World Health Organization

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Prequalification Team Inspection services
WHO INSPECTION REPORT

Desk Assessment of Active Pharmaceutical Ingredient (API) Manufacturer

Part 1	**General information**
Company information	
Name of Manufacturer	KPC Pharmaceuticals Inc.
Corporate address of manufacturer	No.166 Keyi Road, High and New Technology Development Zone, Kunming, Yunnan Province, P. R. China
Contact person	Caesar Schmidlin caesar.schmidlin@holley.cn
Inspected site	
Name & address of manufacturing site	KPC Pharmaceuticals, Inc. Qigongli West Suburb, Kunming City 650100, Yunnan Province, P. R. China.
Synthetic Unit/Block/Workshop	No.4 Phytochemistry Plant
Manufacturing license number	No: Dian 20160102, classification code: HabZbFCb for: Small volume injection, freeze-dried powder injection, tablets, hard capsules, soft capsules, granules, crude drugs, psychoactive drugs, pharmaceutical precursor, chemicals, active pharmaceutical ingredients and extract of traditional Chinese medicine. Licence valid till 31 December 2020.
Desk assessment details	
Start and end dates of review	17 – 18 September 2019
Inspection record number	INSP-2016-0046
Inspector	Iveta Streipa
API covered by this desk assessment	APIMF125 & WHOAPI 125 Artemether
List of documents submitted	1. SMF and its annexes 2. US FDA Establishment Inspection Report 3. US FDA Form 483 4. Response to US FDA Form 483 5. TGA inspection report 6. TGA GMP certificate 7. TGA Close out record 8. Manufacturing authorization 9. List of products manufactured at site 10. PQR for Artemether 11. Batch production and packaging record for Artemether 12. Batch analytical report for Artemether

	13. Blank Master production records 14. Blank Master packaging records 15. GMP certificate 16. Statement of recalls 17. Statement of self-inspection 18. Statement of regulatory action 19. Statement of stock situation	
Any documents missing?	N/A	
Part 2	**Summary of SRA/NRA inspection evidence considered**	
US FDA	Dates of inspection:	02/20/2017 - 02/23/2017
	Type of inspection:	Routine surveillance inspection of an active pharmaceutical ingredient manufacturer
	Block/Unit/Workshop:	No.4 Phytochemistry Plant
	API covered:	Artemether
	Physical areas inspected:	• Training program • Manufacturing / design operations o Manufacturing o Warehouses o Laboratories • Quality o Product release review, o Document control, o Change control, o Deviation control, o Annual product review, o Supplier management, o Internal audits, o Complaint handling, o Qualification, o Validation o Training • Materials o Procedures related to the materials system o Rejected materials o Purified water o Nitrogen gas • Production o Walked through the manufacturing process for Artemether from step one to four, observed: ▪ Reactors, ▪ Filters, ▪ Centrifuges, ▪ Dryers, ▪ Clean room,

		▪ Miller, ▪ Blender, ▪ Packaging room o BMRs review for Artemether step 1 to step 4 • Laboratory o Sample retention and stability o Sample retention and stability o Working, reference standard and finished dosage testing o Raw material testing o Review of audit trails o Review of QC worksheets • Manufacturing codes • Complaints • Recall procedures
	Any sections of GMP not covered?	Reprocessing/reworking, blending, recovery of solvents and mother liquor.
	Summary of major deficiencies observed:	Observations was issued for the following: failure to follow written procedures and materials not being properly stored to avoid mix-up. <u>Observation No I</u> Written procedures are not followed, specifically: Your protocol, Stability Study for Artemether API, states stability samples should be tested within 15 days of being removed from the stability chamber. However, Artemether lot MFB20155023 was pulled from the chamber on 4/15/16 and was not analyzed until 5/6/16, exceeding the 15day requirement <u>Observation No 2</u> Materials are not stored appropriately according to status, specifically: It was observed that Artemether lots JZB20151034, JZB20151035, JZB20151036, JZB20l5l037and IPB20141020 were in the cold warehouse in the released area and labelled released by QA. However, the label didn't clearly indicate re-test information and it was later determined that lots listed above are associated with complaint TS2016-009. AS a result, they need to be further tested and potentially reprocessed prior to use in manufacturing.

