Green Chemistry Institute®
Pharmaceutical Roundtable

ACS GCI Pharmaceutical Roundtable Solvent Selection Guide
Version 2.0 Issued March 21, 2011
www.acs.org/gcipharmaroundtable

1. Background and Disclaimer

The American Chemical Society Green Chemistry Institute® Pharmaceutical Roundtable (ACS GCIPR) has developed a Solvent Selection Guide for use by member companies. This is in support of the group's mission to catalyze the implementation of green chemistry and engineering in the pharmaceutical industry globally. It is recognized that during pharmaceutical process development solvent selection is key in determining the sustainability of future commercial production methods and recent benchmarking has demonstrated that solvents contribute ~50% of materials used in manufacture of bulk active pharmaceutical ingredients. Several individual member companies have developed solvent selection guides internally but this is the first guide developed collaboratively and feedback/questions would be welcomed – please send these to gcipr@acs.org.

Recognizing the educational value of the solvent selection guide, the Roundtable has decided to make this version of the guide available to the public.

This version of the ACS GCI Pharmaceutical Roundtable Solvent Selection Guide reflects ongoing evaluation of publicly available information by the ACS GCI Pharmaceutical Roundtable. Comments may be sent to gcipr@acs.org. No warranty is made and all warranties are expressly disclaimed.

The guide has been developed considering safety, health, environment aspects of solvent selection. Other aspects may need to be considered in process design. The ACS GCI Pharmaceutical Roundtable does not accept responsibility for any errors or omissions.

2. Solvent List

The initial solvent list was developed with input from the member companies. It is anticipated that future versions of the guide will incorporate more solvents but the scoring methodology detailed below should allow the assessment of solvents not included in the guide if relevant data are available.

3. Scoring System

The guide rates the solvents against 5 categories: safety, health, environment (air), environment (water), and environment (waste). Key parameters and criteria were then chosen for each category (e.g. flammability is one of the safety criteria). The summary table assigns a score from 1 to 10 for each solvent under the respective categories, with a score of 10 being of most concern and a score of 1 suggesting few issues. This is further simplified by using color coding with scores in the range 1 to 3 shown as **green**, 4 to 7 as **yellow** and 8 to 10 as **red**. This allows quick comparison between various solvents.

The Solvent Selection Guide scores unavoidably limit detail and reflect considerations that may not all apply in particular circumstances. They suggest candidate solvents and flag possible concerns. They are no substitute for detailed evaluation in connection with specific uses.

