### Part 1: General information

<table>
<thead>
<tr>
<th>Manufacturers details</th>
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</thead>
<tbody>
<tr>
<td>Name of manufacturer</td>
<td>Sequent Scientific Limited</td>
</tr>
<tr>
<td>Corporate address of manufacturer</td>
<td>Corporate: 301, ‘Dosti Pinnacle’, Plot No. E7, Road No.22, Wagle Estate Industrial Area, Thane(W), Mumbai – 400604, India</td>
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<table>
<thead>
<tr>
<th>Inspected site</th>
<th></th>
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<tbody>
<tr>
<td>Name &amp; Address of inspected manufacturing site if different from that given above</td>
<td>Sequent Scientific Limited</td>
</tr>
<tr>
<td>Plot no: B-32, G-2&amp;G-3, MIDC, Mahad, Dist. Raigad -402309, Maharashtra, India</td>
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<tr>
<td>Synthetic Unit/Block/Workshop</td>
<td>Plant 1, Plant 2 and Plant 3</td>
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<table>
<thead>
<tr>
<th>Inspection details</th>
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<tbody>
<tr>
<td>Dates of inspection</td>
<td>29 August - 02 September 2022</td>
</tr>
<tr>
<td>Type of inspection</td>
<td>Initial inspection (New site)</td>
</tr>
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### Introduction

**Brief description of the manufacturing activities**

Production, quality control of intermediates and API products.

**General information about the company and site**

Sequent Scientific Limited (Mahad site) was established in the year of 2001. It is one of the Sequent Scientific Group of company. No beta-lactam antibiotics and high potent drug substances are manufactured on the site.

**History**

This was the initial WHO GMP inspection.

### Brief report of inspection activities undertaken – Scope and limitations

**Areas inspected**

- Quality management system
- Production blocks
- Solvent recovery plant
- Warehouses
- Physical and chemical quality control laboratory
- Microbiology laboratory
- Water system
<table>
<thead>
<tr>
<th>Restrictions</th>
<th>The inspection was restricted to the production of the product listed in the inspection scope.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Out of scope</td>
<td>All other products and production facility on the site were outside of the inspection scope and were not visited.</td>
</tr>
<tr>
<td>WHO APIs (including WHO API or APIMF numbers) covered by the inspection</td>
<td>APIMF 427 Albendazole</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Abbreviations</th>
<th>Meaning</th>
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<tbody>
<tr>
<td>AHU</td>
<td>Air handling unit</td>
</tr>
<tr>
<td>ALCOA</td>
<td>Attributable, legible, contemporaneous, original and accurate</td>
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<tr>
<td>API</td>
<td>Active pharmaceutical ingredient</td>
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<tr>
<td>APR</td>
<td>Annual product review</td>
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<tr>
<td>BMR</td>
<td>Batch manufacturing record</td>
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<td>BPR</td>
<td>Batch production record</td>
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<tr>
<td>CC</td>
<td>Change control</td>
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<tr>
<td>CIP</td>
<td>Cleaning in place</td>
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<td>CoA</td>
<td>Certificate of analysis</td>
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<tr>
<td>CpK</td>
<td>Process capability</td>
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<td>DQ</td>
<td>Design qualification</td>
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<tr>
<td>EDI</td>
<td>Electronic deionization</td>
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<td>EM</td>
<td>Environmental monitoring</td>
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<tr>
<td>FMEA</td>
<td>Failure modes and effects analysis</td>
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<td>FPP</td>
<td>Finished pharmaceutical product</td>
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<td>FTA</td>
<td>Fault tree analysis</td>
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<td>GMP</td>
<td>Good manufacturing practices</td>
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<td>HEPA</td>
<td>High efficiency particulate air</td>
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<td>HPLC</td>
<td>High performance liquid chromatography (or high-performance liquid chromatography equipment)</td>
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<tr>
<td>HVAC</td>
<td>Heating, ventilation and air conditioning</td>
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<td>IQ</td>
<td>Installation qualification</td>
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<tr>
<td>KF</td>
<td>Karl Fisher</td>
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<tr>
<td>LAF</td>
<td>Laminar air flow</td>
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<td>LIMS</td>
<td>Laboratory information management system</td>
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<tr>
<td>MB</td>
<td>Microbiology</td>
</tr>
<tr>
<td>MBL</td>
<td>Microbiology laboratory</td>
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<tr>
<td>MR</td>
<td>Management review</td>
</tr>
<tr>
<td>NC</td>
<td>Non conformity</td>
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<td>NRA</td>
<td>National regulatory agency</td>
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<td>OQ</td>
<td>Operational qualification</td>
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<td>PHA</td>
<td>Process hazard analysis</td>
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<tr>
<td>PLC</td>
<td>Programmable logic controller</td>
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<tr>
<td>PM</td>
<td>Preventive maintenance</td>
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Part 2  Summary of the findings and comments

1. Quality management
The quality management system was generally well established, documented and implemented. The site organizational structure was presented and was acceptable. Quality-related activities were defined and documented. The quality assurance department was independent from production. The persons authorized to release products were specified.