	Description of CAPA:	Response to FDA Inspection February 20 - 23, 2017, FEI number: 3007245623 was submitted and reviewed. CAPAs were found to be adequate
	Final conclusion of the inspection report:	The inspection resulted in a 4- item FDA-483, Inspectional Observations. The inspection was classified VAI. During the current inspection all observations were found to be corrected.
	Comments/observations on the scope and comprehensiveness of the inspection report and on the appropriateness of the CAPAs in lieu of an onsite inspection by WHO:	Inspection report was comprehensive and CAPAs could be accepted in lieu of an onsite inspection by WHO.
TGA Australia	Dates of inspection:	7-9 November 2016
	Type of inspection:	Full inspection / Re-inspection
	Block/Unit/Workshop:	PCP4
	API covered:	Artemether

	Physical areas inspected:	• Quality system
		• Personnel
		• Manufacturing facilities in PCP4
		• Dedicated raw materials and finished product warehouses
		• The shared packing material warehouse
		• QC laboratories (chemistry and microbiology)
		• Quality management
		  o Personnel
		  o Buildings and facilities
		  o Process equipment
		  o Computerizes systems
		  o Documentation / records
		• Materials management
		• Production and in-process controls
		• Packaging and labeling of intermediates and APIs
		• Storage and distribution
		• Laboratory controls
		• Validation
		• Rejection and re-use of materials
		• Complaints and recalls
		• Contract manufacturing

	Sections of GMP not covered:	Reprocessing/reworking, blending, recovery of solvents and mother liquor, self-inspection, supplier qualification
	Summary of major deficiencies observed:	Your response(s) to the deficiency report have been evaluated and have been accepted.

		No critical/major deficiencies reported. Other deficiencies: 1. The requirements of Clause 6.10 that all documents related to the manufacture of APIs should be prepared, reviewed and distributed according to written procedures were not fully satisfied. SOPs that had undergone repeated reviews demonstrated: a. The document control procedure did not describe the required activities to manage the electronic master copy. b. The procedure for sampling tankers did not consider different compartments within the tankers. c. The sampling procedure for liquids in drums did not ensure the very top and bottom of the drum was sampled (potential for precipitate or phase separation not to be detected) d. Several SOPs were reassigned a new 3-year review period although the new version had only been issued due to a change in the logo and the documents had not been fully reviewed.
	Description of CAPA:	Response to TGA Inspection 7-9 November 2016 was submitted and reviewed. CAPAs were found to be adequate
	Final conclusion of the inspection report:	A satisfactory response to the deficiencies reported to the manufacturer was received on 05/12/2016. The manufacturer's corrective actions have been evaluated and accepted, based on the agreement that all corrective actions will be carried out as described in the inspection close out correspondence. The manufacturer operates in accordance with the relevant GMP requirements.
	Comments/observations on the scope and comprehensiveness of the inspection report and on the appropriateness of the CAPAs in lieu of an onsite inspection by WHO:	Inspection report was comprehensive and CAPAs could be accepted in lieu of an onsite inspection by WHO.

Part 3	Summary of the last WHO inspection
Date and conclusion of most recent WHO inspection	16-18 November 2015 Initial conclusion Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the deficiencies listed in the Inspection Report, a decision on the compliance of the Kunming Pharmaceutical Corporation, Phytochemistry Plant No.4 (PCP4), located at No. 141 Chunyu Road, Wuhua Zone, Kunming, Yunnan Province, P. R. China **,** with WHO GMP guidelines will be made after the manufacturer's response to the deficiencies has been assessed. Inspection closing letter, dated 6 April 2016: On the basis of the findings of the inspection and these subsequent response(s) the inspectors have recommended that the API: • Artemether - APIMF125 is considered to be manufactured in compliance with WHO GMPs for Active Pharmaceutical Ingredients published by WHO for the scope activities listed below: • manufacture and packaging of Active Pharmaceutical Ingredients by chemical synthesis • analytical and microbiological testing of raw materials associated intermediates and API
Brief summary of manufacturing activities	Active Pharmaceutical Ingredient, Freeze-drying Powder for Injection, Small Volume Injections and Oral Solid Dosage preparations
General information about the company and manufacturing site (according to the SMF)	KPC Pharmaceuticals, Inc. (hereafter be abbreviated as "KPC") was established in 1951. KPC headquarter is located in No.166 Keyi Road, High and New Technology Development Zone, Kunming, Yunnan Province P. R. China. The company has 1 joint venture, 4 subsidiary companies, 1 drug research institute, and 1 manufacturing center. The staff of KPC is more than 3200. The manufacturing site is located in Qigongli West Suburb, Kunming City 650100, Yunnan Province, P. R. China. It covers an area of 120,000 square meters with a floorage of 60,500 square meters, with a staff of more than 1200 including about 180 technical personnel, accounting for 15% of the total. Manufacturing center currently has an annual production capacity of 360 million ampoules of small volume injections, 3,000 million tablets, 70 million vials of freeze-dried powder for injection and 100 tons of active pharmaceutical ingredient. The product, Artemether DS00 is manufactured in No.4 Phytochemistry Plant (hereafter be abbreviated as "PCP4"), which has been launched in 2005
Focus of the last WHO inspection	APIMF125 Artemether
Areas inspected	• Quality Management • Personnel • Buildings and facilities • Process equipment • Documentation and records • Materials management • Production and in-process controls

