

Supplier/Manufacturer Response Request

FORM 2- Residual Solvents Impurity Information– Basic Information

Background: Based upon ICH Q3C-Impurities–Guideline for Residual Solvents, the European Pharmacopoeia and the United States Pharmacopoeia have adopted criteria consistent with the expectations defined for Residual Solvents according to ICH Guideline Q3C. Application of the guidelines is for both new and existing materials.

Part Number	Material Title

#1	
SOLVENTS <u>NOT</u> USED OR <u>NOT</u> PRODUCED DURING MANUFACTURE/PROCESSING OF MATERIAL	
Yes/No	The material listed above (all lots) is not manufactured with the solvents listed as Class 1, Class 2, or Class 3 in the International Committee on Harmonization (ICH). The product complies with the requirements of the ICH Q3C Guideline.

#2	
SOLVENTS <u>ARE</u> USED OR <u>ARE</u> PRODUCED DURING MANUFACTURE/PROCESSING OF MATERIAL	
Yes/No	The material listed above is manufactured with solvents listed as Class 1, Class 2, or Class 3 in the International Committee on Harmonization (ICH). Additional information is provided below regarding the solvents used or produced by the manufacturing process (including solvents used in the synthesis as well as any solvents used for washing the final crystals).

**FORM 2- Residual Solvents Impurity Information
Detailed Information on Specific Solvents**

Table 1: Class 1 Residual Solvents and Concentration Limit			
Solvent	Concentration Limit (ppm)	Solvent Used Yes/No	IF Yes, Concentration (ppm) present
Benzene	2		
Carbon Tetrachloride	4		
1,2-Dichloroethane	5		
1,1-Dichloroethane	8		
1,1,1-Trichloroethane	1500		

Table 2. Class 2 Residual Solvents and Concentration Limit			
Solvent	Concentration Limit (ppm)	Solvent Used Yes/No	IF Yes, Concentration (ppm) present
Acetonitrile	410		
Chlorobenzene	360		
Chloroform	60		
Cyclohexane	3880		
1,2-Dichloroethene	1870		
1,2-Dimethoxyethane	100		
<i>N,N</i> -Dimethylacetamide	1090		
<i>N,N</i> -Dimethylformamide	880		
1,4-Dioxane	380		
2-Ethoxyethanol	160		
Ethylene Glycol	620		
Formamide	220		
Hexane	290		
Methanol	3000		
2-Methoxyethanol	50		
Methylbutylketone	50		
Methylcyclohexane	1180		
Methylene Chloride	600		
<i>N</i> -Methylpyrrolidone	530		
Nitromethane	50		

**FORM 2- Residual Solvents Impurity Information
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Table 2 (continued). Class 2 Residual Solvents and Concentration Limit			
Solvent	Concentration Limit (ppm)	Solvent Used Yes/No	IF Yes, Concentration (ppm) present
Pyridine	200		
Sulfolane	160		
Tetrahydrofuran	720		
Tetralin	100		
Toluene	890		
Trichloroethene	80		
Xylene	2170		

Table 3. Class 3 Residual Solvents		
Limited by GMP or other quality-based requirements in drug substances, excipients, and drug products. Class 3 residual solvents are limited to 5000 ppm or 0.5%, unless specified in individual monographs		
Solvent	Solvent Used Yes/No	IF Yes, Concentration (ppm) present
Acetic Acid		
Acetone		
Anisole		
1-Butanol		
2-Butanol		
Butyl Acetate		
<i>tert</i> -Butylmethyl Ether		
Cumene		
Dimethyl Sulfoxide		
Ethanol		
Ethyl Acetate		
Ethyl Ether		
Ethyl Formate		
Formic Acid		
Heptane		
Isobutyl Acetate		
Isopropyl Acetate		
Methyl Acetate		
3-Methyl-1-butanol		
Methylethylketone		
Methylisobutylketone		
2-Methyl-1-propanol		
Pentane		
1-Pentanol		
1-Propanol		
2-Propanol		
Propyl Acetate		

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Table 4. Other residual solvents – Specification limits should be listed in the individual monograph.		
Solvent	Solvent Used Yes/No	IF Yes, Concentration (ppm) present
1,1-Diethoxypropane		
1,1-Dimethoxymethane		
2,2-Dimethoxypropane		
Isooctane		
Isopropyl Ether		
Methyl Isopropyl Ketone		
Methyltetrahydrofuran		
Solvent Hexane		
Trichloroacetic Acid		
Trifluoroacetic Acid		

List other Solvents used/produced below (as applicable):

_____	_____	_____
_____	_____	_____

_____	_____	_____
Name	Title	Date

_____	_____ / _____
Name of Manufacturer	Contact Phone # / Internet e-mail address

_____	_____ / _____
Name of Supplier	Contact Phone # / Internet e-mail address