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March 18, 2015

To whom it may concern

STATEMENT

Subject : Calcium Carboxymethyl Cellulose

Re: Residual Solvents

Attached is a form regarding residual solvents requirements for materials we purchase from you for use in the manufacture of pharmaceutical products. Please be advised that if we purchase more than one material from you, separate forms are to be completed for each and every material.

The information we are requesting pertains to *USP <467> Residual Solvents* and the ICH guidance *Q3C Impurities: Residual Solvents*. Manufacturers of pharmaceutical products require residual solvent information to meet the criteria of these documents. The reporting level of residual solvents has been established as follows:

If Class 1 solvents are likely to be present, they should be identified and quantified. If solvents of Class 2 or 3 are present at greater than their Option 1 limits or 0.5%, respectively, they should be identified and quantified.

The phrase "likely to be present" refers to the solvent used or produced in the final manufacturing step and to solvents that are used or produced in earlier manufacturing steps and not removed consistently by a validated process.

When filling out the attached form, please proceed using the following steps:

- Place an *X* or *✓* in the box for each statement that applies.
- Where residual solvents are likely to be present, indicate the name of the solvent.
- State the method used to test for the solvent and the appropriate solvent limit where specified.
- Sign and date at bottom of the form.
- Attach a current Certificate of Analysis for the material.

If there is an equivalent prepared general statement available for the product listed, the statement may be submitted — along with a current Certificate of Analysis -in lieu of this form. The USP provides the following examples of acceptable statements:

- Only Class 3 solvents are likely to be present. Loss on drying is less than 0.5%.
- Only Class 2 solvents X,Y...are likely to be present. All are below the Option 1 limit.
- Only Class 2 solvents X,Y...and Class 3 solvents are likely to be present. Residual Class 2 solvents are below the Option 1 limit and residual Class 3 solvents are below 0.5%

Thank you for your cooperation.

**Compliance to USP <467> Residual Solvents /
ICH guidance Q3C Impurities: Residual Solvents**
(Reference attached residual solvent limit tables)

Material Name:

Paddock Item:

Class 1 solvents likely to be present:

Solvent Name	Method	Limit

Class 2 solvents likely to be present @ or below Option 1 limit:

Solvent

Names: _____

Class 2 solvents likely to be present above Option 1 limit:

Solvent Name	Method	Limit

Class 3 solvents likely to be present @ or below 0.5%:

Solvent Names:

Class 3 solvents likely to be present above 0.5%:

Solvent Name	Method	Limit

Other solvents likely to be present:

Solvent Name	Method	Limit

No residual solvents are likely to be present.

Completed by: Lee, Dal_seok_ (Name & Signature of Authorised Person) January 5 2015_ Date

Signature indicates authorization as a representative of
(manufacturer): bolak company limited

D.S Lee

**Manager
Quality Control**

Table 1. Class 1 Residual Solvents

Solvent	Concentration Limit (ppm)	Concern
Benzene	2	Carcinogen
Carbon tetrachloride	4	Toxic and environmental hazard
1,2-Dichloroethane	5	Toxic
1,1-Dichloroethene	8	Toxic
1,1,1-Trichloroethane	1500	Environmental hazard

Table 2. Class 2 Residual Solvents

Solvent	PDE (mg/day)	Concentration Limit (ppm) (Option 1 limit)
Acetonitrile	4.1	410
Chlorobenzene	3.6	360
Chloroform	0.6	60
Cyclohexane	38.8	3880
1,2-Dichloroethene	18.7	1870
1,2-Dimethoxyethane	1.0	100
<i>N,N</i> -Dimethylacetamide	10.9	1090
<i>N,N</i> -Dimethylformamide	8.8	880
1,4-Dioxane	3.8	380
2-Ethoxyethanol	1.6	160
Ethylene glycol	6.2	620
Formamide	2.2	220
Hexane	2.9	290
Methanol	30.0	3000
2-Methoxyethanol	0.5	50
Methylbutylketone	0.5	50
Methylcyclohexane	11.8	1180
Methylene chloride	6.0	600
<i>N</i> -Methylpyrrolidone	5.3	530
Nitromethane	0.5	50
Pyridine	2.0	200
Sulfolane	1.6	160
Tetrahydrofuran	7.2	720

Solvent	PDE (mg/day)	Concentration Limit (ppm) (Option 1 limit)
Tetralin	1.0	100
Toluene	8.9	890
Trichloroethylen	0.8	80
Xylene	21.7	2170

Table 3. Class 3 Residual Solvents

(limited by GMP or other quality-based requirements in drug substances, excipients, and drug products)

Acetic acid	Heptane
Acetone	Isobutyl acetate
Anisole	Isopropyl acetate
1-Butanol	Methyl acetate
2-Butanol	3-Methyl-1-butanol
Butyl acetate	Methylethylketone
<i>tert</i> -Butylmethyl ether	Methylisobutylketone
Cumene	2-Methyl-1-propanol
Dimethyl sulfoxide	Pentane
Ethanol	1-Pentanol
Ethyl acetate	1-Propanol
Ethyl ether	2-Propanol
Ethyl formate	Propyl acetate
Formic acid	

Table 4. Other Residual Solvents

(for which no adequate toxicological data was found)

1,1-Diethoxypropane	Methyl isopropyl ketone
1,1-Dimethoxymethane	Methyltetrahydrofuran
2,2-Dimethoxypropane	Solvent hexane
Isooctane	Trichloroacetic acid
Isopropyl ether	Trifluoroacetic acid