	• Storage and distribution • Laboratory controls • Validation • Change control • Rejection and reuse of materials • Complaints and recalls • Contract manufacturers (including laboratories)
Out of scope and restrictions (last WHO inspection)	Freeze-drying Powder for Injection, Small Volume Injections and Oral Solid Dosage preparations.
WHO API covered by the last WHO inspection	APIMF125 Artemether
Additional products to be covered by this desk assessment:	N/A
Abbreviations	**Meaning**
BMR	Batch manufacturing record
BPR	Batch production record
CAPA	Corrective and preventive action
CC	Change control
GMP	Good manufacturing practices
NC	Non-conformity
NRA	National regulatory agency
PQR	Product quality review
PQS	Pharmaceutical quality system
QA	Quality assurance
QC	Quality control
QCL	Quality control laboratory
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
RCA	Root cause analysis
SOP	Standard operating procedure

Part 4	Summary of the assessment of supporting documentation

a) Manufacturing authorization and GMP certificate granted by the local authority:
No: Dian 20160102, classification code: HabZbFCb for: Small volume injection, freeze-dried powder injection, tablets, hard capsules, soft capsules, granules, crude drugs, psychoactive drugs, pharmaceutical precursor, chemicals, active pharmaceutical ingredients and extract of traditional Chinese medicine. Licence valid till 31 December 2020.

GMP certificate No YN20190045, issued by Chiba Food nd Drug Administration: "Manufacturer complies with the requirement of Chinese Good Manufacturing Practices for Pharmaceutical Products", valid until 15/08/2024. Scope of inspection: Bulk drug (Artemether).

b) Site master file (SMF):
Submitted – acceptable, prepared according to the WHO TRS No. 961, Annex 14

c) List of all the APIs or other products (intermediates, dosage forms) manufactured on-site:

Sr	Product Name	Strength
1.	Metamizole Sodium Injection	1ml:0.25g
2.	Metamizole Sodium Injection	2ml:0.5g
3.	Caowujiasu Injection	Herbal; 2ml:0.2mg
4.	Quinine Dihydrochloride Injection	1ml:0.25g
5.	Quinine Dihydrochloride Injection	1ml:0.5g
6.	Quinine Dihydrochloride Injection	10ml:0.25g
7.	Compound Amionpyrine and Antipyrine Injection	compound
8.	Vitamin B Injection	compound
9.	Artemether Injection	1ml:80mg
10.	Artemether Injection	0.5ml:40mg
11.	Huangtengsu Injection	Herbal; 2ml:20mg
12.	Ribavirin Injection	1ml:100mg
13.	Ribavirin Injection	2ml:250mg
14.	Amikacin Sulfate Injection	1ml:0.1g
15.	Amikacin Sulfate Injection	2ml:0.2g
16.	Atropine Sulfate Injection	1ml:5mg
17.	Atropine Sulfate Injection	2ml:1mg
18.	Atropine Sulfate Injection	1ml:0.5mg
19.	Kanamycin Sulfate Injection	2ml:0.5g
20.	Gentamycin Sulfate Injection	1ml :20000U
21.	Gentamycin Sulfate Injection	1ml:40000U
22.	Gentamycin Sulfate Injection	2ml:80000U
23.	Tobramycin Sulfate Injection	2ml:80mg
24.	Tobramycin Sulfate Injection	1ml:30mg
25.	Micronomycin Sulfate Injection	2ml:60mg
26.	Micronomycin Sulfate Injection	2ml:80mg
27.	Calcium Chloride Injection	10ml:0.3g
28.	Calcium Chloride Injection	10ml:0.5g
29.	Calcium Chloride Injection	20ml:0.6g
30.	Calcium Chloride Injection	20ml:1g
31.	Potassium Chloride Injection	10ml:1g
32.	Sodium Chloride Injection	10ml:90mg

