dimethyl sulphoxide	67-68-5		189	3	4	4	9	8	6	7	9	9	5
	1,3-Dimethyl-2-imidazolidinone	80-73-9		225	3	4	3	10	7	6	4	8	9	9
	Acetonitrile	75-05-8		82	3	5	1	4	10	8	7	5	6	10
	Propanenitrile	107-12-0		97	4	3	2	5	10	7	4	4	6	10
	Sulfolane	126-33-0		282	3	5	5	10	6	6	1	10	10	10
	Formamide	75-12-7		220	2	4	4	10	10	6	1	10	10	8
	N-Methyl pyrrolidone	872-50-4		202	3	4	3	10	10	6	1	9	9	9
	Dimethyl acetamide	127-19-5		165	3	6	3	9	10	6	1	7	9	9
	N-Ethylpyrrolidone	2687-91-4		212	3	4	3	10	9	6	1	8	9	9
	N-Methylformamide	123-39-7		200	2	5	3	10	10	6	1	5	10	10
	Dimethyl formamide	68-12-2		153	3	6	3	8	10	4	1	6	9	9
	Tetramethylurea	632-22-4		177	3	5	2	9	5	5	1	4	10	10
	Carbon disulfide	75-15-0		46	4	8	7	1	6	4	4	1	1	6

Classification	Solvent Name	CAS Number	Composite Colour	Boiling Point (°C)	Incineration	Recycling	Biotreatment	VOC Emissions	Aquatic Impact	Air Impact	Health Hazard	Exposure potential	Flammability & Explosion	Reactivity & Stability
Halogenated	1,2,4-Trichlorobenzene	120-82-1		214	3	7	7	10	1	9	4	6	9	10
	Chlorobenzene	108-90-7		132	4	9	7	7	2	7	4	4	8	10
	1,2-Dichlorobenzene	95-50-1		180	4	8	6	7	1	6	7	6	8	10
	Trichloroacetonitrile	545-06-2		83	4	8	5	4	3	4	4	3	7	10
	Perfluorotoluene	434-64-0		104	4	4	6	6	1	7	4	4	5	10
	Fluorobenzene	462-06-6		85	4	7	5	4	3	4	4	3	4	10
	Perfluorocyclic ether	335-36-4		103	4	4	6	6	1	7	4	4	5	10
	Dichloromethane	75-09-2		40	2	10	4	1	8	6	7	4	4	10
	1,2-Dichloroethane	107-06-2		84	2	7	5	5	9	7	1	2	5	10
	Perfluorocyclohexane	355-68-0		53	4	9	5	2	4	7	4	2	3	10
	Chloroform	67-66-3		61	3	9	5	3	7	5	4	1	5	10
	Trichloroacetic acid	76-03-9		197	1	4	3	9	2	5	4	6	10	6
	Chloroacetic acid	79-11-8		189	1	4	4	9	6	4	1	5	10	6
	Trifluoracetic acid	76-05-1		72	1	5	2	4	4	4	4	3	7	6
	Perfluorohexane	355-42-0		57	4	10	5	2	1	7	4	2	4	10
	Carbon tetrachloride	56-23-5		77	3	7	5	4	4	1	4	1	4	10
	2,2,2-Trifluoroethanol	75-89-8		74	1	5	2	4	5	4	1	1	6	9
Other	Furfural	98-01-1		162	7	8	8	8	8	4	4	6	9	9
	N,N-Dimethyldecanamide	14433-76-2		291	6	7	6	10	4	6	10	10	10	10
	Dihydrolevoglucosenone	1087696-49-8		203	4	4	5	10	9	6	4	8	10	10
	N,N-Dimethyloctanamide	1118-92-9		261	5	6	5	8	7	5	4	6	9	10
	N,N-Dimethylaniline	121-69-7		194	7	7	6	9	3	4	4	8	9	9
	Acetic anhydride	108-24-7		140	4	6	4	8	8	7	4	4	8	6
	Nitromethane	75-52-5		101	2	1	4	6	6	8	7	5	7	1
	Triethylamine	121-44-8		89	4	4	1	5	8	3	4	3	5	6

Section 4: Selected figures showing useful subsets of solvent guide information



* *The scoring assessment for this solvent includes 4 or more data gaps, therefore there is a lower level of confidence in the solvent's placement on this guide.*

Figure 5: Single page view of GSK Solvent Sustainability Guide, including commonly used solvents and recommended alternatives, sorted by chemical class.

Figure 6: Reverse side of updated GSK Solvent Sustainability Guide single page view, providing scoring breakdowns for selected solvents.