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Substance Information			Scoring Information				
Solvent Class	Solvent Name	CAS Number	Safety	Health	Env (Air)	Env (Water)	Env (Waste)
Acid	ACETIC ACID	64-19-7	3	6	6	3	6
Acid	ACETIC ANHYDRIDE	108-24-7	3	6	6	2	7
Acid	FORMIC ACID	64-18-6	2	6	5	4	7
Acid	METHANE SULPHONIC ACID	75-75-2			6	6	10
Acid	PROPIONIC ACID	79-09-4	2	5	6	4	6
Alcohol	1-BUTANOL	71-36-3	3	5	5	5	3
Alcohol	1-PROPANOL	71-23-8	4	4	6	2	6
Alcohol	2-BUTANOL	78-92-2	4	5	6	3	5
Alcohol	2-METHOXYETHANOL	109-86-4	4	9	5	3	7
Alcohol	BENZYL ALCOHOL	100-51-6	4	3	4	2	4
Alcohol	ETHANOL	64-17-5	4	3	5	1	6
Alcohol	ETHYLENE GLYCOL	107-21-1	3	3	5	1	7
Alcohol	ISOAMYL ALCOHOL	123-51-3	3	4	5	3	4
Alcohol	ISOBUTANOL	78-83-1	3	5	4	3	3
Alcohol	ISOPROPYL ALCOHOL (IPA)	67-63-0	5	5	6	2	6
Alcohol	METHANOL	67-56-1	3	5	6	3	6
Alcohol	T-BUTANOL	75-65-0	3	5	7	2	6
Aromatic	BENZENE	71-43-2	5	10	6	6	2
Aromatic	TOLUENE	108-88-3	5	7	6	6	2
Base	PYRIDINE	110-86-1	3	6	7	7	6
Base	TRIETHYLAMINE (TEA)	121-44-8	4	7	5	7	4
Dipolar aprotic	ACETONITRILE	75-05-8	3	5	6	4	6
Dipolar aprotic	DIMETHYL ACETAMIDE (DMAC)	127-19-5	2	7	3	7	7
Dipolar aprotic	DIMETHYL SULFOXIDE (DMSO)	67-68-5	3	4	4	4	8
Dipolar aprotic	N,N-DIMETHYLFORMAMIDE (DMF)	68-12-2	3	7	3	2	7
Dipolar aprotic	N-METHYL-2-PYRROLIDONE (NMP)	872-50-4	3	6	6	2	7
Dipolar aprotic	DIMETHYLIMIDAZOLIDINONE	80-73-9	3				
Dipolar aprotic	N-ETHYL-PYRROLIDONE (NEP)	2687-91-4					
Dipolar aprotic	TETRAMETHYLUREA	632-22-4	3				
Ester	AMYL ACETATE	628-63-7	3	3	5	5	4
Ester	DIMETHYL CARBONATE	616-38-6		3			5
Ester	ETHYL ACETATE (ETOAC)	141-78-6	5	4	6	4	4
Ester	ISOBUTYL ACETATE (IBUOAC)	110-19-0	5	3	5	2	2
Ester	ISOPROPYL ACETATE (IPAC)	108-21-4	3	4	6	3	3
Ester	METHYL ACETATE	79-20-9	3	5	6	3	5
Ester	METHYL FORMATE	107-31-3	5	7	7		6
Ester	N-BUTYL ACETATE	123-86-4	4	4	6	3	4
Ether	1,2-DIMETHOXYETHANE (DME)	110-71-4		9		3	6
Ether	1,4-DIOXANE	123-91-1	8	7	4	4	6
Ether	2-METHOXYETHYL ETHER (DIGLYME)	111-96-6		8		3	7
Ether	ANISOLE	100-66-3	5	4		3	4
Ether	ETHYL ETHER	60-29-7	9	5	7	4	4
Ether	METHYL TERT-BUTYL ETHER (MTBE)	1634-04-4	8	5	8	5	2
Ether	TETRAHYDROFURAN (THF)	109-99-9	5	6	5	4	5
Ether	2-METHYL TETRAHYDROFURAN	96-47-9	5	6			4
Ether	SULFOLANE	126-33-0	2	3		5	8
Ether	CYCLOPENTYL METHYL ETHER (CPME)	5614-37-9					3
Halogenated	1,2-DICHLOROETHANE (DCE)	107-06-2	4	9	6	6	6
Halogenated	CHLOROBENZENE	108-90-7	3	5	5	8	6
Halogenated	CHLOROFORM	67-66-3	2	9	7	7	6
Halogenated	DICHLOROMETHANE	75-09-2	2	7	9	6	7
Halogenated	CARBON TETRACHLORIDE	56-23-5	3	8	8	5	7
Halogenated	TRIFLUOROTOLUENE	98-08-8		6	7	7	6
Hydrocarbon	CYCLOHEXANE	110-82-7	6	5	4	7	2
Hydrocarbon	METHYL CYCLOHEXANE	108-87-2	6	4	4		2
Hydrocarbon	N-HEPTANE	142-82-5	6	4	4	7	2
Hydrocarbon	N-HEXANE	110-54-3	6	7	5	8	1
Hydrocarbon	XYLENE (MIXED ISOMERS)	1330-20-7	4	4	4	7	3
Hydrocarbon	ISOOCTANE	540-84-1	6	4	4		2
Ketone	ACETONE	67-64-1	4	4	7	1	5
Ketone	CYCLOHEXANONE	108-94-1	4	4	6	3	5
Ketone	METHYL ETHYL KETONE (MEK)	78-93-3	5	4	7	2	5
Ketone	METHYL ISOBUTYL KETONE (MIBK)	108-10-1	5	6	6	4	2

Note: A blank cell indicates that data are missing so a score could not be calculated.