Sr	Product Name	Strength
33.	Chloramphenicol Injection	1ml:0.125g
34.	Chloramphenicol Injection	2ml:0.25g
35.	Clonazepam Injection	1ml:1mg
36.	Chlorphenamine Maleate Injection	1ml:10mg
37.	Chlorphenamine Maleate Injection	2ml:20mg
38.	Sterilized Water for Injection	20ml
39.	Sterilized Water for Injection	10ml
40.	Sterilized Water for Injection	2ml
41.	Sterilized Water for Injection	5ml
42.	Glucose Injection	10ml:2g
43.	Glucose Injection	20ml:5g
44.	Glucose Injection	20ml:10g
45.	Gastrodin Injection	1ml:100mg
46.	Gastrodin Injection	2ml:0.2g
47.	Vitamin B_{12}Injection	1ml:0.05 mg
48.	Vitamin B_{12}Injection	1ml:0.1 mg
49.	Vitamin B_{12}Injection	1ml:0.25 mg
50.	Vitamin B_{12}Injection	1ml:0.5mg
51.	Vitamin B_{12}Injection	1ml:1mg
52.	Vitamin B_1Injection	2ml:50mg
53.	Vitamin B_1Injection	2ml:100mg
54.	Vitamin B_6Injection	1ml:25mg
55.	Vitamin B6Injection	1ml:50mg
56.	Vitamin B_6Injection	2ml:0.1g
57.	Vitamin C Injection	2ml :0.1g
58.	Vitamin C Injection	2ml:0.25g
59.	Vitamin C Injection	2ml:0.5g
60.	Vitamin C Injection	5ml:0.5g
61.	Vitamin C Injection	5ml:1g
62.	Vitamin C Injection	20ml:2.5g
63.	Panax Notoginseng Injection	2ml:100mg
64.	Panax Notoginseng Injection	2ml:200mg
65.	Panax Notoginseng Injection	5ml:250mg
66.	Panax Notoginseng Injection	10ml:250mg
67.	Nicotinamide Injection	1ml:50mg
68.	Nicotinamide Injection	1ml:100mg
69.	Lincomycin Hydrochloride Injection	1ml:0.2g
70.	Lincomycin Hydrochloride Injection	2ml:0.6g
71.	Nefopam Hydrochloride Injection	1ml:20mg
72.	Procaine Hydrochloride Injection	2ml:40mg
73.	Procaine Hydrochloride Injection	10ml:100mg
74.	Procaine Hydrochloride Injection	20ml:50mg
75.	Procaine Hydrochloride Injection	20ml:100mg
76.	Adrenaline Hydrochloride Injection	0.5ml:0.5mg
77.	Adrenaline Hydrochloride Injection	1ml:1mg
78.	Panax Notoginseng Lyophilized Powder for Injection	200mg
		400mg
		100mg
79.	Dapsone Tablets	50mg
80.	Dapsone Tablets	100mg
81.	Aminophylline Tablets	0.1g

Sr	Product Name	Strength
82.	Aminophylline Tablets	0.2g
83.	Metamizole Sodium Tablets	0.25g
84.	Metamizole Sodium Tablets	0.5g
85.	Benorilate tablets	0.2g
86.	Benorilate tablets	0.5g
87.	Pipemidic Acid Tablets	0.25g
88.	Pipemidic Acid Tablets	0.5g
89.	Mentha Laryngitic Tablets	Herbal
90.	Breviscapine Tablets	Herbal
91.	Diazepam Tablets	2.5mg
92.	Diazepam Tablets	5mg
93.	Helicia tablets	Herbal; 25mg
94.	Helicia tablets	Herbal; 50mg
95.	Domiphen Bromide Buccal Tablets	0.5mg
96.	Sodium Aminosalicylate Enteric-coated Tablets	0.5g
97.	Paracetamol Tablets	0.1g
98.	Paracetamol Tablets	0.3g
99.	Paracetamol Tablets	0.5g
100.	Multivitamin Tablets (21)	Compound
101.	Paracetamol,Aminophenazone Tablets	compound
102.	Furazolidone Tablets	10mg
103.	Furazolidone Tablets	30mg
104.	Furazolidone Tablets	100mg
105.	Copmpound Paracetamol Tablets	compound
106.	Compound Glycyrrhiza Tablets	Compound
107.	Compound Artemether Tablets	120mg, 20mg
108.	Compound Sulfamethoxazole Tablets	0.4g; 80mg
109.	Compound Sulfadiazine Tablets	Compound
110.	Compound Reserpine Tablets	Compound
111.	Compound Naphthoquine Phosphate Tablets	Compound
112.	Compound Naphthoquine Phosphate Tablets	Compound
113.	Tabellae Bergenini Compositae	Erbal Compound
114.	Tabellae acidi acetyls Alicylici compositae	Compound
115.	Compound Vitamin B Tablets	Compound
116.	Dry Yeast Tablets	0.2g
117.	Dry Yeast Tablets	0.3g
118.	Dry Yeast Tablets	0.5g
119.	Artemether Tablets	40mg
120.	Artemether Tablets	50mg
121.	Artemether Tablets	25 mg
122.	Erythromycin Enteric-coated Tablets	0.125g
123.	Erythromycin Enteric-coated Tablets	0.25g
124.	Fibrauretine Tablets	0.1g
125.	Fibrauretine Tablets	0.3g

Sr	Product Name	Strength
126.	Sulfamidine Tablets	0.5g
127.	Sulfadiazine Tablets	0.5g
128.	GriseofulvinTablets	0.1g
129.	GriseofulvinTablets	0.25g
130.	Inositol Nicotinate Tablets	0.2g
131.	Inosine Tablets	0.2g
132.	Kitasamycin Tablets	100000U
133.	MetronidazoleTablets	0.2g
134.	Trimethoprim Tablets	0.1g
135.	Jianshenning Tablets	Herbal; 100mg
136.	Pentoxyverine Citrate Tablets	25mg
137.	Captopril Tablets	12.5mg
138.	Captopril Tablets	25mg
139.	Kunming Shanhaitang Tablets	Herbal; 0.25g
140.	Reserpine Tablets	0.25mg
141.	Reserpine Tablets	0.1mg
142.	Chloroquine Phosphate Tablets	0.075g
143.	Chloroquine Phosphate Tablets	0.25g
144.	Atropine Sulfate Tablets	0.3mg
145.	Gentamicin Sulfate Tablets	20mg
146.	Gentamicin Sulfate Tablets	40mg
147.	Diclofenac Sodium Chlorphenamine Maleate Tablets	Compound
148.	RotundineTablets	30 mg
149.	RotundineTablets	60mg
150.	Chloramphenicol Tablets	0.25g
151.	Spiramycin Tablets	750000U
152.	Chlorphenamine Maleate Tablets	4mg
153.	Medemycin Tablets	0.1g
154.	Paracetamol and Chlorphenamine Maleate Tablets	50mg
155.	Norfloxacin Tablets	0.1g
156.	Calcium Gluconate Tablets	0.1g
157.	Calcium Gluconate Tablets	0.5 g
158.	Qiyeanshen Tablets	50mg
159.	Qiyeanshen Tablets	100mg
160.	Qiyeanshen Tablets	0.3g
161.	Colchicine Tablets	0.5mg
162.	Colchicine Tablets	1mg
163.	Compound Aminopyrine Phenacetin Tablets	Compound
164.	Calcium Lactate Tablets	0.25g
165.	Calcium Lactate Tablets	0.5 g
166.	Sanfensan Extract Tablets	10mg
167.	Sanqishang Tablets	/
168.	Tetracycline Tablets	0.05g
169.	Tetracycline Tablets	0.125g
170.	Tetracycline Tablets	0.25g
171.	Sodium Bicarbonate Tablets	0.3g
172.	Sodium Bicarbonate Tablets	0.5 g
173.	Gastrodin Tablets	25mg
174.	Gastrodin Tablets	50mg
175.	Oxytetracycline Tablets	0.25g

Sr	Product Name	Strength
176.	Oxytetracycline Tablets	0.125g
177.	Vitamin B_1 Tablets	5mg
178.	Vitamin B_1 Tablets	10mg
179.	Vitamin B_2 Tablets	5mg
180.	Vitamin B_2Tablets	10mg
181.	Vitamin B_6 Tablets	10mg
182.	Vitamin C Tablets	200mg
183.	Vitamin C Tablets	500mg
184.	Vitamin C Tablets	25mg
185.	Vitamin C Tablets	50mg
186.	Vitamin C Tablets	100mg
187.	Urotropine Tablets	0.3g
188.	Urotropine Tablets	0.5g
189.	Cimetidine Tablets	0.2g
190.	Cimetidine Tablets	0.4g
191.	Cimetidine Tablets	0.8g
192.	Nicotinic Acid Tablets	50mg
193.	Nicotinic Acid Tablets	100mg
194.	Diltiazem Hydrochloride Sustained Release Tablets	30mg
195.	Diltiazem Hydrochloride Sustained Release Tablets	60mg
196.	Ciprofloxacin Hydrochloride Tablets	0.25g
197.	Chlorpromazine Hydrochloride Tablets	12.5mg
198.	Chlorpromazine Hydrochloride Tablets	25mg
199.	Chlorpromazine Hydrochloride Tablets	50mg
200.	Ephedrine Hydrochloride Tablets	15mg
201.	Ephedrine Hydrochloride Tablets	25mg
202.	Ephedrine Hydrochloride Tablets	30mg
203.	Berberine Hydrochloride Tablets	0.1g
204.	Berberine Hydrochloride Tablets	0.025g
205.	Berberine Hydrochloride Tablets	0.05g
206.	Levamisole Hydrochloride Tablets	25mg
207.	Levamisole Hydrochloride Tablets	50mg
208.	Ofloxacin Tablets	0.1g
209.	Pyrimethamine Tablets	6.25mg
210.	Acetylspiramycin Tablets	0.1g
211.	Acetylspiramycin Tablets	0.2g
212.	Acetagastrodin Tablets	25mg
213.	Acetagastrodin Tablets	50mg
214.	Isoniazid Tablets	50mg
215.	Isoniazid Tablets	100mg
216.	Isoniazid Tablets	300m g
217.	Alginic Sodium Diester Tablets	50mg
218.	Lumefantrine Soft Capsules	100mg
219.	Bulleyaconitine Soft Capsules	0.4mg
220.	Dengyinnaotong Capsules	Herbal; 0.26g
221.	Ethyl Polyenoate Soft Capsules	1g
222.	Ethyl Polyenoate Soft Capsules	0.45g
223.	Ethyl Polyenoate Soft Capsules	0.3g
224.	Ethyl Polyenoate Soft Capsules	0.25g
225.	Artemether Capsules	40mg
226.	Artemether Capsules	40mg

Sr	Product Name	Strength
227.	Artemether Capsules	100mg
228.	Bismuth Potassium Citrate Capsules	0.3g
229.	Luoshuicao Capsules	0.17g
230.	Midecamycin Capsules	0.1g
231.	Norfloxacin Capsules	0.1g
232.	Gastrodin Capsules	50mg
233.	Panax Notoginseng Soft Capsules	Herbal; 100mg
234.	Ranitidine Hydrochloride Capsules	150mg
235.	Minocycline Hydrochloride Capsule	50mg
236.	Yinqin Capsule	Herbal; 0.2g
237.	Paracetamol,Aminophenazone Phenacetin,Caffeine and Chlorphenamine Maleate Granules	Compound
238.	Paracetamol and Chlorphenamine Maleate Granules	Compound
239.	Bismuth Potassium Citrate Granules	1.0g
240.	Nanbanlangen Granules	15g
241.	Pediatric Paracetamol,Atificial Cow-bezoar and Chlorphenamine Maleate Granules	Compound
242.	Sulfogaiacol,Pentoxyverine and Promethazine Granules	Compound
243.	Zhikequtan Granules	Herbal; 10g
244.	Compound Artemisinin Liniments	5ml
		25ml
		50ml
245.	Artemisinin Liniments	5ml
		25ml
		50ml
246.	Compound Artemisinin Spray	5ml
		15ml
		20ml
		50ml
247.	Yunnanshe Medicine	Herbal
248.	Lumefantrine	API
249.	Hiliedum	API
250.	Artemether	API
251.	Reserpine	API
252.	Artemisinin	API
253.	Colchicine	API
254.	Gastrodin	API
255.	Acetagastrodin	API
256.	Calcium Laevulinate	API
257.	BisMuth PotassiuM Citrate	API
258.	Ethanol	/
259.	Peanut Oil	/
260.	Breviscapine	API
261.	Panax Notoginseng	API