Classification	Solvent Name	CAS Number	Composite Colour‡	Boiling Point (°C)	Incineration	Recycling	Biotreatment	VOC Emissions	Aquatic Impact	Air Impact	Health Hazard	Exposure potential	Flammability & Explosion	Reactivity & Stability	Life Cycle Analysis†
Water & Acids	Water	7732-18-5		100	4	2	4	6	10	8	10	9	8	10	10
	Acetic Acid	64-19-7		118	3	5	4	7	8	4	7	5	8	6	8
	*Trifluoroacetic acid**	76-05-1		72	1	5	2	4	4	4	4	3	7	6	
Alcohols	1-Heptanol	111-70-6		178	9	8	10	9	8	4	10	7	9	10	
	Ethylene glycol	107-21-1		197	4	5	5	10	10	8	7	10	10	10	9
	1-Octanol	111-87-5		195	9	7	8	10	5	4	7	10	9	10	
	1-Butanol	71-36-3		118	6	7	5	8	9	3	7	7	8	9	5
	1-Propanol	71-23-8		97	5	3	3	6	10	4	10	7	8	10	7
	Ethanol	64-17-5		78	5	5	3	4	9	5	10	8	6	10	
	2-Propanol	67-63-0		82	5	5	3	5	8	7	10	6	6	8	4
	t-Butanol	75-65-0		82	5	5	3	5	9	7	7	5	6	10	8
	IMS (ethanol, denatured)	64-17-5		78	5	5	3	5	9	5	4	7	6	10	
	Methanol	67-56-1		65	4	7	3	3	10	7	4	6	5	10	9
Esters	Glycerol diacetate	111-55-7		187	5	6	6	10	6	8	10	8	10	10	
	Isobutyl acetate	110-19-0		116	7	9	8	6	9	6	10	6	8	10	
	Isoamyl acetate	123-92-2		142	9	9	8	8	4	6	7	8	8	10	
	Isopropyl acetate	108-21-4		89	6	7	5	5	9	5	10	6	6	10	7
	Ethyl acetate	141-78-6		77	5	6	5	4	9	5	10	7	5	10	6
Carbonates	*Propylene carbonate**	108-32-7		242	4	5	6	10	10	10	10	10	10	10	
	*Diethyl carbonate**	105-58-8		126	7	9	9	7	9	8	4	5	8	10	
	Dimethyl carbonate	616-38-6		91	4	3	5	5	9	7	10	6	6	10	8
Ketones	Cyclopentanone	120-92-3		131	8	9	6	7	10	5	7	6	8	10	6
	Methylisobutyl ketone	108-10-1		117	7	8	5	7	9	3	7	6	7	9	2
	Methylethyl ketone	78-93-3		80	5	5	3	4	8	4	10	6	5	9	3
	Acetone	67-64-1		56	5	6	2	2	10	6	10	6	4	9	7
Aromatics	Anisole	100-66-3		154	8	8	8	8	7	6	7	8	7	9	5
	p-Xylene	106-42-3		138	10	9	6	7	5	2	7	7	5	10	7
	*p-Cymene**	99-87-6		177	10	8	7	9	3	2	10	6	6	9	
	Toluene	108-88-3		111	10	7	6	7	7	2	7	6	5	10	7
	Trifluorotoluene	98-08-8		102	4	4	5	6	3	8	10	4	4	10	
	Pyridine	110-86-1		115	3	6	2	7	7	3	4	4	8	9	2
	Benzene	71-43-2		80	9	6	6	4	7	5	1	1	3	10	7
Hydrocarbons	Isooctane	540-84-1		99	10	4	5	6	2	5	10	7	3	10	7
	Heptane	142-82-5		98	10	4	5	6	3	5	10	6	3	10	7
	Cyclohexane	110-82-7		81	10	6	5	4	3	5	10	6	2	10	7
	Hexane	110-54-3		69	10	8	4	3	3	5	7	4	2	10	7
	Petroleum spirits	8032-32-4		55	8	9	4	2	5	5	1	6	2	10	7
Ethers	*Dimethyl isosorbide**	5306-85-4		236	4	4	5	10	9	6	4	9	9	8	
	Cyclopentyl methyl ether	5614-37-9		106	8	4	5	6	4	3	4	4	6	9	4
	*2-Methyltetrahydrofuran**	96-47-9		78	6	5	3	4	7	4	4	3	4	6	4
	t-Butylmethyl ether	1634-04-4		55	7	8	4	2	7	5	7	4	3	9	8
	Diisopropyl ether	108-20-3		68	9	7	6	3	5	4	10	6	4	3	9
	Tetrahydrofuran	109-99-9		65	5	5	2	3	9	3	7	5	4	6	4
	1,4-Dioxane	123-91-1		102	4	1	3	6	8	4	4	3	4	6	6
	Diethyl ether	60-29-7		35	7	7	3	1	5	3	10	4	2	6	6
	1,2-Dimethoxyethane	110-71-4		85	4	4	3	5	8	7	1	4	4	6	7
Dipolar Aprotics	Dimethyl sulphoxide	67-68-5		189	3	4	4	9	8	6	7	9	9	5	6
	Acetonitrile	75-05-8		82	3	5	1	4	10	8	7	5	6	10	4
	N-Methyl pyrrolidone	872-50-4		202	3	4	3	10	10	6	1	9	9	9	4
	N,N-Dimethyl acetamide	127-19-5		165	3	6	3	9	10	6	1	7	9	9	2
	N,N-Dimethyl formamide	68-12-2		153	3	6	3	8	10	4	1	6	9	9	7
Chlorinated	Dichloromethane	75-09-2		40	2	10	4	1	8	6	7	4	4	10	7
	1,2-Dichloroethane	107-06-2		84	2	7	5	5	9	7	1	2	5	10	7
	Chloroform	67-66-3		61	3	9	5	3	7	5	4	1	5	10	6
	Carbon tetrachloride	56-23-5		77	3	7	5	4	4	1	4	1	4	10	7

GSK Solvent Sustainability Guide

Column Headings Colour Key

	Waste
	Environment
	Human Health
	Safety

Composite Colour Key

	Few Known Issues
	Some Known Issues
	Major Known Issues

The scoring assessment for this solvent includes 4 or more data gaps, therefore there is a lower level of confidence in the solvent's placement on this guide.

†A blank value for Life Cycle Analysis (LCA) indicates that this data is currently not available.

‡The composite colour represents an overall categorization of the holistic sustainability of a solvent, taking all category scores into consideration.

Figure 7: Data chart for the 44 newly scored solvents, showing all category scores and the total number of data gaps for each solvent. Solvents are rank ordered by composite score within each colour designation.