Annual Product Quality Review (PQR)
The Company had a procedure for annual product quality review. The APQR was required to be prepared from January to December and the compilation was to be completed before the end of March of the subsequent year in principle. At the time of the inspection, Albendazole API has not been prequalified by PQ. The APQRs for Albendazole 2021 and 2020 for the other quality grades were reviewed. The Company utilized one manufacturing process to produce API with different quality specifications supplied to commercial markets. The list of testing parameters differs based on the customer requirements or pharmacopeial (EP/BP/USP/IP) specifications. The APQR reported the key elements for the review period and was in general acceptable.

It was noted that the stability study data for Albendazole batches applied for WHO PQ were generated at another site: Sequent Research Limited located at 120 A&B, Industrial Area, Baikampady, New Mangalore – 575 011, India.

Quality Risk Management
Quality risk management and risk assessment was handled and performed according to an approved procedure. Risk assessment register for 2021 was checked and discussed.
Management review (MR)
Quality management review followed an approved procedure. MR meeting minutes dated July 2022 and the presentation prepared for the meeting were reviewed and found to be generally acceptable.

Deviations
Deviations were managed according to an approved procedure. The procedure and deviation management in Albendazole APQR 2021 were reviewed and found generally acceptable.

CAPAs
The CAPA events were handled with an established procedure. The QA department was responsible for issuing the CAPA number. The review of the CAPA register, CAPA effectiveness and trending of CAPA were performed. The CAPA procedure and flow chart depicted the steps leading change control raised to inform permanent changes.

Product release
The QA department was authorized to release the finished API batches manufactured at the Mahad site. The SOP for API product batch release and dispatch were reviewed and discussed.

Internal Audits:
The procedure for internal audits described the audit plan and the requirement for audits to be conducted. The audit form was used and included the check points to be audited for each department which was found acceptable.

2. Personnel

Personnel qualifications
An organization chart was available. 370 people were employed by the company at the time of the inspection. There appeared to be a sufficient number of personnel for the current manufacturing activities. Personnel were qualified through qualifications, experience, and training. Responsibilities in position descriptions for key personnel were reviewed. The positions of the Head Production and Head Quality were separate with independent responsibilities.

Training
The procedures for training and assessment of staff were reviewed and found acceptable. Training program for staff was in place with criteria for trainers established. The training protocol and record for an analytical analyst reviewed showed that the analyst met the criteria and was deemed competent to perform HPLC analyses.

Personnel hygiene
Personnel were required to wear protective clothing suitable for the type and stage of manufacturing. Suitable sanitation and change room facilities were provided.
3. Buildings and facilities

**Design and construction**
The buildings and facilities inspected were generally designed and constructed to facilitate cleaning, maintenance, and operations as appropriate to the type and stage of manufacture. Manufacturing areas provided adequate space for the placement of equipment.

Albendazole API manufacturing took place within three separate production plant units. A Grade D clean area was located in one of the plants for the final drying and packaging activities. The recovery of solvents was performed in the distillation facility on the site.

**HVAC System**
The company had established procedures for environmental control. The following documents were checked and found acceptable.
- The SOP for HVAC re-qualification for the ISO 8.
- The HVAC P&ID
- The qualification an AHU with the parameters results which supported the re-qualification of the AHU for ISO 8 criteria.

**Water System**
Purified water (PW) was used in the production and QC laboratory and PW was not used in the final purification stage of Albendazole API manufacture.

Portable water was supplied by the local government. The PW Generation and Distribution P&ID was checked. The company had sampling points for the generation and distribution system as indicated on P&ID. The detailed sampling plan was available for each sampling point. The re-qualification of PW system and the annual purified water monitoring report was check and was found acceptable.

