15 September 2011 **ANNEX**

Draft Exchange of Information with SFDA

This document provides a draft text for exchange of information in the area of pharmaceuticals to increase mutual confidence between EU and SFDA.

1. Advanced Notification of GMP/GDP Inspection

1.1. GMP Inspections

SFDA agrees to notify the relevant established contact point at EMA in advance of any planned inspection to be carried out by SFDA within the territory of the European Union with details of the site(s) to be inspected and the dates.

SFDA agrees to allow inspectors from the National Competent Authorities of the EU Member States in which these inspections take place to participate as observers in these inspections.

EMA and the European Commission agree to request the National Competent Authorities of the EU Member States planning to perform GMP inspections in the People's Republic of China to notify the relevant established contact point at SFDA in advance with details of the site(s) to be inspected and the dates.

Inspectors from SFDA will be permitted to participate as observers in these inspections.

1.2. GCP Inspections

SFDA agrees to notify the relevant established contact point at EMA in advance of any planned inspection to be carried out by SFDA within the territory of the European Union with details of the site(s) to be inspected and the dates.

SFDA agrees to allow inspectors from the National Competent Authority of the EU Member States in which these inspections take place to participate as observers.

EMA agrees to notify the relevant established contact point at SFDA in advance of any GCP inspection planned to be carried out by an EU authority at the request of EMA in the People's Republic of China, with details of the site(s) to be inspected and the dates.

EMA and European Commission agree to request the National Competent Authorities of the EU Member States planning to perform GCP inspections in the People's Republic of China that are not being performed at the request of EMA, to notify the relevant established contact point at SFDA in advance with details of the site(s) to be inspected and the dates.

Inspectors from SFDA will be permitted to participate as observers in these inspections.

2. GMP for APIs

SFDA agrees to exchange information on the GMP status of API manufacturers located in the People's Republic of China at the request of EMA, European Commission, or a National Competent Authority of an EU Member State. The format for this exchange is attached to this annex.

SFDA agrees that it will inform the person requesting a GMP certificate as well as the EMA and European Commission, if the site in question ceases to operate in compliance with GMP in the view of SFDA.

SFDA is hereby informed that certificates for API manufacturers located in EU can be found in the EudraGMP database:
http://eudragmp.eudra.org/inspections/displayWelcome.do;jsessionid=ac10292ad31c6ad3713fbc94b60a614c9bc932b008c.rlmNb38InljyqA4IpR9BcxaNbNq

Where a GMP certificate cannot be found in EudraGMP EMA agrees, following an enquiry by SFDA to the nominated EMA contact point for GMP, to provide information on the GMP status of the site in question. If necessary, EMA and European Commission agree to request the National Competent Authority of the EU Member State in which the manufacturing site is located to perform an inspection and to place the resulting GMP certificate into EudraGMP, or information on non-compliance, as appropriate. In the case of non-compliance EMA will inform SFDA.

Attachment

(LETTERHEAD of SFDA)

Certificate No: _ _ _/_ _ _/_ _ _

CERTIFICATE OF GMP COMPLIANCE OF AN API MANUFACTURER

Part 1

The State Food and Drug Administration of the People's Republic of China (SFDA) confirms the following:

The manufacturer …….

Site address…….

……

Is an active substance manufacturer that has been inspected by SFDA in accordance with [Reference to relevant legislation of the People's Republic of China].

SFDA confirms that this legislation provides for regular, strict and transparent controls and to the effective enforcement of GMP standards, including repeated and unannounced inspections, so as to ensure a protection of public health equivalent to that in the European Union.

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on …../……/…… *[date]*, it is considered that the plant complies the Good Manufacturing Practice requirements laid down in [Reference to relevant GMP legislation of People's Republic of China] which are equivalent to those laid down in Directive 2003/94/EC.

SFDA confirms that should the site be subsequently found to be non-compliant that it will notify the recipients of this certificate, the European Medicines Agency and the European Commission without any delay with details of the non-compliance.