d) List of all regulatory inspections performed in the last 3 years and their outcomes:

Inspection Scope	Time	Agency
PCP4 (Artemether API)	2015.11	WHO
Injection Plant	2016.08	WHO
Oral Dosage Plant and Injection Plant	2016.04	Zanzibar Food and Drug Board
PCP4 (Artemether API)	2016.09	Japan PMDA
Injection Plant	2016.11	Yunnan FDA
PCP4 (Artemether API)	2016.11	TGA, Australia
PCP4 (Artemether API)	2017.02	U.S. FDA
Oral Dosage Plant and Injection Plant	2017.06	NDA, Uganda
Soft Capsule Plant	2018.10	Yunnan FDA
Oral Dosage Plant, Soft Capsule Plant and Injection Plant	2018.10	Sudan
Oral Dosage Plant, Soft Capsule Plant and Injection Plant	2018.11	NAFDAC, Tanzania
Lyophilized Powder for Injection Plant, and Extraction Plant	2019.03	Yunnan FDA
PCP4 (Artemether API)	2019.07	Yunnan FDA
Oral Dosage Plant, Soft Capsule Plant and Injection Plant	2019.08	Yemen

e) Most recent product quality review (PQR) of the concerned WHO API:

Submitted and reviewed for (1 January - 31 December 2018):

Artemether (DS00), document code APR9000600-2019-1.01, including Dihydroartemisin, Artemether crude and Artemether was submitted and reviewed.

49 batches of Dihydroartemisin and 42 batches of Artemether Crude were produced.

18 batches of Artemether were produced.

Cpk was used for process performance evaluation.

Change controls (CC):

- 3 CC related to production
- 8 CC related to QC

Deviations 2 related to QC

No OOE reported

1 OOS reported

1 complaint reported

No unqualified, scrapped, reworked and re-processed batches, no returns / recalls

f) Batch manufacturing and packaging records, including the analytical part, for the most recently released batch of relevant API:

Submitted and reviewed for:

Artemether DS00 batch No I20191012 (BMR/BPR)

Artemether DS00 batch No I20191007 (analytical part)

g) Master batch manufacturing and packaging record(s) of the API(s) of interest:

Submitted and reviewed for:

Artemether DS00

h) Recalls in the past three years related to APIs with quality defects:
Submitted: statement – no recalls in last 3 years

i) Confirmation by the senior quality assurance representative that a full self-inspection or external audit dedicated to the API has been performed and all matters dealt with:
Submitted and reviewed.

j) Copy of any warning letter, or equivalent regulatory action, issued by any authority for their market, to which the site provides or has applied to provide the API:
Submitted:
Form 483, related the US FDA inspection 02/20/2017 - 02/23/2017.

k) Out-of-stock situations:
Submitted, none reported.

l) Additional documents submitted:
N/A

Part 5	**Conclusion – Desk assessment outcome**

Based on the previous WHO inspections and on the GMP evidence received and reviewed, it is considered that a desk assessment is acceptable in lieu of a WHO onsite inspection. The *site* ***KPC Pharmaceuticals, Inc., No.4 Phytochemistry Plant*** located at ***Qigongli West Suburb, Kunming City 650100, Yunnan Province, P. R. China*** is considered to be operating at an acceptable level of compliance with WHO GMP guidelines for APIs.

This compliance status shall be valid until 23 February 2020 (3 years from US FDA inspection) or when another inspection is conducted by WHO or by a stringent regulatory authority.

