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Presentation by
Livzon Group Fuzhou Fuxing Pharmaceutical Co., Ltd.

Plant Aeroview

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Fermentation Facility

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Extraction Facility

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Down Stream Purification and Solid Handling

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Clean Room Operation

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GLove Box

Registration in U.S. FDA

- Kanamycin Monosulfate DMF no.: 28275
- Vancomycin HCL, Lyophilized DMF no.: 26030
- Vancomycin HCL, Precipitated DMF no.: 26310
- Colistimethate sodium DMF no.: 28350
- Daptomycin DMF no.: 29137

Registration in EDQM

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EDQM

- **Colistin Sulfate**

  CEP No：R0-CEP 2011-372-Rev 00

- **Vancomycin HCL, Precipitated**

  CEP No.: R0-CEP 2012-235-Rev 00

- **Teicoplanin**

  CEP No.：R0-CEP 2015-093-Rev 00

Confirmation of WHO API Prequalification (CPQ)

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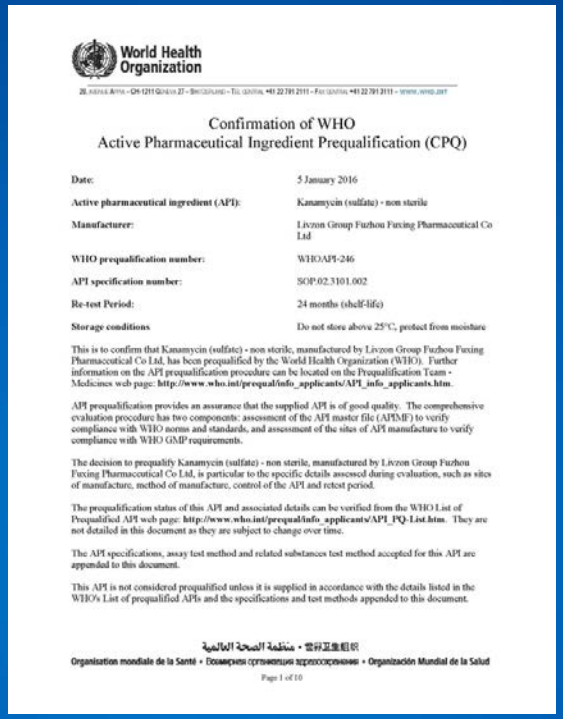
- Kanamycin Monosulfate
- Ref. No.: APIMF-246
- Kanamycin Acid Sulfate
- Ref. No.: APIMF-241



World Health Organization

Confirmation of WHO
Active Pharmaceutical Ingredient Prequalification (CPQ)

Date:	5 January 2016
Active pharmaceutical ingredient (API):	Kanamycin (sulfate) - non sterile
Manufacturer:	Livzon Group Fuzhou Fuxing Pharmaceutical Co Ltd
WHO prequalification number:	WHOAPI-246
API specification number:	SOP.02.3101.002
Re-test Period:	24 months (shelf-life)
Storage conditions	Do not store above 25°C, protect from moisture

This is to confirm that Kanamycin (sulfate) - non sterile, manufactured by Livzon Group Fuzhou Fuxing Pharmaceutical Co Ltd, has been prequalified by the World Health Organization (WHO). Further information on the API prequalification procedure can be located on the Prequalification Team - Medicines web page: **http://www.who.int/prequal/info_applicants/API_info_applicants.htm**.

API prequalification provides an assurance that the supplied API is of good quality. The comprehensive evaluation procedure has two components: assessment of the API master file (APIMF) to verify compliance with WHO norms and standards, and assessment of the sites of API manufacture to verify compliance with WHO GMP requirements.

The decision to prequalify Kanamycin (sulfate) - non sterile, manufactured by Livzon Group Fuzhou Fuxing Pharmaceutical Co Ltd, is particular to the specific details assessed during evaluation, such as sites of manufacture, method of manufacture, control of the API and retest period.