Data for Newly Assessed Solvent Options

Few Issues → Major Issues

Solvent Name	CAS Number	Solvent Classification	Composite Colour	Boiling Point (°C)	Incineration	Recycle	Biotreatment	VOC Emissions	Environmental Impact: Aqueous	Environmental Impact: Air	Health Hazard	Exposure potential	Safety: Flammability & Explosion	Safety: Reactivity	Number of Data Gaps*
Glycerol triacetate	102-76-1	Ester		259	5	5	7	10	9	10	10	10	9	10	4
1-Pentanol	71-41-0	Alcohol		137	7	8	8	9	9	4	10	9	9	10	0
1-Heptanol	111-70-6	Alcohol		178	9	8	10	9	8	4	10	7	9	10	3
Glycerol diacetate	111-55-7	Ester		187	5	6	6	10	6	8	10	8	10	10	1
Isobutyl acetate	110-19-0	Ester		116	7	9	8	6	9	6	10	6	8	10	1
Amyl acetate	628-63-7	Ester		146	7	8	8	8	9	5	7	8	8	10	2
2,4,6-Collidine	108-75-8	Aromatic		171	7	9	6	8	10	5	7	8	9	9	4
2-Ethylhexyl acetate	103-09-3	Ester		199	9	7	9	10	4	6	10	7	9	10	2
1-Octanol	111-87-5	Alcohol		195	9	7	8	10	5	4	7	10	9	10	1
Methyl oleate	112-62-9	Ester		218	9	6	8	10	5	8	4	10	7	10	3
Isoamyl acetate	123-92-2	Ester		142	9	9	8	8	4	6	7	8	8	10	1
Diethyl carbonate	105-58-8	Carbonate		126	7	9	9	7	9	8	4	5	8	10	4
Isobutanol	78-83-1	Alcohol		108	6	3	5	7	10	6	7	7	8	9	0
1-Hexanol	111-27-3	Alcohol		157	5	6	3	9	8	5	7	9	9	10	1
Dimethyl succinate	106-65-0	Ester		200	4	5	6	10	9	7	4	7	9	10	4
Lactic acid	50-21-5	Acid		122	3	6	5	10	9	6	4	9	10	8	4
Furfural	98-01-1	Other		162	7	8	8	8	8	4	4	6	9	9	1
t-Amyl alcohol	75-85-4	Alcohol		102	6	3	4	7	9	5	7	6	8	10	2
Diethyl succinate	123-25-1	Ester		218	7	7	9	10	9	8	4	8	9	10	6
N,N-Dimethyldecanamide	14433-76-2	Other		291	6	7	6	10	4	6	10	10	10	10	5
Dimethyl adipate	627-93-0	Ester		110	8	5	10	10	8	8	4	8	9	10	5
Butylene carbonate	4437-85-8	Carbonate		250	5	5	7	10	9	9	4	9	9	10	9
γ-Valerolactone	108-29-2	Ester		207	8	7	10	9	10	6	4	7	9	10	9
Diisopropyl adipate	6938-94-9	Ester		136	5	7	6	10	7	8	4	10	9	10	8
Dihydrolevoglucosenone	1087696-49-8	Other		203	4	4	5	10	9	6	4	8	10	10	9
Dimethyl isosorbide	5306-85-4	Ether		236	4	4	5	10	9	6	4	9	9	8	10
1,2-Isopropylideneglycerol	100-79-8	Alcohol		192	6	5	5	10	4	6	4	8	10	10	5
N,N-Dimethyloctanamide	1118-92-9	Other		261	5	6	5	8	7	5	4	6	9	10	6
1,3-Dimethyl-2-imidazolidinone	80-73-9	Dipolar aprotic		225	3	4	3	10	7	6	4	8	9	9	6
Methanesulfonic acid	75-75-2	Acid		167	2	5	5	10	6	6	4	10	9	6	2
Formic acid	64-18-6	Acid		101	5	4	8	6	8	8	4	4	7	7	0
1,2,3-Trimethoxypropane	20637-49-4	Ether		143	4	5	4	8	7	7	4	5	8	9	10
Methyl propionate	554-12-1	Ester		79	5	5	5	4	10	6	7	3	4	10	4
L-Limonene	5989-54-8	Hydrocarbon		175	10	8	7	9	3	3	4	6	5	10	2
D-Limonene	5989-27-5	Hydrocarbon		175	10	8	7	9	3	3	4	7	5	10	1
p-Cymene	99-87-6	Aromatic		177	10	8	7	9	3	2	4	6	6	9	5
1,3-Dioxolane	646-06-0	Ether		75	4	4	3	4	7	5	7	5	2	9	2
Diethoxymethane	462-95-3	Ether		88	6	5	4	4	5	5	4	3	4	8	5
N-Ethylpyrrolidone	2687-91-4	Dipolar aprotic		212	3	4	3	10	9	6	1	8	9	9	6
Methyl formate	107-31-3	Ester		33	3	7	3	1	9	9	7	4	3	9	0
Dimethoxymethane	109-87-5	Ether		42	5	6	3	1	6	6	10	7	3	5	2
Tetrahydrofurfuryl alcohol	97-99-4	Alcohol		178	4	4	4	8	9	6	1	5	9	6	3

At least one piece of data is not available as part of this subscore. Values have been estimated where possible via calculation or comparison to structurally similar solvents.

*A red value in the number of data gaps column highlights those solvents with 4 or more data gaps.

Section 5: Data Gap Analysis List.

The charts below details all data gaps within the dataset for the GSK Solvent Sustainability Guide and specifies how these gaps are filled for the purposes of reaching assessment endpoints.