**Containment**
The final synthesis, purification, and packaging of Albendazole API took place in a dedicated facility.

**Lighting**
The lighting in all warehouses and production areas, and the QC laboratory was suitable.

**Sanitation and maintenance**
All areas inspected were clean and appeared to be well maintained.

4. Process equipment

Equipment used in the manufacture of Albendazole API was dedicated and appeared to be of appropriate design and size for its intended use, cleaning, and maintenance. In general, equipment appeared to be well maintained. Measuring equipment was required to be labelled with its calibration status and all examples viewed were within their calibration dates.
The company had a preventive maintenance and serving procedure for equipment in place and was prepared annually and generated by SAP. The records were kept by the engineering department. The cleaning of the dust extractor collector filters was checked. The cleaning was required to be conducted on a regular basis and the integrity check for the filters should be covered.

5. Documentation and records
The company had corporate QA procedures for good documentation practices. The site had procedures and record control established. A procedure for the preparation, revision, and distribution was in place. Appropriately designed forms were used for the management of documents and records. QA department was responsible for the document control and retention of archival documents. The procedure for the disposal of documents was reviewed and found acceptable.

*Batch numbering system*
The batch numbering system was reviewed. There were several product codes assigned to Albendazole APIs corresponding to the different quality specifications.

*Batch manufacturing and packaging records*
BMR documents were prepared, reviewed, and approved according to written procedures. QA was responsible for the review of records and approval for the release of API batches produced. The SOP for issue and retrieval of batch manufacturing and packing record was reviewed and discussed.
Several BMRs of Albendazole API were briefly reviewed. The quantity of input materials was recorded and verified. The instructions were provided for the operators. The manufacturing activities were verified by the production supervisor. The holding time of the materials and in-process control were checked and discussed.

6. Materials management
The material management system was in place for the receipt and tracking of inventory. Starting materials and finished goods were stored in a dedicated area within the warehouse. There was a tank farm for the receipt of solvents and an external drum store. These appeared to be tidy and well managed and appropriately labelled. The raw material warehouse and finished goods warehouse were visited during the inspection.

*Raw Materials*
Procedures were established for managing all starting materials and packaging materials, received by approved suppliers. The company utilized the SAP system for materials management. The quarantined, approved and rejected material status were applicable and indicated by affixed labels.

The rejected raw material storage area was secured, no materials were stored in the area during the inspection. The rejected/returned raw material registered was checked and discussed.
**Finished Products**
There were two finish product warehouses on the site. The temperature was controlled below 25°C. The products stored during the inspection had customer dispatch labels.

**Vendor qualification**
A qualification system for starting material suppliers had been established. The procedures for the supplier audit and the quality agreement with suppliers were available. A supplier audit report for key staring material and the quality agreement were checked and found acceptable.

7. **Production and in-process controls**
The production was in operation at the time of inspection. The production block Plant 1, 2 and 3 were visited. The manufacturing processes of Albendazole API were performed and recorded according to instructions in the batch production records. The SOP for blending batches was reviewed and discussed.

8. **Packaging and identification labelling of APIs and intermediates**
The primary packaging operation was carried out in a Grade D environment. The labelling of the API was performed according to an approved procedure. The finished API product was packed in HDPE polybags and Fibre drums. The drums were sealed with unique seal number. Product labels were attached to the drums.

9. **Storage and distribution**
The APIs and intermediates were stored in a designated warehouse and held in quarantine until released for distribution by QA department.

10. **Laboratory controls**
The company had an established QC laboratory with wet chemistry, chromatography, and separate microbiology laboratory. Sample receiving and distribution, retention sample room were spot checked during the inspection.

   **Physical and chemical Laboratory**
The laboratory operations had the LIMS electronic management system, however the analytical instruments were all managed as standalone equipment, and data was manually transferred to LIMS. The chromatographic analyses procedure for integration and the HPLC analysis for WHO grade Albendazole batch were checked.

The data integrity management procedures were established, e.g. the instrument procedure for access management, project creation, roles/privileges and audit trial review which was reviewed and discussed. The calibration status of the QC equipment was spot check, and found acceptable.

**OOS and OOT management**
The procedure for OOS and OOT was reviewed. A flow chart outlined the steps for investigations. Trending was performed for OOS events. The OOS register and the investigation of an OOS of a Albendazole batch (IP) were reviewed and discussed.
Microbiology laboratory
The company had a small microbiology laboratory established. It was briefly visited. The PW microbiological limit test was checked. The results for the annual microbiological monitoring for purified water were discussed.

11. Validation

Validation policy
The validation policy was described in the VMP. The company had validation policies, procedures established and documented validation records.

Process Validation
The SOP for process validation was in place and reviewed. The process validation protocol and report for Albendazole API with three process validation batches were reviewed. The PV protocol and report for Albendazole micronization were also checked and discussed.

Cleaning validation:
The equipment line was dedicated for the Albendazole production. The SOP for cleaning validation, the cleaning validation protocol and report of Albendazole were reviewed during the inspection.

The periodic cleaning procedure of the equipment used for manufacturing of Albendazole was checked. The procedure defined the conditions and requirements for a complete equipment cleaning to be performed.

Analytical Method Validation
The analytical method validation for EP Grade Albendazole was available as described in the protocol and report. This validation was performed at Mangalore Site. The transfer of the analytical method was discussed.

Computerised Systems:
The company had a SAP system for material management and QC laboratory LIMS with Server and Acronis Cloud Backup procedures. The validation plan presented a full life cycle approach of the systems. The procedure for computerized system validation was reviewed and addresses the validation components to ensure data security, integrity and disaster recovery. There was an annual review for re-validation and systems to be migrate and data secured.

12. Change Control
An approved procedure for change control was established. The change controls for increased batch size of the API production and a CC for the trial conducted to use a recovered material were reviewed and discussed during the inspection.
13. Rejection and re-use of materials
   The company had a procedure for re-use of materials. Albendazole manufacturing involved the
   use of recovered solvents. The specifications set for the recovered solvents to be used in the
   Albendazole production were available.
   Reprocessing and reworking for the API production was allowed as per the company’s procedure.
   The APQR 2020 for Albendazole API reported reprocessed batches.

14. Complaints and recalls
   Procedures were established for complaints, returns, and recalls.

   **Complaints**
   The procedure and record for complaints was reviewed and found acceptable. The complaint
   register was available and the investigation of the reported complaints of Albendazole API were
   checked and discussed.

   **Recalls**
   The procedure for recalls was reviewed and found acceptable. QA was responsible for the recall
   process. Recall class 1, 2, 3, and the triggers for recalls were described. A flow chart directed the
   procedure. The recall register showed no Albendazole recall. The company conducted a mock
   recall periodically for Albendazole.

15. Contract manufacturers (including laboratories)
   A contract laboratory Sequent Research Limited, 120 A&B, Industrial Area, Baikampady, New
   Mangalore – 575 011, India was used for analytical method validation and stability study.

<table>
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<tr>
<th>Part 3</th>
<th>Initial conclusion – Inspection outcome</th>
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</table>
|        | Based on the areas inspected, the people met and the documents reviewed, and considering the 
        | findings of the inspection, including the observations listed in the Inspection Report, **Sequent
        | Scientific Limited** located at **Plot no: B-32, G-2&G-3, MIDC, Mahad, Dist. Raigad -402309, 
        | Maharashtra, India** was considered to be operating at an acceptable level of compliance with WHO
        | GMP Guidelines. |

All the non-compliances observed during the inspection that were listed in the full report as well as
those reflected in the WHOPIR, were addressed by the manufacturer, to a satisfactory level, prior to
the publication of the WHOPIR.

This WHOPIR will remain valid for 3 years, provided that the outcome of any inspection conducted
during this period is positive.
Part 4  List of GMP guidelines referenced in the inspection report

   [untitled (digicollections.net)]

   [https://digicollections.net/medicinedocs/documents/s21467en/s21467en.pdf]

   [https://digicollections.net/medicinedocs/documents/s23457en/s23457en.pdf]

   [9789240020900-eng.pdf (who.int)]

   [https://digicollections.net/medicinedocs/documents/s21440en/s21440en.pdf]

   [https://digicollections.net/medicinedocs/documents/s23455en/s23455en.pdf]
*Short name: WHO TRS No. 937, Annex 4*

*Short name: WHO TRS No. 961, 957), Annex 1*

*Short name: WHO TRS No. 957, Annex 3*

*Short name: WHO TRS No. 961, Annex 6*

*Short name: WHO TRS No. 961, Annex 7*

*Short name: WHO TRS No. 961, Annex 9*

*Short name: WHO TRS No. 943, Annex 3*
https://digicollections.net/medicinedocs/#d/s21438en
Short name: WHO TRS No. 961, Annex 2

Short name: WHO TRS No. 981, Annex 2
https://digicollections.net/medicinedocs/#d/s20177en/

Short name: WHO TRS No. 981, Annex 3
https://digicollections.net/medicinedocs/#d/s20175en/

Short name: WHO TRS No. 961, Annex 14
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1


Essential Medicines and Health Products Information Portal (digicollections.net)


9789240001824-eng.pdf (who.int)