The prequalification status of this API and associated details can be verified from the WHO List of Prequalified API web page: **http://www.who.int/prequal/info_applicants/API_PQ-List.htm**. They are not detailed in this document as they are subject to change over time.

The API specifications, assay test method and related substances test method accepted for this API are appended to this document.

This API is not considered prequalified unless it is supplied in accordance with the details listed in the WHO's List of prequalified APIs and the specifications and test methods appended to this document.

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World Health Organization

Confirmation of WHO
Active Pharmaceutical Ingredient Prequalification (CPQ)

Date:	3 February 2016
Active pharmaceutical ingredient (API):	Kanamycin (acid sulfate) - sterile
Manufacturer:	Livzon Group Fuzhou Fuxing Pharmaceutical Co Ltd
WHO prequalification number:	WHOAPI-241
API specification number:	SOP.02.3102.003
Re-test Period:	48 months
Storage conditions	(Shelf life) Do not store above 25°C, protect from moisture

This is to confirm that Kanamycin (acid sulfate) - sterile, manufactured by Livzon Group Fuzhou Fuxing Pharmaceutical Co Ltd, has been prequalified by the World Health Organization (WHO). Further information on the API prequalification procedure can be located on the Prequalification Team - Medicines Assessment web page: **http://www.who.int/prequal/info_applicants/API_info_applicants.htm**.

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WHO PQ Experiences 1

2011 WHO PQ made numerous requested to have a site GMP Inspection on sterile Kanamycin Acid Sulfate.
At the time, Livzon Fuzhou Fuxing did not submitted APIMF to WHO PQ.

In order to accommodate WHO PQ's need to address kanamycin sulfate FPP shortage, the first WHO PQ site inspection is hosted at the end of 2011.

Dr. Andre Van Zyl l led the GMP inspection resulted some critical observations
(non data-integrity related)

At the exit meeting, there was no conclusion that the GMP inspection was not in compliances with WHO PQ GMP guidelines.

WHO PQ Experiences 2

2012 USP GPH PQM directly involved to provide technical assistance on how to complete CAPA plan with some completed CAPAs.

However, in April 2012, WHO PQ issued a closing letter to announce Fuzhou Fuxing Sterile Kanamycin Acid Sulfate was no in compliance with WHO PQ GMP.

It was interrelated that this process was hopeless to pass WHO PQ inspite numerous USFDA and EDQM approvals for the other APIs on the site.

April 22,2012	PQM made a site visit to emphasis the importance of WHO PQ to the management while remote technical assistance were on going.
May 12, 2012	PQM provided an audit on the CAPA results.
June 6, 2012	A site technical assistance on CAPA was conducted as necessary.
Aug 8, 2012	PQM was on site to make sure all the CAPAs were completed for WHO PQ reviews.

WHO PQ Experiences 3

Jan 2014	USP GPH PQM brought WHO PQ Sterile expert David Buckley for a mock audit (who became a third party GMP consultant for WHO PQ, also for manufacturers)
Jan-Feb 2014	PQM provided technical assistance to the CAPA based on the mock audit.
Feb 14, 2014	WHO PQ 2nd inspection Some observation required bench mark GMP to complete the CAPA
Sept 2014	PQM provided a site visit for the CAPA follow up.
May 2015	PQM conducted another mock audit for the WHO PQ inspection.
July 2015	WHO PQ inspection resulted a WHO PQ GMP compliance.
Feb 2016	WHO Prequalification acheived.

Besides the site visits, USP GPH PQM provided invaluable remote technical assistances To GMP issues and dossier questions from WHO PQ dossier assessment team.

Conclusions

- Technical Assistance are hands-on and technically intensive.
- Overcoming Communication and cultural barriers is as important as technical matters
- Requiring mental strengthen to deal with world renowned inspectors
- Without USP GPH PQM's Technical Assistance, a WHO PQ process could be much longer

Acknowledgement

The technical assistance from USAID aided USP GPH PQM towards kanamycin acid sulfate API for WHO PQ is great appreciated to enable Livzon Fuzhou Fuxing Pharma to make a
contribution to the global public health.

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Thank You