Solvent	Property	Type of Gap (default, nearest neighbour, chemical class, calculation)	Source or Reference for Approximation
Butylene carbonate	Enthalpy of combustion	default	N/A
Dihydrolevoglucosenone	Enthalpy of combustion	default	N/A
Diisopropyl adipate	Enthalpy of combustion	default	N/A
Dimethyl adipate	Enthalpy of combustion	default	N/A
Dimethyl isosorbide	Enthalpy of combustion	default	N/A
1,3-Dimethyl-2-imidazolidinone	Enthalpy of combustion	default	N/A
N,*N*-Dimethyldecanamide	Enthalpy of combustion	default	N/A
N,*N*-Dimethyloctanamide	Enthalpy of combustion	default	N/A
Dimethylpropylene urea	Enthalpy of combustion	default	N/A
N-Ethylpyrrolidone	Enthalpy of combustion	default	N/A
Perfluorocyclic ether	Enthalpy of combustion	default	N/A
Perfluorocyclohexane	Enthalpy of combustion	default	N/A
Perfluorohexane	Enthalpy of combustion	default	N/A
Perfluorotoluene	Enthalpy of combustion	default	N/A
Petroleum spirit	Enthalpy of combustion	default	N/A
Trichloroacetonitrile	Enthalpy of combustion	default	N/A
1,2,3-Trimethoxypropane	Enthalpy of combustion	default	N/A
Water	Enthalpy of combustion	default	N/A
1,2,3-Trimethoxypropane	Water solubility	calculated	ACD prediction from SciFinder

Table 12: Data Gaps within Incineration Category

Solvent	Property	Type of Gap (default, nearest neighbour, chemical class, calculation)	Source or Reference for Approximation
1,2,3-Trimethoxypropane	Melting point	calculated	http://www.qsardb.org/repository/predictor/10967/104
Butylene carbonate	Presence of azeotrope with water	default	N/A
Dihydrolevoglucosenone	Presence of azeotrope with water	default	N/A
Diisopropyl adipate	Presence of azeotrope with water	default	N/A
Dimethyl adipate	Presence of azeotrope with water	default	N/A
Dimethyl isosorbide	Presence of azeotrope with water	default	N/A
Dimethyl succinate	Presence of azeotrope with water	default	N/A
N,*N*-Dimethyldecanamide	Presence of azeotrope with water	default	N/A
N,*N*-Dimethyloctanamide	Presence of azeotrope with water	default	N/A
N-Ethylpyrrolidone	Presence of azeotrope with water	default	N/A
Glycerol triacetate	Presence of azeotrope with water	default	N/A
Methyl oleate	Presence of azeotrope with water	default	N/A
Tetrahydrofurfuryl alcohol	Presence of azeotrope with water	default	N/A
Tetramethylurea	Presence of azeotrope with water	default	N/A
1,2,3-Trimethoxypropane	Presence of azeotrope with water	default	N/A

Table 13: Data Gaps within Recycling Category

Solvent	Property	Type of Gap (default, nearest neighbour, chemical class, calculation)	Source or Reference for Approximation
Diisopropyl adipate	Vapour pressure	calculated	ACD prediction from SciFinder
1,2,3-Trimethoxypropane	Vapour pressure	calculated	ACD prediction from SciFinder

Table 14: Data Gaps within VOC Emissions Category

Solvent	Property	Type of Gap (default, nearest neighbour, chemical class, calculation)	Source or Reference for Approximation
Perfluorocyclic ether	Aquatic toxicity	calculated	QSAR
Perfluorocyclohexane	Aquatic toxicity	calculated	QSAR
Perfluorohexane	Aquatic toxicity	calculated	QSAR
Perfluorotoluene	Aquatic toxicity	calculated	QSAR
γ-Valerolactone	Aquatic toxicity	nearest neighbour	Propylene carbonate
Butylene carbonate	Biodegradation	calculated	EPISuite Biowin MITI Linear model
Diethyl succinate	Biodegradation	calculated	EPISuite Biowin MITI Linear model
Dimethyl isosorbide	Biodegradation	calculated	EPISuite Biowin MITI Linear model
Ethyl lactate	Biodegradation	calculated	EPISuite Biowin MITI Linear model
Ethyl propionate	Biodegradation	calculated	EPISuite Biowin MITI Linear model
Methylcyclohexane	Biodegradation	calculated	EPISuite Biowin MITI Linear model
Methylcyclopentane	Biodegradation	calculated	EPISuite Biowin MITI Linear model
Methyl propionate	Biodegradation	calculated	EPISuite Biowin MITI Linear model
2-Pentanol	Biodegradation	calculated	EPISuite Biowin MITI Linear model
Perfluorocyclic ether	Biodegradation	chemical class	http://www.epa.gov/hpv/pubs/summaries/perfluro/c13244rs.pdf suggests that perfluorocarbons are not biodegradable.
Perfluorocyclohexane	Biodegradation	chemical class	http://www.epa.gov/hpv/pubs/summaries/perfluro/c13244rs.pdf suggests that perfluorocarbons are not biodegradable.
Perfluorohexane	Biodegradation	chemical class	http://www.epa.gov/hpv/pubs/summaries/perfluro/c13244rs.pdf suggests that perfluorocarbons are not biodegradable.
Perfluorotoluene	Biodegradation	chemical class	http://www.epa.gov/hpv/pubs/summaries/perfluro/c13244rs.pdf suggests that perfluorocarbons are not biodegradable.
Propanenitrile	Biodegradation	calculated	EPISuite Biowin MITI Linear model
Trichloroacetonitrile	Biodegradation	calculated	EPISuite Biowin MITI Linear model
Trifluorotoluene	Biodegradation	calculated	EPISuite Biowin MITI Linear model
γ-Valerolactone	Biodegradation	calculated	EPISuite Biowin MITI Linear model
Butylene carbonate	Partition coefficient	calculated	http://www.epa.gov/hpvis/rbp/108-32-7_Propylene%20Carbonate_Web_April%202009.pdf
Di(ethylene glycol)	Partition coefficient	calculated	QSAR from ECHA registered chemicals database
Dihydrolevoglucosenone	Partition coefficient	calculated	clogP daylight
Dimethoxymethane	Partition coefficient	calculated	Chemspider EPISuite
Dimethyl ether	Partition coefficient	calculated	QSAR from ECHA registered chemicals database
Dimethyl isosorbide	Partition coefficient	calculated	http://www.perflavory.com/episys/ps1252931.html
Ethyl lactate	Partition coefficient	calculated	http://chem.sis.nlm.nih.gov/chemidplus/rn/97-64-3
Methyl lactate	Partition coefficient	calculated	http://chem.sis.nlm.nih.gov/chemidplus/rn/547-64-8
2-Methyltetrahydrofuran	Partition coefficient	calculated	QSAR from ECHA registered chemicals database

n-Octyl acetate	Partition coefficient	calculated	http://webnet.oecd.org/CCRWEB/ChemicalDetails.aspx?ChemicalID=9d720ec0-d5c6-42de-9d25-fa1efd8ab761
Perfluorocyclic ether	Partition coefficient	calculated	http://chem.sis.nlm.nih.gov/chemidplus/rn/335-36-4
Perfluorohexane	Partition coefficient	calculated	http://chem.sis.nlm.nih.gov/chemidplus/rn/355-42-0
Perfluorotoluene	Partition coefficient	calculated	http://chem.sis.nlm.nih.gov/chemidplus/rn/434-64-0
1,3-Propanediol	Partition coefficient	calculated	QSAR from ECHA registered chemicals database
γ-Valerolactone	Partition coefficient	calculated	Chemspider EPISuite

Table 15: Data Gaps within Environment - Aquatic Impact Category

Solvent	**Property**	**Type of Gap (default, nearest neighbour, chemical class, calculation)**	**Source or Reference for Approximation**
t-Amyl alcohol	odour threshold	nearest neighbour	2-Pentanol
Bis(2-methoxyethyl) ether	odour threshold	default	N/A
1,4-Butanediol	odour threshold	nearest neighbour	1,2-Propanediol
Butylene carbonate	odour threshold	default	N/A
2,4,6-Collidine	odour threshold	default	N/A
Cyclopentanone	odour threshold	nearest neighbour	Cyclohexanone
p-Cymene	odour threshold	nearest neighbour	Cumene
cis-Decalin	odour threshold	default	N/A
Di(ethylene glycol)	odour threshold	default	N/A
Diethoxymethane	odour threshold	default	N/A
Diethyl carbonate	odour threshold	default	N/A
Diethyl succinate	odour threshold	default	N/A
Diethylene glycol monobutyl ether	odour threshold	default	N/A
Dihydrolevoglucosenone	odour threshold	default	N/A
Diisopropyl adipate	odour threshold	default	N/A
Dimethoxymethane	odour threshold	default	N/A
Dimethyl adipate	odour threshold	default	N/A
Dimethyl carbonate	odour threshold	default	N/A
Dimethyl isosorbide	odour threshold	default	N/A
Dimethyl succinate	odour threshold	default	N/A
Dimethyl sulphoxide	odour threshold	default	N/A
1,3-Dimethyl-2-imidazolidinone	odour threshold	default	N/A
N,*N*-Dimethyldecanamide	odour threshold	default	N/A
N,*N*-Dimethyloctanamide	odour threshold	default	N/A
Dimethylpropylene urea	odour threshold	default	N/A
1,3-Dioxolane	odour threshold	nearest neighbour	1,4-Dioxane
Ethoxybenzene	odour threshold	default	N/A
Ethyl propionate	odour threshold	nearest neighbour	N/A
Ethylene carbonate	odour threshold	default	N/A
N-Ethylpyrrolidone	odour threshold	default	N/A
Fluorobenzene	odour threshold	default	N/A
Glycerol	odour threshold	default	N/A
Glycerol triacetate	odour threshold	default	N/A
Isooctane	odour threshold	nearest neighbour	Heptane
1,2-Isopropylideneglycerol	odour threshold	default	N/A
Lactic acid	odour threshold	default	N/A
Methanesulfonic acid	odour threshold	default	N/A

Methyl lactate	odour threshold	nearest neighbour	Ethyl lactate
Methyl oleate	odour threshold	default	N/A
Methylcyclopentane	odour threshold	nearest neighbour	Methylcyclohexane
N-Methylformamide	odour threshold	default	N/A
2-Methyltetrahydrofuran	odour threshold	default	N/A
Perfluorocyclic ether	odour threshold	default	N/A
Perfluorocyclohexane	odour threshold	default	N/A
Perfluorohexane	odour threshold	default	N/A
Perfluorotoluene	odour threshold	default	N/A
1,3-Propanediol	odour threshold	nearest neighbour	1,2-Propanediol
Propylene carbonate	odour threshold	default	N/A
Sulfolane	odour threshold	default	N/A
Tetramethylurea	odour threshold	default	N/A
Tri(ethylene glycol)	odour threshold	default	N/A
Trichloroacetonitrile	odour threshold	default	N/A
Trifluoracetic acid	odour threshold	default	N/A
2,2,2-Trifluoroethanol	odour threshold	default	N/A
1,2,3-Trimethoxypropane	odour threshold	default	N/A
Water	odour threshold	default	N/A
γ-Valerolactone	odour threshold	default	N/A
Amyl acetate	POCP	chemical class	Acetates
t-Amyl methyl ether	POCP	nearest neighbour	*t*-Butyl methyl ether, *t*-Butyl ethyl ether[37]
Anisole	POCP	default	
Bis(2-methoxyethyl) ether	POCP	default	N/A
1,4-Butanediol	POCP	default	N/A
Butylene carbonate	POCP	nearest neighbour	Dimethyl carbonate
Carbon tetrachloride	POCP	nearest neighbour	Chloroform
Chloroacetic acid	POCP	default	N/A
2,4,6-Collidine	POCP	nearest neighbour	Pyridine
Cyclopentanone	POCP	nearest neighbour	Cyclohexanone
p-Cymene	POCP	nearest neighbour	Toluene, Cumene[38]
Dibutyl ether	POCP	nearest neighbour	Diethyl ether
Diethoxymethane	POCP	nearest neighbour	Dimethoxymethane
Diethyl carbonate	POCP	nearest neighbour	Dimethyl carbonate
Diethyl succinate	POCP	chemical class	Esters
Dihydrolevoglucosenone	POCP	default	N/A
Diisopropyl adipate	POCP	chemical class	Esters
1,2-Dimethoxyethane	POCP	nearest neighbour	Dimethoxymethane
Dimethyl acetamide	POCP	default	N/A
Dimethyl adipate	POCP	chemical class	Esters
Dimethyl isosorbide	POCP	default	N/A

Dimethyl succinate	POCP	chemical class	Esters
Dimethyl sulphoxide	POCP	default	N/A
1,3-Dimethyl-2-imidazolidinone	POCP	default	N/A
N,*N*-Dimethylaniline	POCP	default	N/A
N,*N*-Dimethyldecanamide	POCP	default	N/A
N,*N*-Dimethyloctanamide	POCP	default	N/A
Dimethylpropylene urea	POCP	default	N/A
1,4-Dioxane	POCP	nearest neighbour	1,3-Dioxolane
Ethoxybenzene	POCP	nearest neighbour	Anisole
Ethyl formate	POCP	nearest neighbour	Methyl formate
Ethylene carbonate	POCP	nearest neighbour	Dimethyl carbonate
2-Ethylhexyl acetate	POCP	chemical class	Acetates
N-Ethylpyrrolidone	POCP	nearest neighbour	*N*-Methylpyrrolidone
Fluorobenzene	POCP	default	N/A
Formamide	POCP	default	N/A
Furfural	POCP	default	N/A
1-Heptanol	POCP	nearest neighbour	1-Pentanol
1-Hexanol	POCP	nearest neighbour	1-Pentanol
Isoamyl acetate	POCP	chemical class	Acetates
Isobutyl acetate	POCP	chemical class	Acetates
Isooctane	POCP	nearest neighbour	Heptane
1,2-Isopropylidene glycerol	POCP	default	N/A
Lactic acid	POCP	default	N/A
Methanesulfonic acid	POCP	default	N/A
Methyl lactate	POCP	nearest neighbour	Ethyl lactate
Methyl oleate	POCP	chemical class	Esters
Methyl propionate	POCP	nearest neighbour	Ethyl propionate
N-Methylformamide	POCP	nearest neighbour	*N*,*N*-Dimethylformamide
1-Octanol	POCP	nearest neighbour	1-Pentanol
n-Octyl acetate	POCP	chemical class	Esters
2-Pentanol	POCP	nearest neighbour	2-Butanol
Perfluorocyclic ether	POCP	chemical class	perfluorinated solvents via http://www.epa.gov/hpv/pubs/summaries/perfluro/c13244rs.pdf
Perfluorocyclohexane	POCP	chemical class	perfluorinated solvents via http://www.epa.gov/hpv/pubs/summaries/perfluro/c13244rs.pdf
Perfluorohexane	POCP	chemical class	perfluorinated solvents via http://www.epa.gov/hpv/pubs/summaries/perfluro/c13244rs.pdf
Perfluorotoluene	POCP	chemical class	perfluorinated solvents via http://www.epa.gov/hpv/pubs/summaries/perfluro/c13244rs.pdf
Petroleum spirit	POCP	nearest neighbour	Pentane

Propylene carbonate	POCP	nearest neighbour	Dimethyl carbonate
Sulfolane	POCP	default	N/A
Tetrahydrofurfuryl alcohol	POCP	nearest neighbour	Benzyl alcohol
Tetramethylurea	POCP	default	N/A
Trichloroacetic acid	POCP	default	N/A
Trichloroacetonitrile	POCP	default	N/A
1,2,4-Trichlorobenzene	POCP	nearest neighbour	1,2-Dichlorobenzene
Trifluoracetic acid	POCP	default	N/A
2,2,2-Trifluoroethanol	POCP	default	N/A
γ-Valerolactone	POCP	default	N/A
Water	POCP		

Table 16: Data Gaps within Environment - Air Impact Category

Solvent	Property	Type of Gap (default, nearest neighbour, chemical class, calculation)	Source or Reference for Approximation
Butylene carbonate	OEL	default	N/A
Cyclopentyl methyl ether	OEL	default	N/A
p-Cymene	OEL	default	N/A
Dibutyl ether	OEL	default	N/A
Diethoxymethane	OEL	default	N/A
Diethyl carbonate	OEL	default	N/A
Diethyl succinate	OEL	default	N/A
Dihydrolevoglucosenone	OEL	default	N/A
Diisopropyl adipate	OEL	default	N/A
1,3-Dimethyl-2-imidazolidinone	OEL	default	N/A
Dimethyl isosorbide	OEL	default	N/A
N,*N*-Dimethyldecanamide	OEL	default	N/A
N,*N*-Dimethyloctanamide	OEL	default	N/A
Dimethylpropylene urea	OEL	default	N/A
Ethoxybenzene	OEL	default	N/A
Ethyl propionate	OEL	default	N/A
Ethylene carbonate	OEL	default	N/A
2-Ethylhexyl acetate	OEL	default	N/A
N-Ethylpyrrolidone	OEL	default	N/A
Fluorobenzene	OEL	default	N/A
Glycerol diacetate	OEL	default	N/A
Glycerol triacetate	OEL	default	N/A
1-Heptanol	OEL	default	N/A
1,2-Isopropylideneglycerol	OEL	default	N/A
Lactic acid	OEL	default	N/A
L-Limonene	OEL	default	N/A
Methyl lactate	OEL	default	N/A
Methyl propionate	OEL	default	N/A
N-Methylformamide	OEL	default	H360 severe health risk corresponds to health hazard score of 1 of 10.
2-Methyltetrahydrofuran	OEL	default	N/A
n-Octyl acetate	OEL	default	N/A
Perfluorocyclic ether	OEL	default	N/A
Perfluorocyclohexane	OEL	default	N/A
Perfluorohexane	OEL	default	N/A
Perfluorotoluene	OEL	default	N/A
1,3-Propanediol	OEL	default	N/A
Propylene carbonate	OEL	default	N/A

Tetramethylurea	OEL	default	H360 severe health risk corresponds to health hazard score of 1 of 10.
Trichloroacetonitrile	OEL	default	N/A
Trifluoroacetic acid	OEL	default	N/A
Trifluorotoluene	OEL	default	N/A
1,2,3-Trimethoxypropane	OEL	default	N/A
γ-Valerolactone	OEL	default	N/A

Table 17: Data Gaps within Exposure Potential Category

Solvent	**Property**	**Type of Gap (default, nearest neighbour, chemical class, calculation)**	**Source or Reference for Approximation**
2,4,6-Collidine	Autoignition Temperature	nearest neighbour	Pyridine, Mesitylene[35]
Dimethyl isosorbide	Autoignition Temperature	chemical class	Ethers
Perfluorocyclic ether	Autoignition Temperature	chemical class	Halogenated
Perfluorocyclohexane	Autoignition Temperature	chemical class	Halogenated
Perfluorohexane	Autoignition Temperature	chemical class	Halogenated
Perfluorotoluene	Autoignition Temperature	chemical class	Halogenated
Trichloroacetonitrile	Autoignition Temperature	chemical class	Halogenated
Trifluoracetic acid	Autoignition Temperature	chemical class	Halogenated
1,2,3-Trimethoxypropane	Autoignition Temperature	chemical class	Glycol derivatives
γ-Valerolactone	Autoignition Temperature	chemical class	Esters
Amyl acetate	Electrical conductivity	chemical class	Esters
t-Amyl alcohol	Electrical conductivity	chemical class	Alcohols
t-Amyl methyl ether	Electrical conductivity	nearest neighbour	TBME
Bis(2-methoxyethyl) ether	Electrical conductivity	default	N/A
1,4-Butanediol	Electrical conductivity	chemical class	Alcohols
t-Butyl acetate	Electrical conductivity	chemical class	Esters
t-Butyl ethyl ether	Electrical conductivity	nearest neighbour	TBME
Butylene carbonate	Electrical conductivity	chemical class	Carbonates
2,4,6-Collidine	Electrical conductivity	chemical class	Aromatics
Cumene	Electrical conductivity	chemical class	Aromatics
Cyclopentanone	Electrical conductivity	chemical class	Ketones
p-Cymene	Electrical conductivity	chemical class	Hydrocarbon
Dibutyl ether	Electrical conductivity	nearest neighbour	Diethyl ether, Diisopropyl ether[35]
1,2-Dichlorobenzene	Electrical conductivity	default	N/A
Diethoxymethane	Electrical conductivity	nearest neighbour	Dimethoxymethane, Dimethoxyethane[35]
Diethyl succinate	Electrical conductivity	chemical class	Esters
Dihydrolevoglucosenone	Electrical conductivity	chemical class	Ketones
Diisopropyl adipate	Electrical conductivity	chemical class	Esters
1,2-Dimethoxyethane	Electrical conductivity	nearest neighbour	Dimethoxymethane
Dimethyl adipate	Electrical conductivity	chemical class	Esters
Dimethyl ether	Electrical conductivity	nearest neighbour	Diethyl ether, Diisopropyl ether[35]
1,3-Dimethyl-2-imidazolidinone	Electrical conductivity	chemical class	Dipolar aprotics
Dimethyl isosorbide	Electrical conductivity	nearest neighbour	CPME, THF
Dimethyl succinate	Electrical conductivity	chemical class	Esters
N,*N*-Dimethylaniline	Electrical conductivity	default	N/A
N,*N*-Dimethyldecanamide	Electrical conductivity	chemical class	*N*,*N*-Dimethylformamide, *N*,*N*-Dimethylacetamide
N,*N*-Dimethyloctanamide	Electrical conductivity	chemical class	*N*,*N*-Dimethylformamide, *N*,*N*-