This certificate reflects the status of the manufacturing site at the time of the inspection noted above and should not be relied upon to reflect the compliance status if more than three years have elapsed since the date of that inspection, after which time the issuing authority should be consulted.

This certificate is valid only when presented with all pages and both Parts 1 and 2.

The authenticity of this certificate may be verified with the issuing authority.

Part 2

Delete activities that do not apply and specify where needed:

A **Manufacture of Active Substance by Chemical Synthesis**

1. Upstream Chemical Synthesis (Manufacture of intermediates)
2. Downstream Chemical Synthesis (Final synthetic steps)
3. Salt formation/Purification steps : <free text> *(e.g. crystallisation)*
4. Other <free text>

B **Extraction of Active Substance from Natural Sources**

1. Extraction of substance from plant source
2. Extraction of substance from animal source
3. Extraction of substance from human source
4. Extraction of substance from mineral source
5. Modification of extracted substance <specify source 1,2,3,4>
6. Purification of extracted substance <specify source 1,2,3,4 >
7. Other <free text>

C **Manufacture of Active Substance using a Biological Processes**

1. Fermentation
2. Cell Culture <specify cell type> (e.g. mammalian/bacterial)
3. Isolation/Purification
4. Modification
5. Other <free text>

D **Manufacture of sterile active substance (Note: Parts A, B &C, to be completed as applicable)**

1. Aseptically prepared
2. Terminally sterilised

E **General Finishing Steps**

1. Physical processing steps < specify > *(e.g. drying, milling/micronization, sieving.)*
2. Primary Packaging
3. Secondary Packaging
4. Other <free text> *(for operations not described above)*

F **Quality Control Testing**

1. Physical/Chemical testing
2. Microbiological testing (excluding sterility testing)
3. Microbiological testing (including sterility testing)
4. Biological Testing

G **<u>Other activities relating to active substances</u>**

1. Importation
2. Distribution
3. Other <specify>

Names of active substances subject to last inspection <specify>

Any restrictions or clarifying remarks related to the scope of this certificate <specify>

……./……./……. *[date]*

Name and signature of the authorised person of SFDA

.....

.....

[name, title, phone & fax numbers]

<u>Note: This is not part of the API written confirmation format</u>

Definitions

Primary Packaging: *Enclosing/sealing the active substance within a packaging material which is in direct contact with the substance.*

Secondary Packaging: *Placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance.*

Certificates issued by EU authorities

Part 1 of GMP certificates issued by EU authorities for API manufacturers appears as follows.

Issued following an inspection in accordance with Art. 111(5) of Directive 2001/83/EC or Art. 80(5) of Directive 2001/82/EC as amended

The competent authority of ……*[Member State]* confirms the following:

The manufacturer …….

Site address…….

……

Has been inspected in connection with marketing authorisation(s) listing manufacturers located outside of the European Economic Area in accordance with Art. 8(2)/33(2)/19(3)/44(3) of Regulation (EC) 726/2004 or Art. 111(4) of Directive 2001/83/EC/Art. 80(4) of Directive 2001/82/EC transposed in the following national legislation:

……

or

Is an active substance manufacturer that has been inspected in accordance with Art. 111(1) of Directive 2001/83/EC/ Art. 80(1) of Directive 2001/82/EC* transposed in the following national legislation: ……

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on …../……/…… *[date]*, it is considered that it complies with the principles of GMP for active substances referred to in Article 47 of Directive 2001/83/EC/ Article 51 of Directive 2001/82/EC.

This certificate reflects the status of the manufacturing site at the time of the inspection noted above and should not be relied upon to reflect the compliance status if more than three years have elapsed since the date of that inspection, after which time the issuing authority should be consulted.

This certificate is valid only when presented with all pages and both Parts 1 and 2.

The authenticity of this certificate may be verified with the issuing authority.

…….../……../……. *[date]*

Name and signature of the authorised person of the Competent Authority of <country>

.....

.....

[name, title, phone & fax numbers]

Part 2 of GMP certificates issued by EU authorities for API manufacturers will follow the same format as Part 2 above.