Name	Iveta Streipa
Signature	
Date of signature	9/27/2019

Part 6	**List of guidelines referenced in this inspection report**

1. WHO good manufacturing practices for active pharmaceutical ingredients. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Forty-Fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2. ***Short name: WHO GMP for APIs*** or ***TRS No. 957, Annex 2***
   http://apps.who.int/medicinedocs/documents/s20119en/s20119en.pdf

2. WHO good manufacturing practices for pharmaceutical products: main principles. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Forty-Eighth Report. Geneva, World

Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2. ***Short name: WHO GMP Guidelines or WHO TRS No. 986, Annex 2***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/

3. WHO guidance on good practices for desk assessment of compliance with good manufacturing practices, good laboratory practices and good clinical practices for medical products regulatory decisions. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Fifty-Second Report. Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 9. ***Short name: WHO TRS 1010, Annex 9***
https://www.who.int/medicines/areas/quality_safety/quality_assurance/TRS1010annex9.pdf?ua=1

4. WHO Good Manufacturing Practices: water for pharmaceutical use. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Forty-Sixth Report. Geneva, World Health Organization, 2012 (WHO Technical Report Series, No. 970), Annex 2. ***Short name: WHO TRS No. 970, Annex 2***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_970/en/

5. WHO guidelines for sampling of pharmaceutical products and related materials. *WHO Expert Committee on Specifications for Pharmaceutical Preparations.* Thirty-Ninth Report. Geneva, World Health Organization, 2005 (WHO Technical Report Series, No. 929), Annex 4. ***Short name: WHO TRS No. 929, Annex 4***
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6. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. Part 2: Interpretation of Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Fifty-Third Report Geneva, World Health Organization, 2019 (WHO Technical Report Series, No. 1019), Annex 2. **Short name: WHO TRS No. 1019, Annex 2**
https://apps.who.int/iris/bitstream/handle/10665/312316/9789241210287-eng.pdf?ua=1

7. Good manufacturing practices: guidelines on validation. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Fifty-Third Report Geneva, World Health Organization, 2019 (WHO Technical Report Series, No. 1019), Annex 3. **Short name: WHO TRS No. 1019, Annex 3**
https://apps.who.int/iris/bitstream/handle/10665/312316/9789241210287-eng.pdf?ua=1

8. WHO Good Practices for pharmaceutical quality control laboratories. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Forty-Fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 1. ***Short name: WHO TRS No. 957, Annex 1***
http://www.who.int/medicines/publications/44threport/en/

9. WHO good practices for pharmaceutical products containing hazardous substances. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Forty-Fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 3. ***Short name: WHO TRS No. 957, Annex 3***
http://www.who.int/medicines/publications/44threport/en/

10. WHO good manufacturing practices for sterile pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 6.

Short name: WHO TRS No. 961, Annex 6
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

11. WHO guidelines on transfer of technology in pharmaceutical manufacturing. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 7.
Short name: WHO TRS No. 961, Annex 7
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12. Model guidance for the storage and transport of time-and temperature-sensitive pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 9.
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13. General guidelines for the establishment maintenance and distribution of chemical reference substances. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Forty-First Report Geneva, World Health Organization 2007 (WHO Technical Report Series, No.943) Annex 3.
Short name: WHO TRS No. 943, Annex 3
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14. WHO good practices for pharmaceutical microbiology laboratories. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 2.
Short name: WHO TRS No. 961, Annex 2
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15. WHO guidelines on quality risk management. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Forty-Seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 2.
Short name: WHO TRS No. 981, Annex 2
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

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17. WHO guidelines for drafting a site master file. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 14.
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http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

18. WHO Guidelines on good manufacturing practices: validation, Appendix 7: non-sterile process validation. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 3.
Short name: WHO TRS No. 992, Annex 3

http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

19. WHO General guidance on hold-time studies *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 4. ***Short name: WHO TRS No. 992, Annex 4***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

20. WHO Technical supplements to Model Guidance for storage and transport of time – and temperature – sensitive pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 5. ***Short name: WHO TRS No. 992, Annex 5***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

21. Guidance on good data and record management practices. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Fiftieth Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 5.
Short name: WHO TRS No. 996, Annex 5
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex05.pdf

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24. WHO Recommendations for quality requirements when plant – derived artemisin is used as a starting material in the prosecution of antimalarial active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 6
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