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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Desk Assessment of Finished Pharmaceutical Product (FPP) Manufacturer

Part 1	**General information**
Company information	
Name of Manufacturer	Strides Pharma Science Limited.
Corporate address of manufacturer	Strides House, Bilekahalli, Bannerghatta Road, Bangalore-560076, India. Phone: 91-80-67840521 Fax: 91-80-67840800
Inspected site	
Name & address of manufacturing site	Strides Pharma Science Limited. 36/7, KRS Gardens, Suragajakkanahalli, Indlawadi Cross, Anekal Taluk, Bangalore South-562106, India D-U-N-S Number: 918513263
Unit/Block/Workshop	Formulations 1
Desk assessment details	
Date of review	28 October 2019
FPPs covered by this desk assessment	

PQ number	**Product**
ANDA 090457 USFDA	Lamivudine 300mg tablets
ANDA 21988 USFDA	Lamivudine/zidovudine+Nevirapine-150mg/300mg+200mg tablets
HA268	Nevirapine 200mg tablets
HA291	Lamivudine/Zidovudine 150mg/300mg film coated tablets
HA389	Efavirenz 200mg film-coated tablets
HA390	Efavirenz 600mg coated tablets
HA494	Abacavir sulphate 300mg film-coated tablets
HA524	Lamivudine/Nevirapine/Zidovudine 150mg/200mg/300mg film coated tablets
HA535	Tenofovir disoproxil fumarate 300mg film coated tablets
HA552	Emtricitabine/tenofovir disoproxil fumarate 200mg/300mg film coated tablets
HA553	Efavirenz/Emtricitabine/tenofovir disoproxil fumarate 600mg/200mg/300mg film coated tablets.
HA557	Lamivudine/Nevirapine/Zidovudine 30mg/50mg/60mg dispersible tablets
HA729	Dolutegravir sodium/lamivudine/tenofovir disoproxil fumarate 50mg/300mg/300mg film-coated tablets
HP009	Sofosbuvir 400mg film coated tablets

	HP013	Ledipasvir/sofosbuvir 90mg/400mg film coated tablets
	IN002	Oseltamivir phosphate 75mg hard gelatin capsules
	MA088	Artemether/Lumefantrine 20mg/120mg tablets
	MA110	Artemether/Lumefantrine 20mg/120mg dispersible tablets
	MA123	Artesunate 100mg rectal soft capsule
	MA138	Artemether/Lumefantrine 80mg/480mg tablets
	The site mentioned the discontinuation of the products below:	
	NDA 21837a USFDA	Lamivudine/Nevirapine/Stavudine 150mg/200mg/30mg tablets.
	TB085	Isoniazid/Rifampicin 75mg/150mg coated tablets
	TB090	Ethambutol hydrochloride/isoniazid/pyrazinamide/Rifampicin 275mg/75mg/400mg/150mg film-coated tablets
List of documents submitted	a. Manufacturing licenses issued by the Government of Karnataka, numbers; KTK/25/415/98, KTK/28/301/98 valid till 31.12.2021 and KTK/25F/2/2009 valid till 22.09.2019. b. Site master file, effective on 30.08.2018. c. A list of all the products (medicinal or other) manufactured on site. d. A list of regulatory inspections conducted in the last five years e. Inspection reports for inspections conducted within the last 3 years along with CAPAs and proof of CAPAs implementation related to the inspection report observations/deficiencies or any warning letter or equivalent regulatory action. f. PQRs for 10 WHO prequalified products. g. Completed batch manufacturing and packaging records, including the analytical records for 10 WHO prequalified products. h. A confirmation by the Assistant vice president-QA representative that a full self-inspection or external audit has been performed and all matters dealt with. i. A list of any recalls in the last three years. j. A statement on out of stock situations. k. Blank master batch manufacturing and packaging records for PQ products.	
Part 2	**Summary of SRA/NRA inspection evidence considered (from most recent to last)**	
Health and Youth Care Inspectorate, Ministry of Health, Welfare and Sport	Dates of inspection:	11-14 June 2019
	Type of inspection:	Routine inspection
	Block/Unit/Workshop:	Blocks for packaging operations, manufacturing of Oral Liquids forms and manufacturing of tablets and hard/soft capsules.
	Type of dosage forms covered:	Non-sterile products: • Capsules, hard shell • Capsules, soft shell • Liquids for internal use