			Dimethylacetamide
Dimethylpropylene urea	Electrical conductivity	chemical class	Dipolar aprotics
1,3-Dioxolane	Electrical conductivity	nearest neighbour	1,4-Dioxane
Ethyl lactate	Electrical conductivity	chemical class	Esters
Ethylene carbonate	Electrical conductivity	chemical class	Carbonates
N-Ethylpyrrolidone	Electrical conductivity	nearest neighbour	*N*-Methylpyrrolidone
Fluorobenzene	Electrical conductivity	nearest neighbour	Bromobenzene, Chlorobenzene, Nitrobenzene[35]
Glycerol triacetate	Electrical conductivity	chemical class	Alcohols
1-Heptanol	Electrical conductivity	chemical class	Alcohols
Isooctane	Electrical conductivity	chemical class	Hydrocarbon
1,2-Isopropylideneglycerol	Electrical conductivity	chemical class	Alcohols
Lactic acid	Electrical conductivity	chemical class	Acids
D-Limonene	Electrical conductivity	chemical class	Hydrocarbon
L-Limonene	Electrical conductivity	chemical class	Hydrocarbon
Mesitylene	Electrical conductivity	chemical class	Hydrocarbon
2-Methoxyethanol	Electrical conductivity	chemical class	Alcohols
Methyl lactate	Electrical conductivity	chemical class	Esters
Methyl propionate	Electrical conductivity	chemical class	Alcohols
Methylcyclohexane	Electrical conductivity	chemical class	Hydrocarbon
Methylcyclopentane	Electrical conductivity	chemical class	Hydrocarbon
2-Methylpentane	Electrical conductivity	chemical class	Hydrocarbon
2-Methyltetrahydrofuran	Electrical conductivity	nearest neighbour	Tetrahydrofuran
2-Pentanol	Electrical conductivity	chemical class	Alcohols
Perfluorocyclic ether	Electrical conductivity	nearest neighbour	Perfluorohexane
Perfluorocyclohexane	Electrical conductivity	nearest neighbour	Perfluorohexane
Perfluorotoluene	Electrical conductivity	nearest neighbour	Perfluorohexane
Petroleum spirit	Electrical conductivity	chemical class	Hydrocarbon
1,3-Propanediol	Electrical conductivity	chemical class	Alcohols
Propylene carbonate	Electrical conductivity	chemical class	Carbonates
Tetrahydrofurfuryl alcohol	Electrical conductivity	chemical class	Alcohols
Tetramethylurea	Electrical conductivity	chemical class	Alcohols
Trichloroacetonitrile	Electrical conductivity	chemical class	Dipolar aprotics
1,2,4-Trichlorobenzene	Electrical conductivity	default	N/A
Triethylamine	Electrical conductivity	nearest neighbour	Trimethylamine
Trifluoracetic acid	Electrical conductivity	chemical class	Acids
2,2,2-Trifluoroethanol	Electrical conductivity	nearest neighbour	Pyridine
1,2,3-Trimethoxypropane	Electrical conductivity	nearest neighbour	Ethylene glycol
γ-Valerolactone	Electrical conductivity	chemical class	Esters
Perfluorocyclohexane	Flash point	calculated	J. Phys. Chem. Ref. Data, Vol. 33, No. 4, 2004, 1083

Table 18: Data Gaps within Flammability & Explosivity Category

Solvent	Property	Type of Gap (default, nearest neighbour, chemical class, calculation)	Source or Reference for Approximation
1,2,3-Trimethoxypropane	NFPA Reactivity Rating	default	N/A

Table 19: Data Gaps for Reactivity Category

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[26] Such cases were determined by using SciFinder to search for instances of a given chemical classified with role of "solvent" in published reactions. Any literature sources returned were then evaluated by the authors to determine if they were relevant to this work.
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[28] The geometric mean scores for Flammability & Explosivity and Reactivity, are here normalised to a scale from 1.0 to 4.0, using the formula:

$$Score = \left(\frac{Score_{calc} - Min\ Score}{Max\ Score - Min\ Score} \times 3\right) + 1$$

where the Flammability & Explosivity score has a minimum of 1.3 and a maximum of 4.0 and the reactivity score has a minimum of 1.7 and a maximum of 4.0.
[29] http://www.ilo.org/legacy/english/protection/safework/ghs/ghsfinal/ghsc14.pdf
[30] Sources used for regulatory data include internal GSK OEL values, threshold limit values (TLVs) from: American Conference of Governmental Industrial Hygienists (ACGIH), National Institute for Occupational Safety and Health (NIOSH), Occupational Safety and Health Administration (OSHA); time weighted average (TWA) values from: European Agency for Safety and Health at Work (EU-OSHA) Directive 2000/39/EC, EU-OSHA Directive 2006/15/EC, EU-OSHA Directive 2009/161/EU, EU-OSHA Directive 91/322/EEC, American Industrial Hygiene Association (AIHA) Workplace Environmental Exposure Levels (WEELs), ACGIH 8 hour values, United Kingdom - Workplace Exposure Limits (WELs); and German OEL values from the Technische Regel für Gefahrstoffe 900 (TRGS 900).
[31] In two cases, *N*-methylformamide and tetramethyl urea, no formal guidance can be sourced on regulatory OEL values. However in both of these cases GHS hazard phrases indicate significant risk of reprotoxicity. In line with GSK's general health risk guidelines, these two solvents have therefore been assigned a default OEL value of 0.1 ppm, rather than the standard 2.5 ppm default.
[32] Sources utilised include: European Chemicals Agency (ECHA) Classification & Labeling (C&L) Inventory database (http://echa.europa.eu/information-on-chemicals/cl-inventory-database, ECHA Registered Substances Database (http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances), and UK versions of MSDS from both Sigma Aldrich and Acros Organics websites, websites last accessed 13Jan2016.
[33] In addition to the resources from ECHA and vendor MSDS as described previously, we also consulted the National Institute of Health (NIH) Toxnet Hazardous Substances Data Bank (HSDB): http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB.
[34] http://echa.europa.eu/regulations/reach/registration/information-requirements and http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2007:136:0003:0280:EN:PDF, last accessed 13Jan2016.

[35] As listed in ECHA Registered Substances Database (http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances) or the 2007 OECD (Organisation for Economic Co-operation and Development) List of High Production Volume Chemicals (http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2009)40&doclanguage=en).

[36] For perfluorocyclohexane, no flash point data can be sourced. For this data point, a method to calculate flash point from boiling point and enthalpy of vaporization (as described in L. Catoire, V. Naudet, *J. Phys. Chem. Ref. Data*, 2004, **33**, 1083-1110.) is utilised.

[37] In cases where multiple solvents could reasonably considered to be the "nearest" neighbour to a given solvent, the data and/or scoring for the point of interest were examined for all neighbors, and the one which results in the more stringent evaluation was chosen.

[38] In cases where multiple solvents could reasonably considered to be the "nearest" neighbour to a given solvent, the data and/or scoring for the point of interest were examined for all neighbors, and the one which results in the more stringent evaluation was chosen.