		• Semi-solids • Tablets • Other: Sachets
US Food and Drug Administration (US FDA)	Dates of inspection:	16-17,20-24 May 2019
	Type of inspection:	Routine inspection
	Block/Unit/Workshop:	Not mentioned
	Type of products/dosage forms covered:	•The inspection covered profile classes POW (non-sterile powder), CHG (capsules prompt release), LIQ (non-sterile liquid), TCM (tablets prompt release), OIN (non-sterile ointment or cream) and CSG (soft gelatin capsules). •Post-approval Review: capsules and tablets
US Food and Drug Administration (US FDA)	Dates of inspection:	29.10.2018 to 02.11.2018
	Type of inspection:	Pre-approval inspection
	Block/Unit/Workshop:	Soft gelatin block
	Type of products/dosage forms covered:	Soft gel capsules
US Food and Drug Administration (US FDA)	Dates of inspection:	20- 24 August 2018
	Type of inspection:	Pre-approval inspection
	Block/Unit/Workshop:	Oral liquids and topical solutions block
	Type of products/dosage forms covered:	Oral and topical solutions
US Food and Drug Administration (US FDA)	Dates of inspection:	22- 26 May 2017
	Type of inspection:	Pre-approval inspection
	Block/Unit/Workshop:	Soft gelatin block
	Type of products/dosage forms covered:	Soft gelatin capsules
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	The manufacturing site of Strides KRS in Bangalore was last inspected by the WHO from the 13-17 June 2016. The site was found compliant after the submission of CAPA to two major findings and 9 classified as "Others".	
Brief description of manufacturing activities	The manufacturing site performs production and quality control for general tablets, hard gelatin capsules, oral liquids and soft gelatin capsules. No beta lactam or other hazardous products were manufactured at the site. Contract laboratories were used to perform certain tests.	
General information about the company and manufacturing site	Strides Pharma Science Limited is a global pharmaceutical company with headquarters in Bangalore India. The company is involved in the development, and manufacture of nutritional, active pharmaceutical ingredients and pharmaceutical products. The company has six manufacturing units spread across three continents. The Bangalore site is spread across 23 acres and consists of four production departments engaged in the manufacture of tablets, capsules, ointments and	

	creams and soft gel capsules and has a dedicated block for packaging operations, consisting of 17 packaging lines.
Focus of the last WHO inspection	The focus of the last WHO inspection was the film coated and dispersible tablet, hard and soft gelatine capsule lines.
Areas inspected	The areas inspected during the last WHO inspection were, the quality management systems, QC laboratories and OSD production departments for tablets, soft and hard gelatine capsules.
Out of scope and restrictions (last WHO inspection)	The last WHO inspection did not cover the oral liquids line. Furthermore, the microbiology laboratory and tablet and hard gelatin capsule HVAC systems were not covered due to time constraints.
WHO products ~~APIs~~ covered by the last WHO inspection	**Product** Lamivudine 300mg tablets Lamivudine/zidovudine+Nevirapine-150mg/300mg+200mg tablets Nevirapine 200mg tablets. Lamivudine/Zidovudine 150mg/300mg film coated tablets Efavirenz 200mg film-coated tablets Efavirenz 600mg coated tablets Abacavir sulphate 300mg film-coated tablets Lamivudine/Nevirapine/Zidovudine 150mg/200mg/300mg film coated tablets Tenofovir disoproxil fumarate 300mg film coated tablets Emtricitabine/tenofovir disoproxil fumarate 200mg/300mg film coated tablets Efavirenz/Emtricitabine/tenofovir disoproxil fumarate 600mg/200mg/300mg film coated tablets. Lamivudine/Nevirapine/Zidovudine 30mg/50mg/60mg dispersible tablets Oseltamivir phosphate 75mg hard gelatin capsules Artemether/Lumefantrine 20mg/120mg tablets Artemether/Lumefantrine 20mg/120mg dispersible tablets Artesunate 100mg rectal soft capsule. Artemether/Lumefantrine 80mg/480mg tablets. Lamivudine/Nevirapine/Stavudine 150mg/200mg/30mg tablets. Isoniazid/Rifampicin 75mg/150mg coated tablets Ethambutol hydrochloride/isoniazid/pyrazinamide/Rifampicin 275mg/75mg/400mg/150mg film-coated tablets
Additional products covered by this desk	None

assessment:	
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:

Manufacturing licenses issued by the Government of Karnataka, numbers; KTK/25/415/98, KTK/28/301/98 valid till 31.12.2021 and KTK/25F/2/2009 valid till 22.09.2019 respectively were submitted.

b) Site master file (SMF):

Site master file, effective on 30.08.2018, was reviewed and found acceptable and in line with the WHO guidance for Site master files for manufacturers.

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

List of all products manufactured at the site was provided. There were dedicated sections for tablets, soft gelatine capsules, and oral liquids There are no penicillin or other beta lactams manufactured at the site, therefore no foreseen risks of cross-contamination from highly sensitising products.

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

A list of all regulatory inspections performed in the last 3 years and the corresponding CAPA where required were submitted. The US FDA inspections conducted in the last 3 years covered the soft capsule, Tablets, Hard Gelatine Capsules, Oral liquid lines. There were various SRA inspections covering the production of tablets , hard gelatine capsules and Softgel capsules lines over the last 3 years.

e) Most recent product quality review(s) (PQR)(s) of the concerned WHO products(s):
PQR for emtricitabine and tenofovir disoproxil fumarate 200/300mg film coated tablets, dated 11.10.2018 for the period 01.01.2017 to 31.08.2018 was reviewed. It was mentioned that this is the first PQR for this product, therefore no recommendations from the past PQR was applicable. Only two batches were manufactured during the review period. The PQR included a review of raw and packaging materials, batches manufactured and their disposition, trending of CQAs including impurity levels, equipment qualification, deviations, changes, complaints, recalls, OOT, OOS, CAPA, stability study results, environmental monitoring results, regulatory data review, and technical agreement status review. It was concluded that the manufacturing process was robust and under a state of control, although no statistical analysis was performed.

PQR for Artemether/Lumefantrine 20/120mg tablets for the review period 01.01.2017 to 28.02.2018 was also reviewed. 128 batches had been manufactured during the review period, out of which, 127 were released while 1 batch was rejected due to an OOS result. Parameters as indicated above were reviewed and where applicable, trended. CPK was calculated and showed the manufacturing process was robust and under a state of control. No issues of concern were noted with regards to the PQR.

PQR for Artesunate rectal capsules 100mg for the period 01.01.2017 to 31.08.2018 dated 4.10.2018 was reviewed. 2 batches of batch size 125,000 soft gels were manufactured and released. No rejects, deviations, complaints, recalls were reported. Statistical evaluations were not done as the number of batches manufactured were inadequate to provide statistically meaningful results.

PQR for other products were confirmed to be available and their summary reports perused. No issues of concern were noted.

f) Batch manufacturing and packaging record(s), including the analytical part, for the most recently released batch of relevant product (s):
BMR for emtricitabine and tenofovir 200/300mg tablets, batch number *XXX* and Artemether and lumefantrine 20mg/120mg tablets batch number *XXX* were sampled for review. The records were generally well assembled and detailed, and included line clearance before each critical stage, environmental monitoring records, raw material testing and approval records, potency adjustment calculations, raw material dispensing records, instructions for each processing stage with time duration where required, sampling for in-process controls and records of in-process test results, process yields at various stages, primary packaging, reconciliation of packaging material, finished product CoA , along with supporting raw analytical data and batch release records. All batches were released for dispatch. BMRs for the other six products were confirmed to be available and briefly perused.

g) Master batch manufacturing and packaging record(s) of the product (s) ~~API(s)~~ of interest:
Master batch manufacturing records of the WHO PQ products covered by this desk assessment were submitted.

h) Recalls in the past three years related to products with quality defects:
A list of recalls was provided. A total of 11 recalls were reported by the firm in the last 3 years. 7 of these were related to products failing testing of stability indicating parameters. It is important to note that the complaint currently under investigation relates to Artesunate soft gel rectal caps failing the assay test during stability testing. The rather significant number of recalls related to products failing stability could signal a weakness in product/process development or proper control of the manufacturing processes. The firm should consider an overall review of these recalls.

i) Confirmation by the senior quality assurance representative that a full self-inspection or external audit dedicated to the products has been performed and all matters dealt with:
A confirmation by the Assistant vice president-QA representative that a full self-inspection or external audit has been performed and all matters dealt with was provided.

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 product(s):
A statement signed by the group leader quality assurance, dated 11.07.2019 mentioning that no regulatory actions or warning letters were issued to the site was submitted. Although it should be noted that a warning letter number 320-19-28 was issued by the US FDA to the Strides Puducherry site on the 1.07.2019 for significant violations to GMP. It is therefore imperative to verify whether these issues might exist in the Strides Bangalore site as well.

k) Out-of-stock situations:
A signed statement by the group leader quality assurance mentioning that no communication regarding out of stock situations has so far been received.

l) Additional documents submitted:
Notification dated 28.06.2019 regarding OOS for MA123 Artesunate rectal capsules 100mg, regarding low assay results observed during stability studies performed at 30^0C/75% RH for batch number *XXX* (24 months) and *XXX* (18 months).

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 **Strides Pharma Science Limited *(Formulations 1),*** located at ***36/7, KRS Gardens, Suragajakkanahalli, Indlawadi Cross, Anekal Taluk, Bangalore South-562106, India,*** is considered to be operating at an acceptable level of compliance with WHO GMP guidelines for FPP.

This WHOPIR will remain valid for 14 June 2021(2 years from the last Netherlands GMP inspection), provided that the outcome of any inspection conducted during this period is positive.

Part 6	List of guidelines referenced in this inspection report

1. 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 TRS No. 986, Annex 2***
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/

2. 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

3. 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/

4. 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
   http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf?ua=1

5. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Fifty-Second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 8. **Short name: WHO TRS No. 1010, Annex 8**
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_1010/en/

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
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

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.
Short name: WHO TRS No. 961, Annex 9
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

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
http://whqlibdoc.who.int/trs/WHO_TRS_943_eng.pdf?ua=1

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
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

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/

16. WHO guidelines on variation to a prequalified product. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Forty-Seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 3.
Short name: WHO TRS No. 981, Annex 3
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

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.
Short name: WHO TRS No. 961, Annex 14
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

22. Stability testing of active pharmaceutical ingredients and finished pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 10.
Short name: WHO TRS No. 1010, Annex 10
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

23. WHO general guidance on variations to multisource pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Fiftieth Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 10.
Short name: WHO TRS No. 996, Annex 10
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf