s22
Quality Assurance Manager
GMP Pharmaceuticals Pty Ltd
7 – 9 Amax Avenue
Girraween
NSW 2145

Ref: PH21/7232

Dear s22

RE: GMP INSPECTION of Company GMP Pharmaceuticals Pty Ltd

Please find attached the inspection report for the 7 – 9 Amax Avenue and 14 Amax Avenue, Girraween site and s22 on the 30th May s22 .

Your response(s) to the deficiencies reported in the post inspection letter have been evaluated and have been accepted. Effective implementation will be reviewed at the next GMP inspection.

Should you have any questions regarding the inspection, please do not hesitate to contact me.

Yours sincerely,

(Signed electronically; contains no visible signature)

s22
s22
Manufacturing Quality Branch
Date: 05th March 2024

Tel: s22
E-mail: s22 @health.gov.au

Australian Government

Department of Health

Therapeutic Goods Administration

Manufacturer: GMP Pharmaceuticals Pty Ltd

Inspected site/s: 7 – 9 Amax Avenue, Girraween, NSW 2145

Activities carried out by manufacturer:

- ☑ Manufacture of finished medicinal product
- ☐ Manufacture of intermediate or bulk
- ☑ Packaging
- ☑ Laboratory testing
- ☑ Release for supply
- ☐ Other:

Type of inspection:

- ☐ Initial inspection
- ☑ Re-inspection
- ☑ Full inspection
- ☑ Special inspection

Applicable sections of the *Therapeutic Goods Act 1989*:

- ☐ section 37(2)(b) (licence application)
- ☑ section 40B(10)(a) (licence variation)
- ☑ section 40(4)(b) (re-inspection of licensed site)
- ☐ section 25(1)(g) (overseas in relation to registration)
- ☐ sections 26(1)(g), 26A(3) (overseas in relation to listing)

Scope of Inspection:

MI-2023-03143-1
Primary Site: 7-9 Amax Ave, Girraween, NSW 2145
Full Product Manufacture excluding Microbiological Testing Listed Therapeutic Goods - Powder
Full Product Manufacture excluding Microbiological Testing Listed Therapeutic Goods – Solid Unit Dosage Forms
Full Product Manufacture excluding Microbiological Testing Listed Therapeutic Goods – Liquids Group
Full Product Manufacture excluding Microbiological Testing Listed Therapeutic Goods – Capsule, soft
Full Product Manufacture excluding Microbiological Testing Listed Therapeutic Goods – Tea
Full Product Manufacture excluding Microbiological Testing Listed Therapeutic Goods – Semi Solids

Secondary Site: Unit 15 Long Street, Smithfield, NSW 2145
Storage Listed Therapeutic Goods – All Dosage Forms

Secondary Site: 14 Amax Ave, Girraween, NSW 2145

Secondary packaging Listed Therapeutic Goods – All Dosage Forms
Storage Listed Therapeutic Goods – All Dosage Forms
Release for supply Listed Therapeutic Goods – All Dosage Forms

This licence does not authorise the manufacture of medicinal products in the dosage form 'Spray – pressurised'

MI-2023-LI-13492-1
Primary Site: 14 Amax Ave, Girraween, NSW 2145
Full Product Manufacture excluding Microbiological Testing Listed Therapeutic Goods – Capsule, soft
Full Product Manufacture excluding Microbiological Testing Listed Therapeutic Goods – Liquids Group
Full Product Manufacture excluding Microbiological Testing Listed Therapeutic Goods – Powders Group
Full Product Manufacture excluding Microbiological Testing Listed Therapeutic Goods – All Dosage Forms
Full Product Manufacture excluding Microbiological Testing Listed Therapeutic Goods – Semi Solids

Secondary Site: Unit 7 – 9 Amax Ave, Girraween, NSW 2145
Storage Listed Therapeutic Goods – All Dosage Forms

Secondary Site: Unit 15 Long Street, Smithfield, NSW 2145
Storage Listed Therapeutic Goods – All Dosage Forms

This licence excludes the manufacture of the dosage form 'spray pressurised' contained within the liquids group.

APVMA Licence: 2205

Inspection date/s: 30th May to 02nd June 2023

Inspector/s: s22

Manufacturing Standard used: PIC/S Guide to Good Manufacturing Practice for Medicinal Products – 01 May 2021
(Referred to as GMP code in this report)

References: Certificate number: MI-2023-LI-03143-1 / MI-2023-LI-03144-1
File reference number/s: E21-434863

Introduction

GMP Pharmaceuticals Pty Ltd, known hereafter as GMP Pharma is a contract manufacturer of listed therapeutic goods located in Smithfield NSW. Commencing in 1994, GMP Pharma has undergone multiple site changes due to various expansions and increased business needs to support approximately 500 full time and casual employees working over multiple shifts over 5 or 6 days dependant on contractual requirements.

In total, the buildings occupy over 12,800 square metres over 25,100 square metres of site and are constructed over many years of various differing materials.

Date of previous inspection: 10th to 17th February 2020
Names of inspectors involved in previous inspection: s22

Brief report of the inspection activities undertaken
Scope of inspection
As covered in the previous table.

Inspected areas
General areas covered at the 2 production sites included sampling, dispensing, liquid mixing, powder blending, hard shell encapsulation, primary & secondary packaging, warehousing, laboratories, heating ventilation air conditioning (HVAC), compressed air system and purified water system (PWS) utilities for the site. The secondary site to be added to the licence was inspected for the step of storage. In addition, the quality system and associated records for compliance to the GMP code were reviewed. This inspection also ensured their previous secondary site was no longer in use and not put of the company's operations.

This inspection also included an assessment of their compliance with their current APVMA licence.

This inspection also included an assessment of corrective and preventative actions that were implemented to address the deficiencies identified in the 2020 TGA inspection.

Personnel met during the inspection

Please refer to the Inspection Attendance Sheet.

Inspection findings and observations

Major changes since the previous inspection:
- Removal of the warehouse at Unit 1/29 Amax Avenue, Girraween, NSW 2145
- s22
- Laboratory is only used for In Process Testing
- All testing now contracted to the Huntingwood site
- New automated Liquids line
- Manufacture of Capsule in Capsule.

Future Planned Changes:
- Potential movement of some manufacturing to the Huntingwood site including tablet manufacturing
- Automated and faster equipment
- New bottling capabilities
- Different packing forms.

Action taken since the last inspection
The inspector noted that the company had effectively addressed all of the deficiencies issued at the last TGA inspection.

Quality Management

GMP Pharma had implemented an effective system of quality management that generally met the requirements of the cGMP. Any deficiencies noted at inspection have been recorded in this report.

The company had established regular management review meetings every 3 months to review the quality system and production operations.

GMP Pharma had established a generally appropriate procedure for quality risk management. However, the system did not link to all other relevant company quality management systems (Deficiency #7d).

The company had generally established an appropriate system to manage and investigate planned and unplanned deviations and non-conformances and implement corrective and preventative actions (CAPA). However, the inspector noted some issues (Deficiency #6g) and (Deficiency #6h). When the inspector reviewed some examples of deviations and non-conformances it was found that GMP Pharma had not recorded, documented and trended the deviations and non-conformances to an appropriate depth as well as a number of other issues that required rectification (Deficiency #8).

GMP Pharma had generally implemented an appropriate change control system. However, the inspector noted several issues with the use of electronic documents (Deficiency #2c) and (Deficiency #6h).

The company had established a compliant system for product quality reviews (PQR). The inspector reviewed the 2022 PQR for Bio Island Cod Liver Oil and Fish Oil SG Capsules and found no issues.

GMP Pharma conducted the PQRs on each individual product and did not utilise any groupings. The company had appropriately defined all PQR relevant responsibilities for contract manufactured products in GMP agreements.

GMP Pharma had generally established an appropriate system for release for supply. However, the inspector noted some issues (Deficiency #1b). The Quality Assurance (QA) Manager and delegates were responsible for release. Documented procedures and checklists were utilised to cover the relevant areas, including checking the complete batch documentation package, certification that product was manufactured in compliance with the marketing authorisation and that the product quality review and on-going stability information was available.

Personnel

GMP Pharma had established position descriptions for key personnel and company organisation charts provided clear reporting and authority flows. The inspector confirmed that the heads of production and quality were independent.

The company had established a compliant system for training and assessment of all personnel. The inspector reviewed training procedures, plans and records and found no issues.

GMP Pharma had implemented appropriate arrangements for personal hygiene practices, including clothing of personnel and visitors in the controlled manufacturing areas.

The company had implemented appropriate systems to ensure that staff with infectious diseases, or other relevant health issues could not adversely affect product quality. Medical examinations were conducted upon recruitment.

Premises and Equipment

The design for personnel and material flows were generally appropriate for the activities undertaken on site. The inspector found many areas of the site were not clean and tidy at the time of the inspection (Deficiency #3).

The warehouse had separate locations for goods receipt, staging, sampling, quarantine, storage, rejected goods and returned goods. However, the inspector noted some issues (Deficiency #3b). The warehouse was not air-conditioned, however was temperature mapped. The temperature was monitored and recorded manually daily to ensure storage conditions were maintained at ≤ 30^0C.

Although status was controlled electronically in the GMP Pharma Pronto inventory management system, the company manually controlled status via physical location and status control labels. However, the inspector noted multiple issues with labelling of stock (Deficiency #9) and segregation of stock (Deficiency #3biv) & (Deficiency #3bv). The reject area was locked and the electronic status systems added extra security and would not allow picking or use of rejected materials or goods.

The second site warehouse had a large warehouse area that provided adequate storage space for materials in racking. However, the inspector noted some issues with the facility (Deficiency #3bviii), the materials stored within (Deficiency #1a) and movement of stock between sites (Deficiency #6f).

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The main site contained a sampling room, located in the warehouse. The sampling room was generally appropriate. However, the inspector noted some issues (Deficiency #3aiv). The HVAC system for the sampling room was appropriate.

The company maintained appropriate usage and cleaning records for the sampling area. The company ensured that sampling tools were used, cleaned and stored appropriately.

The dispensing areas were appropriately designed for the weighing activities undertaken. Staff maintained appropriate records to demonstrate an area clearance and clean after dispensing activities were completed.

The company had a dedicated gowning, hygiene and jewellery procedure that suitably covered all production areas and ensured protection of the production processes and personnel.

The site production area was constructed over 2 floors, across 2 sites. Manufacturing rooms were located off main manufacturing corridors. The site contained manufacturing areas for: aqueous and non-aqueous liquid mixing, powder blending, wet and dry granulation, hard shell encapsulation, tablet compression, tablet coating, gel cooking, soft capsule encapsulation, soft capsule drying and sorting and primary & secondary packaging.

Production equipment was generally located in self-contained rooms dedicated to the specified activity. The manufacturing areas were generally designed for both concurrent manufacture of multiple product batches and campaign

manufacture for longer runs as required. However, the inspector noted some issues (Deficiency #10a).

The company manufactured powders in an “Intermediate Bulk Container” (IBC) mixing system. The IBC system was an enclosed system that mixed and transferred the blended powders to the filling lines.

The packaging areas were contained in a number of different rooms and included a primary packaging area and secondary packaging room. There was quite a bit of segregation of manufacturing areas due to the design of the facility and the company’s ability to utilise the space available.

The company had installed a similar default setup on the packaging lines which included the following units where relevant: bottle inverter/blower, gel inserter, filling head/unit counter, check weigher, induction sealer, capper, labeller, batch and expiry print coder with 100% manual checking performed and a metal detector.

Pre-printed packaging was generally appropriately controlled on site. Labels were stored in a secure label room. However, the inspector noted some issues with the label counter (Deficiency #11).

The company had generally appropriately maintained the facility to a reasonable standard. However, the inspector noted some issues (Deficiency #3).

The company did not manufacture any highly toxic or high pharmacological activity materials.

The company had generally established compliant maintenance and calibration systems. However, the inspector noted multiple issues that required to be addressed (Deficiency #3), (Deficiency #6k) and (Deficiency #6l).

The HVAC systems supplied controlled air to each of the different areas in the multiple facilities. GMP Pharma ensured that air quality in all areas where products, starting materials and product contact surfaces were exposed to the environment were appropriately controlled. The HVAC system was described in the site master file (SMF).

The basic HVAC philosophy was configured to prevent external infiltration of uncontrolled air, dedicated containment where required and to ensure that air flowed from clean to less clean environments. Generally the manufacturing rooms were maintained at a 5Pa pressure differential to manufacturing corridors for containment and a higher pressure differential of 10-15Pa was required between controlled clean areas to the external uncontrolled environment.

The site contained a reverse osmosis PWS. Details of the system were described in the SMF.

The systems were established systems installed at the manufacturing site, The system was sanitised at defined intervals and appropriate records of these activities were maintained.

GMP Pharma sampled appropriate volumes of purified water taken from several points of use in the ring main. The company had defined appropriate alert and action limits to comply with BP specifications. The company had appropriate records to demonstrate that the system was calibrated and maintained to provide purified water to the BP standard.

he site contained 2 compressed air units. Both Atlas Copco screw compressors were utilised based on operational loading as required. The company ensured

the systems were externally serviced and maintained. The inspector found them compliant with no issues identified.

GMP Pharma received nitrogen in as bulk currently from Air Liquide. The company ensures the gas is suitable following a check of the certificate of analysis for compliance.

GMP Pharma had implemented an appropriate system for pest control at both sites. The system included documented procedures, approved chemicals, device location maps, control devices for rodents and crawling insects, and relevant records of activities undertaken. A contract pest control company was utilised to visit the sites monthly or more frequently as required.

The company had implemented an appropriate process for secure waste disposal that ensured products and printed packaging were unusable and unrecoverable.

Documentation

GMP Pharma had implemented a manual system for document control. The system allowed employees to view company documents as controlled hard copies were issued to relevant areas. The company required SOPs to be reviewed at least every 3 years to ensure that they remain current. The inspector reviewed a selection of various SOPs during the inspection. These documents were not appropriately detailed and the company had not maintained them to reflect current practice (Deficiency #6).

The company had implemented a generally appropriate system for the back-up of electronic data. However, the inspector noted multiple issues that required rectification (Deficiency #2a), (Deficiency #4), (Deficiency #6b) and (Deficiency #8e).

GMP Pharma had established appropriate specifications for raw materials, packaging and finished products.

The company had prepared, checked and authorised compliant master batch records. Master batch records were generated in word and saved as electronic files. The batch document was printed out with the batch number placed in the document electronically prior to printing. The batch number was generated as a consecutive number from Pronto after the generation of the Work Order by the Planning Officer. However, the inspector identified some issues with the associated instructions (Deficiency #6d).

The records allowed for good product traceability for the history of each batch of product produced. However, the inspector found some issues when the selected batch records were reviewed (Deficiency #1b).

GMP Pharma had implemented a policy to ensure that GMP relevant records were stored securely for specified periods meeting or exceeding minimum cGMP requirements.

Production

The inspector reviewed production and packaging processes and procedures relating to the manufacture of all therapeutic products covered under the company licence/certification. GMP Pharma maintained generally appropriate in-process controls and records for the products manufactured. However, the inspector noted some issues (Deficiency #10c) and (Deficiency #12). The company had generally established detailed instructions for the operation and cleaning of critical production equipment and had maintained usage/cleaning records for major pieces of production equipment. However, the inspector noted some issues (Deficiency #10b).

The company had established a compliant supplier qualification and control system. The starting material vendors were assessed and qualified for each material supplied, according to GMP Pharma procedure. The process could include reviewing vendor information through vendor questionnaires or on-site GMP inspections and full testing of the first three samples of materials for checking of compliance to company specifications and trial batches as required. For vendors who had a vendor assurance questionnaire returned and reviewed (or an on-site inspection had been conducted) reduced sampling and testing was appropriately allowed for the qualified vendors. The reduced testing system allowed for rotational testing of non-critical tests. The inspector reviewed several examples of the supplier qualification reports and found no issues.

The inspector found that starting materials were generally appropriately controlled.

Company staff checked receipt information against order information and packaging integrity, cleanliness, the standard name and that the materials were received from an approved supplier with a relevant certificate of analysis.

The materials were logged into the Goods Inwards Number (GIN) logbook for all log-in details as well as being receipted into the company inventory management system – Pronto for management of stock movement and status control.

Sampling staff performed sampling activities in accordance with the company documented procedures. The inspector reviewed the sampling plans and found them acceptable.

However, the inspector noted some issues with status control (Deficiency #6e) and (Deficiency #9).

GMP Pharma had established appropriate controls over the receipt of pre-printed labels to ensure version and identity.

GMP Pharma had installed appropriate wash bays, drying rooms and clean equipment store rooms. The company had documented cleaning and sanitation instructions and records were available to demonstrate compliance. GMP Pharma had documented different types of cleans including: housekeeping clean, major clean between different product formulations, minor clean and follow on for same products. The company had appropriately defined the definitions for each type of clean in the relevant cleaning procedures. However, the inspector noted some issues (Deficiency #10a). Cleaning status labels were generally in use and accurately reflected the state of the equipment at the time of inspection. However, the inspector noted some issues (Deficiency #13).

GMP Pharma had implemented an appropriate environmental monitoring program. Air quality in the controlled production areas was monitored, for viable particulates with a high volume air sampler, settle plates and contact plates.

The company had documented appropriate action and alert limits for the various areas monitored. GMP Pharma conducted appropriate trending of data and the inspector confirmed that all records reviewed demonstrated that monitored areas were controlled. When GMP Pharma staff detected excursions, they raised appropriate non-conformance and or CAPA as required.

The company appropriately managed rejected materials. Although materials were appropriately controlled with electronic status, the company also labelled rejected materials as such and placed them into a physical reject location.

The company had generally implemented an appropriate system to manage rework and reprocessing of goods. GMP Pharma staff ensured that generally appropriate considerations were given to the potential impact on product quality

including additional testing and stability studies when required. However, the inspector noted some issues (Deficiency #7).

GMP Pharma had established a documented procedure to manage the return of goods.

The company had documented site validation requirements in the validation master plan (VMP). The inspector reviewed this document and found that it had appropriately covered all relevant areas for the site. GMP Pharma maintained appropriate logs and schedules to manage current requalification and new validation project activities.

GMP Pharma had appropriately documented equipment / facility qualification requirements in several company SOPs.

The next inspector should review examples of equipment / facility qualification to determine effectiveness.

GMP Pharma had undertaken process validation for the various processes used for manufacturing activities on site. The company utilised product grouping with worst case products selected to represent the relevant groups. Groups were established based on the dosage form, the product formulation and the worst case within the group.

The inspector reviewed the process validation documentation for the tablet manufacturing of One a Day OAD Tablets conducted in 2022. However, the inspector noted multiple issues (Deficiency #5).

GMP Pharma had undertaken cleaning validation for the various equipment trains and representative products selected as worst case examples for cleaning. The company criteria used to identify the worst case within the dosage form and formulation included the toxicity, dosage, micro contamination potential, allergen, solubility, cleaning agent residue and the most difficult to clean. The company chose visual acceptance cleaning criteria along with micro bioburden, cleaning agent residues, allergen residues and previous product residues in the cleaning validation reports, to represent the worst case

The inspector reviewed the cleaning validation documentation for the Filling and Plugging Machine conducted in 2022 and found no issues.

The company had generally established a computer validation master plan to ensure that all relevant computer systems used for GMP activities would be validated and a risk assessment on validation for computer based systems. However, when the inspector reviewed these documents, several issues were found (Deficiency #6). The inspector also noted that multiple computer validations were yet to be conducted (Deficiency #2).

Quality Control

The site only contained an analytical testing laboratory for In Process testing of production operations, all other testing was contracted out. However, the inspector noted some issues (Deficiency #1c).

The company supplied records to demonstrate that all laboratory equipment reviewed by the inspector was appropriately calibrated, qualified and maintained. The inspector found no issues.

The company ensured that there was a sufficient number of appropriately qualified and trained staff to undertake all necessary testing functions.

GMP Pharma ensured that there was a suitable QA samples retention room that ensured materials were stored in an appropriate format, conditions and effectively traceable.

	The company had established an appropriate system for managing and investigating out of specification (OOS) / out of trend (OOT) events in the laboratory. However, the inspector noted some issues (Deficiency #8b). The company had established an appropriate on-going stability programme for finished products using a documented grouping strategy that followed ICH guidelines.
Contract Manufacture and Analysis	The company had generally established appropriate some GMP agreements with contract manufacturers and some contract testing laboratories. However, the inspector noted some issues (Deficiency #4).
Complaints and Product Recall	The company had established an appropriate system for receipt, recording, investigation and analysis of customer complaints. Customer Service staff were trained and responsible for receiving customer complaints and forwarding them to the correct relevant departments. All quality complaints were logged into the complaints register. The inspector reviewed the customer complaints and chose several examples of complaints for a detailed assessment of the system and found no issues. The inspector reviewed the system for product recalls and found it to be generally compliant. Although a mock recall was conducted every annually, the inspector noted some issues (Deficiency #6o).
Self-Inspection	The company had a compliant system for self-inspection.
Compliance with Marketing Authorisations	GMP Pharma had generally established an appropriate system to ensure that market authorisation aspects for products were covered. However, the inspector noted some issues (Deficiency #1b).
Specific Annexes	The Annexes of the Standard applicable to the inspection were Annexes 8, 9, 11, 15 and 19.

Other specific issues identified
None

Site Master File
The company provided a copy of their SMF No. 07 – 09 version 019 dated 10 May 2023, which appropriately covered the company activities undertaken.

Miscellaneous

Samples taken:
None

Distribution of Report:
Company and TGA files E21-434863

Attachments:

None

List of Deficiencies observed during the inspection

Critical deficiencies:
None observed

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[redacted]

Comments

Any comments made to the company, in reference to their response to correct deficiencies raised at the inspection, during the closeout process can be found in the close out record.

Summary and conclusions

Assessment of manufacturer's responses

A response to the deficiencies reported to the manufacturer was received on 06th / Oct / 2023. Following requests for further information, a final satisfactory response was received on 14th / Feb / 2024.

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.

Final evaluation and recommendations:

1. The manufacturer operates in accordance with the relevant GMP requirements.

2. As discussed during the inspection and throughout the close out process, the following steps in manufacture, known as authorisations under section 40A of the *Therapeutic Goods Act 1989*, have been submitted to the delegate for approval: *Removal of Unit 1/29 Amax Avenue. Inclusion* s22 [redacted] If approved, the Licence will be issued with these amendments.

3. TGA records have been updated to show a final compliance rating of your facility of A2: satisfactory compliance with the manufacturing standard established under the *Therapeutic Goods Act 1989*.

4. The next re inspection is expected to be performed within 30 months.

5. The duration of the next inspection is estimated at this time to be 4 days.

(Signed electronically; contains no visible signature)

s22 [redacted]
s22 [redacted]
Manufacturing Quality Branch
Date: 05th March 2024

Tel: s22 [redacted]
E-mail: s22 [redacted]@health.gov.au

DEFINITIONS

Marketing Authorisation

Compliance with regulatory requirements specified on the ARTG and any other requirements imposed by a relevant Delegate of Secretary upon product listing or registration.

Examples of regulatory requirements include but not limited to the following: compliance with registered formulations, special storage and transportation conditions, shelf life, labelling, batch release testing requirements etc.

Critical Deficiency

A deficiency in a practice or process that has produced, or may result in, a significant risk of producing a product that is harmful to the user. Also occurs when it is observed that the manufacturer has engaged in fraud, misrepresentation or falsification of products or data.

Major Deficiency

A non-critical deficiency that:

- has produced or may produce a product which does not comply with its marketing authorisation; and/or
- indicates a major deviation from the Good Manufacturing Practice; and/or
- indicates a major deviation from the terms of the manufacturing licence or GMP approval (overseas manufacturers); and/or
- indicates a failure to carry out satisfactory procedures for release of batches; and/or
- indicates a failure of the person responsible for QA/QC to fulfil his/her duties; and/or
- consists of several other deficiencies, none of which on its own may be major, but which may together represent a major deficiency and should be explained and reported as such.

Other Deficiency

A deficiency that cannot be classified as either critical or major, but indicates a departure from good manufacturing practice.

A deficiency may be "other" either because it is judged as minor, or because there is insufficient information to classify it as major or critical.

One-off minor lapses or less significant issues are usually not formally reported, but are brought to the attention of the manufacturer.

Note:

1. Classification of a deficiency is based on the assessed risk level and may vary depending on the nature of products manufactured, e.g. in some circumstances an example of major deficiency may be categorised as critical.
2. A deficiency that was reported at a previous inspection and not corrected may be reported in a higher classification.

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Australian Government
Department of Health
Therapeutic Goods Administration

Manufacturing Quality Branch

Inspection attendance sheet

Manufacturer name:	GMP Pharmaceuticals Pty Ltd
Manufacturer address:	7 – 9 Amax Avenue, Girraween, NSW 2145
Inspection type:	Re-inspection / Special inspection
Inspection date/s:	30th May to 02nd June 2023
Inspector/s	Lead Inspector s22
Inspection standard:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products - 01 May 2021

Opening meeting starting time: 30 MAY 2023 09:02
Closing meeting starting time: 02 JUN 2023 16:20

Name (please print)	Position (please print)	Opening meeting (initials)	Closing meeting (initials)
s22			

Australian Government
Department of Health
Therapeutic Goods Administration

s22
s22
GMP Pharmaceuticals Pty Limited
14 Amax Avenue
Girraween NSW 2145

Dear s22

RE: GMP Inspection of GMP Pharmaceuticals Pty Ltd

Please find attached the inspection report for the inspection that took place at GMP Pharmaceuticals Pty Ltd Girraween sites on 10 – 17 February 2020.

Your responses to the deficiencies reported in the post inspection letter have been evaluated and have been accepted.

Should you have any questions regarding the inspection, please do not hesitate to contact me.

Yours sincerely

Signed and authorised by

s22
s22
Manufacturing Quality Branch
Date: 14th August 2020

Tel: s22
Mobile: s22
E-mail: s22 @health.gov.au

Australian Government
Department of Health
Therapeutic Goods Administration

Manufacturer:	GMP Pharmaceuticals Pty Ltd
Inspected sites:	• s22 • 7-9 Amax Ave, Girraween NSW • s22
Activities carried out by manufacturer:	☑ Manufacture of finished medicinal product ☐ Manufacture of intermediate or bulk ☐ Packaging ☐ Laboratory testing ☐ Release for supply ☐ Other:
Type of inspection:	☐ Initial inspection ☑ Re-inspection ☑ Full inspection ☐ Special inspection ☐ Reduced scope inspection Applicable sections of the *Therapeutic Goods Act 1989*: ☐ section 37(2)(b) (licence application) ☑ section 40B(10)(a) (licence variation) ☑ section 40(4)(b) (re-inspection of licensed site) ☐ section 25(1)(g) (overseas in relation to registration) ☐ sections 26(1)(g), 26A(3) (overseas in relation to listing)
Scope of Inspection	s22 **7-9 Amax Ave, Girraween NSW** - Full product manufacture, excluding microbiological testing, of listed medicines in the dosage forms of powder, liquids, soft capsules, tea, and all solid unit dosage forms. Chemical & physical testing of listed medicines in the dosage form of semi-solids. s22

PO Box 100 Woden ACT 2606 ABN 40 939 406 804
Phone: 02 6232 8444 Fax: 02 6232 8605 Email: info@tga.gov.au www.tga.gov.au

TGA Health Safety Regulation

Inspection date/s:	10 – 17 February 2020
Inspector:	s22
Manufacturing Standard used:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products (PE009-13)
References:	**Manufacturing Licence numbers**: MI-21042005-LI-000516-1 & MI-2016-LI-12063-1 **Inspection Tracking Numbers:** MI-2019-LI-08036-1 & MI-2019-LI-07840-1 **Licence variation numbers:** MI-2019-LI-04776-1 **File reference number/s:** PH19/54570 (inspection files), 2014/012527 & E17-10432 (licence files)

Introduction

GMP Pharmaceuticals Pty Ltd, hereafter referred to as GMP Pharmaceuticals, is a contract manufacturer of listed therapeutic goods in multiple solid, semi-solid and liquid dosage forms. The majority of production at the Girraween facilities is soft gel capsules (approximately 30 products).

The manufacturer holds two licences for sites in Girraween NSW for 7-9 Amax Ave and 14 Amax Ave. The existing licences also include secondary storage sites at s22 The head count across all Girraween sites of 363.

The Girraween facilities of GMP Pharmaceuticals also undertake manufacture of cosmetic, food and nutritional products. The sites hold a licence from NSW Food Authority, and organic certification from National Association for Sustainable Agriculture Australia (NASSAA).

Date of previous inspection: 20 August 2018 & 10-14 September 2018

Names of inspector involved in previous inspection: s22

Brief report of the inspection activities undertaken

Scope of inspection

The inspection was conducted to review compliance to the PIC/S GMP Guide for activities encompassed by licences MI-21042005-LI-000516-1 and MI-2016-LI-12063-1 for operations at GMP Pharmaceuticals Pty Limited's Girraween sites as per the manufacturing authorisations:

s22

7-9 Amax Ave, Girraween NSW - Full product manufacture, excluding microbiological testing, of listed medicines in the dosage forms of powder, liquids, soft capsules, tea, and all solid unit dosage forms. Chemical & physical testing of listed medicines in the dosage form of semi-solids.

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Licence variation MI-2019-LI-04776-1 was also included in the scope of this inspection for addition of the following steps in manufacture to licence MI-2016-LI-12063-1 at 14 Amax Ave, Girraween: Full product manufacture, excluding testing, of listed medicines in the dosage forms of liquids group, powders group & semi-solids.

Neither licence authorises the manufacture of preparations containing any drug to which any Schedule of the Poisons Standard applies, and the licences do not authorise the manufacture of medicinal products in the dosage form 'spray, pressurised'.

The manufacture of cosmetic, food and nutritional products were excluded from the scope of this inspection.

Inspected areas

The inspection reviewed all activities and areas related to the scope of the inspection for compliance to the PIC/S Guide to GMP for Medicinal Products (PE009-13).

Personnel met during the inspection

Refer to attached inspection attendance sheet.

Inspection findings and observations

Major changes since the previous inspection:

- A new site manager has been engaged necessitating a change to the licence nominee for production for both medicinal product licences i.e. change of licence nominee for production to Rocky Lu.

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- Refurbishment of rooms in the dry powder manufacturing area of Unit 9 to undertake capsule-in-capsule manufacture for probotic products (refurbishment on-going at time of inspection).

Future Planned Changes:

- Transfer of semi-solid manufacture from 7-9 Amax Ave to s22 (included in scope of this inspection).

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Action taken since the last inspection: Corrective actions for deficiencies identified at the previous inspection had been implemented as per the inspection close-out correspondence.

Quality Management

GMP Pharmaceuticals had an established and effective pharmaceutical quality system (PQS) in place. This PQS was in use across all GMP Pharmaceuticals' Girraween sites.

GMP Pharmaceuticals undertook quality management reviews on a quarterly basis. These reviews were undertaken with the involvement of senior management and included the key elements of operations across the sites. The inspector reviewed meeting minutes for a recent Quality Management Review meeting and noted it fulfilled cGMP requirements.

GMP Pharmaceuticals had integrated quality risk management into procedures including those associated with deviations, non-conformances, change control and complaints. Site personnel routinely conducted product impact evaluations and root cause analysis demonstrating a systematic process for assessment, control, communication and review of risks. The risk to product quality was adequately controlled and appropriate for the products manufactured at the site.

Procedures were available for the management of deviations and non-conformances. The inspector reviewed the procedures and several non-conforming product, and deviation, investigations. Multiple issues were identified (deficiency 1).

A process was available to control the implementation of corrective and preventative actions (CAPA) arising from quality related incidents. The CAPA process was used extensively by GMP Pharmaceuticals staff; however, some quality incidents were not appropriately addressed (deficiency 1b & 1c).

A procedure for the management of proposed changes was available. The procedure addressed most cGMP requirements; however, not all changes were captured by the procedure (deficiency 2). The inspector reviewed the documentation associated with recent facility and product changes and found it acceptable.

A procedure for the preparation of product quality reviews (PQRs) was available. The procedure encompassed all cGMP requirements. The inspector reviewed the program and recent reviews and identified an issue (deficiency 4).

There was an appropriate system in place for the release for supply of finished products. Release for supply activities were restricted to specified QA personnel and conducted according to a detailed procedure and checklist.

Systems were in place to ensure that products released from the site were in

accordance with the relevant marketing authorisations.

Personnel

Organisation charts provided clear reporting and authority flows with the heads of production and quality independent of each other. Key personnel were suitably experienced and effective in their roles with written job descriptions available for each position.

A training program was available that included induction and GMP training, and job related development, based on individual staff training plans. GMP refresher training was routinely implemented. The effectiveness of training activities was evaluated by oral, written or task based evaluations and individual records were kept for all employees. The inspector noted that there was no formalised process to recognise and evaluate the prior learning of new staff (deficiency 5).

The manufacturer had implemented appropriate arrangements for personal hygiene practices, including clothing of personnel and visitors in the controlled manufacturing areas. The types of gowning requirements were acceptable for the therapeutic products manufactured at the sites including hair nets, dedicated uniforms for staff, over garments for visitors, and dedicated factory shoes or shoe covers. Adequate hand washing and sanitising facilities were provided.

All employees were subjected to a pre-employment medical evaluation.

Premises and Equipment

The four GMP Pharmaceuticals sites, which are the subject of this inspection, are sited along Amax Ave, in the Sydney suburb of Girraween.

7-9 Amax Ave

7-9 Amax Ave consisted of multiple structures that had been renovated over time to become a single interconnected building, which occupied approximately 900 m^2 of a 1500 m^2 site.

Rooms of the building sited at 7 Amax Ave were dedicated to individual processes associated with dosage form manufacture of soft gel capsules, tablets and powders. Some food products were also manufactured in these areas using common equipment.

s22 [redacted]

7-9 Amax Ave also housed a QC laboratory.

s22 [redacted]

Multiple manufacturing activities were undertaken in s22 [redacted]
These occurred in dedicated clean rooms used for the following:

- Sampling for all starting materials used in medicinal product manufactured at 7-9, and s22 [redacted] (undergoing final fit-out at time of inspection)
- Dosage form manufacture of soft gel capsules
- Dosage form manufacture of liquids and semi-solids
- Finished product manufacture of powders, packaged into sachets

s22 [redacted]

Warehousing facilities across the Girraween sites were adequate for the receipt and storage of raw materials, packaging components and finished products. Materials were appropriately stored with designated quarantine and approved storage areas available. Documented procedures were available detailing receipt and storage operations and the warehouses were of a suitable size with locked, rejected goods areas and secure storage of printed packaging components.

The system for monitoring and recording temperatures in all storage areas was generally acceptable; however, some issues were identified with cool temperature storage areas (deficiency 1d).

Staff conducted sampling of raw materials within sampling rooms situated in the warehouse. The sampling rooms were of acceptable construction with a separate, filtered air supply. Procedures and records were available for review that documented appropriate cleaning arrangements for the sampling rooms.

The dispensing areas were appropriately designed for the weighing activities undertaken. Dispensing was conducted in dedicated rooms within the various manufacturing clean rooms. Staff maintained appropriate records to demonstrate an area clearance and clean after each dispensing activity was completed.

All manufacturing areas were suitably designed and constructed with sealed floors, smooth walls and ceilings, and covered lights. All were supplied with suitably filtered, temperature controlled air and were contained with pressure differentials and air locks.

Inspected rooms contained appropriate status labelling and usage/cleaning logs.

The design and construction of all production and packaging equipment reviewed was suitable with inert product contact surfaces and appropriate capacities for the manufacturing processes undertaken on site.

The inspector noted that the production areas of 7-9 Amax Ave had no equipment or defined area for the manufacture of semi-solids. s22 [redacted]

Personnel and material flows were appropriate. Staff maintained acceptable housekeeping practises and the inspector found the site to be clean and tidy at the time of the inspection.

GMP Pharmaceuticals had a program and associated schedule in place for the calibration of equipment. The inspector's review of calibration activities indicated

procedures and records were available and activities were conducted within appropriate timeframes, to an acceptable standard.

A procedure was available that addressed the general principles associated with equipment maintenance; however, procedures and records of activities were unavailable for some preventative maintenance tasks (deficiency 7d).

Multiple HVAC systems supplied controlled air to the clean room areas across the two manufacturing sites. The HVAC systems were designed to prevent airborne cross contamination between process rooms by creating positive pressure differentials as required.

The HVAC systems had been qualified to demonstrate compliance to Grade D air quality for non-viable particles. s22 The inspector also reviewed re-qualification data for existing HVAC systems and identified some issues (deficiency 1b).

Three reverse osmosis water systems were available to supply purified water to the soft gel capsule manufacturing areas s22 and 9 Amax Ave, s22 Qualification, maintenance activities and sanitation processes were well documented and acceptable. The inspector's review of qualification and on-going monitoring results identified some issues (deficiency 1c).

Compressed air systems were in place to supply air to manufacturing suites. The inspector's review of new and established compressed air systems across both sites demonstrated the supplied air was suitably filtered, and the systems were appropriately qualified and maintained.

There was a suitable pest control program in place and there was no evidence of pest infestation in any area of the facility.

Waste materials were disposed from the site in an appropriate and controlled manner.

Documentation

GMP Pharmaceuticals appropriately administered the generation, approval, issue and control of GMP related documents. Review periods were defined and acceptable. Documentation was available as hard copy. Some mandatory GMP documents were not available (deficiency 7).

There were appropriate specifications in place for all raw materials, packaging materials, semi-finished goods and finished products.

Master batch records (MBRs) were generated, issued and controlled by QA. Hard copy production/packaging batch documents were appropriately prepared from the MBRs. These were reviewed prior to issue to production.

Batch records were sufficiently detailed to allow full traceability of materials and provide an accurate account of the production activities performed. The inspector reviewed examples of batch records in use at the time of inspection, and fully completed batch records, and found that the records were of a high standard.

Computerised systems

GMP Pharmaceuticals utilised several GMP critical computer systems. These included laboratory data acquisition systems, electronic document storage, spreadsheets, and PLC controllers for production equipment.

An ERP system, *Pronto*, was available that assisted in purchasing, recorded quantities, and tracked the status of materials across the sites; however, the ERP had not been validated and GMP Pharmaceuticals supported the system with manual records, thus reducing the GMP criticality of the ERP to a suitable level.

GMP Pharmaceuticals had implemented data management and validation

requirements for computerised systems; however, some issues were identified (deficiency 3).

Equipment based PLC units had been appropriately qualified in association with individual equipment qualifications.

Production

The inspector reviewed production processes and procedures relating to the manufacture of dosage forms encompassed by GMP Pharmaceuticals existing Girraween site licences, and the licence variation, as outlined in the scope of this inspection. Packaging activities reviewed were bottle packing of liquids and solid unit doses, sachet packing of powders and tube filling of semi-solids.

GMP Pharmaceuticals had a system in place for the assessment of suppliers of raw materials. This system included an evaluation of the manufacturer via a questionnaire and/or testing of samples initially supplied. Overall, the supplier evaluation system was well managed; however, it did not support the current regime of reduced sampling and testing (deficiency 6).

Production and packaging processes and procedures were generally well managed and under appropriate control. In-process controls and records were appropriate for the products manufactured and packaged.

Production and packaging equipment was generally located in self-contained rooms dedicated to the specified activity. The manufacturing areas were designed for both concurrent manufacture of multiple product batches and campaign manufacture for longer runs as required. Individual batches of product were adequately separated at each stage of production.

GMP Pharmaceuticals had established detailed instructions for the operation and cleaning of most manufacturing equipment. Usage and cleaning records were maintained for all production equipment. Cleaning status labels were in use and accurately reflected the state of the equipment at the time of inspection.

Segregated wash bays were available in each clean room suite/area.

s22 [redacted]

An environmental monitoring program was in place. Testing was conducted on a risk based schedule using settle plates and surface swabs. Records were available to demonstrate that the monitored areas were under good control.

Rejected goods were adequately controlled on-site.

GMP Pharmaceuticals conducted rework of bulk products under the planned deviation processes discussed previously. All rework activities required detailed rework instructions to be developed, which required approval by QA after risks had been formally assessed and documented. The inspector reviewed some recent rework activities and found them acceptable.

GMP Pharmaceuticals had an established procedure to manage the return of goods. The procedure required the assessment of appropriate information relating to the traceability and control of the goods for storage and transport conditions to ensure that any goods considered for resale met the required safety, efficacy and quality criteria.

A Validation Master Plan (VMP) was available, which addressed all of the requirements of the manufacturing standard including requalification requirements. s22 [redacted]

s22

The inspector reviewed the equipment qualification associated with a liquid filling and capping machine associated with the licence variation. Design, installation and operational qualification had been completed and were acceptable. Performance qualification on a single batch of food product had been conducted.

Process validation (PV) studies were conducted on a grouped product basis using worst case product. The inspector's review of PV activities for soft gel manufacture demonstrated this activity was adequately controlled and documented. The studies included a review of critical quality attributes and used representative sampling across the validation batches. The VMP identified several PV studies that were still to be conducted.

GMP Pharmaceuticals had established a cleaning validation plan that included consideration of allergens, difficulty to clean, product colourants and solubility, and microbial load. The inspector reviewed a cleaning validation report to support the 10 batch campaign length for soft gel encapsulation of a milk calcium product. The study was run across 10 consecutive days. The report did not indicate how many batches were produced in this period and therefore does not support the acceptability across 10 batches. This was discussed with staff.

Quality Control

GMP Pharmaceuticals had a Quality Control laboratory at 7-9 Amax Ave. The laboratory was adequately equipped with analytical instrumentation to conduct the required chemical and physical testing of materials and products. The laboratory consisted of several testing areas including a physical testing room, wet chemistry room, and two rooms for instrumentation.

The arrangements for receipt, registration, storage and retention of samples were acceptable. The manufacturer retained samples under appropriate storage conditions and these could be retrieved as necessary.

Records were available to demonstrate that laboratory equipment was appropriately qualified, calibrated and maintained.

Laboratory staff were suitably qualified and trained to undertake all necessary testing functions.

Specifications and test methods were available for starting materials, in process materials and finished products.

There was a procedure in place for the investigation of out of specification (OOS) results that included a laboratory investigation and extended to uncover root cause analysis. The inspector's review of non-conforming product investigations indicated OOS results were appropriately managed.

Analytical method validation not reviewed at this inspection.

GMP Pharmaceuticals' arrangements for on-going stability testing were summarised in a procedure. ICH storage conditions and stability indicating test methods were prescribed. The inspector's review of the stability program identified some issues (deficiency 9).

The laboratory demonstrated good control of laboratory reagents, volumetric solutions and chemical reference materials. All were prepared, stored and/or used according to written procedures. However, the electronic reference standard spectra in the FTIR spectral library were not appropriately controlled (deficiency 8).

The inspector reviewed testing records and results for a selection of starting materials, excipients, packaging material and finished products. Testing activities were conducted in accordance with the documented methods, were appropriately recorded and raw data retained. Some issues were identified concerning the

	review of electronic data (deficiency 3c).
Outsourced Activities	GMP agreements were in place between GMP Pharmaceuticals and their clients. Agreements were reviewed annually as part of the PQR process. The inspector reviewed the agreement between GMP Pharmaceuticals and JBX Pty Ltd, which addressed all cGMP responsibilities and assigned them to acceptable parties. Technical agreements were also in place with contractors responsible for maintenance and calibration of equipment and utilities.
Complaints and Product Recall	GMP Pharmaceuticals had an established procedure for receiving, recording, investigating and completing client complaints. The procedure included an evaluation of risk to other batches of product and where necessary, corrective actions were made using the CAPA system. The inspector reviewed several complaint investigations and found they had been adequately investigated and documented; however, these were not documented in accordance with the current procedure (deficiency 7c). GMP Pharmaceuticals had a recall procedure in place that appropriately identified responsible personnel and requirements for investigation and product reconciliation. The inspector reviewed documentation from a recent mock recall activity and found it acceptable.
Self Inspection	GMP Pharmaceuticals had a documented system for self-inspection. Inspections were conducted by on-site staff throughout the year in accordance with a comprehensive schedule. Records of self-inspections were available but not reviewed as part of this inspection.
Compliance with Marketing Authorisations	The inspector undertook a comprehensive review of several formulations manufactured by GMP Pharmaceuticals and determined they complied with most market authorisation requirements. On-going stability data was not available for all products reviewed (deficiency 9).
Specific Annexes	The Annexes of the Standard applicable to the inspection were Annexes 7, 8, 9, 11, 15 and 19.

s22 [redacted]

- Appointment of a new Quality nominee for both Girraween sites: s22

Site Master File

Site Master Files for the two sites were supplied for review.

- s22
- Site 7-9 version 14, dated January 2020

The documents covered all necessary aspects of the sites and were acceptable.

Miscellaneous

Samples taken: None

Distribution of Report: GMP Pharmaceuticals Pty Ltd, TGA electronic file no. PH19/54570

Attachments: Inspection Attendance Sheet

List of Deficiencies observed during the inspection

Critical deficiencies:

None observed.

s47G

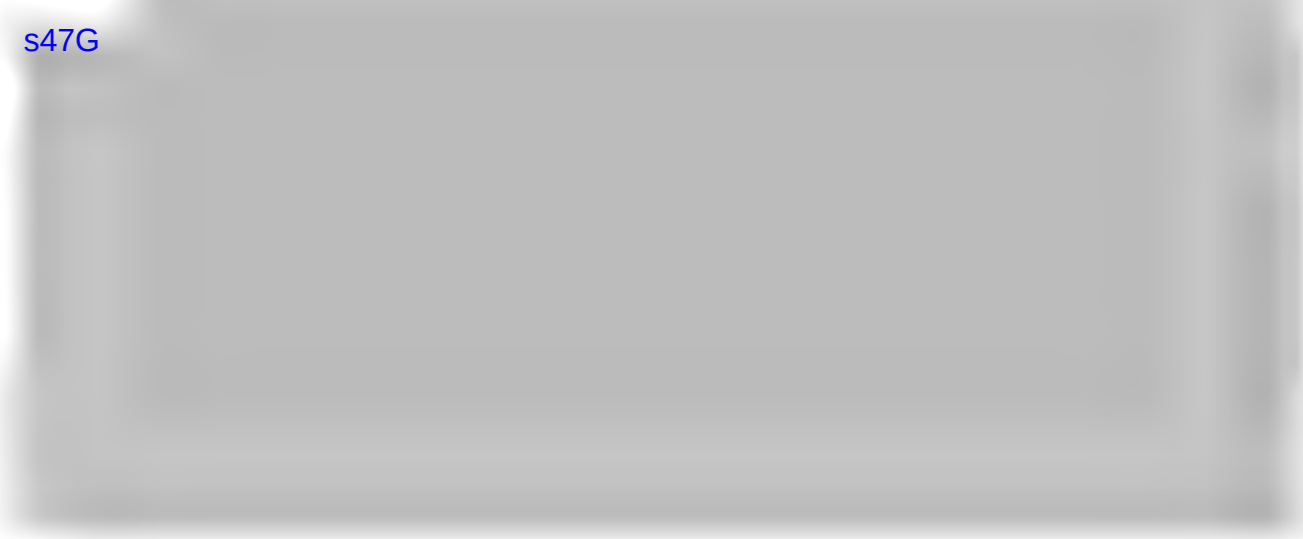
s22

s47G

s47G

s22

s47G



s47G

[redacted]

Summary and conclusions

Assessment of manufacturer's responses
A response to the deficiencies reported to the manufacturer was received on 23rd March 2020. This response was reviewed and found satisfactory.

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.

Final evaluation and recommendations:

1. The manufacturer operates in accordance with the relevant GMP requirements.

2. As discussed during the inspection and throughout the close out process, the following amendments to your Licences, for approved steps in manufacture, known as authorisations under section 40A of the *Therapeutic Goods Act 1989,* have been submitted to the delegate for approval:

s22 [redacted]

- For licence number MI-21042005-LI-000516-1 (7-9 Amax Ave Girraween) the removal of the authorisation of full product manufacture, excluding microbiological testing, of listed medicines in the dosage form of 'semi-solids'.
- For licence number MI-21042005-LI-000516-1 (7-9 Amax Ave Girraween) the addition of the authorisation for chemical & physical testing of listed medicines in the dosage form of 'semi-solids'.

s22 [redacted]

- Updating of the licence nominees for QC and Production to s22 respectively for licences MI-21042005-LI-000516-1 & MI-2016-LI-12063-1.

If approved, licence numbers MI-21042005-LI-000516-1 & MI-2016-LI-12063-1 will be re-issued with these amendments.

3. TGA records have been updated to show a final compliance rating of your facility of A2: satisfactory compliance with the manufacturing standard established under the *Therapeutic Goods Act 1989*.

4. The next routine re-inspection is expected to be performed within 30 months of this inspection.

5. The duration of the next inspection is estimated at this time to be 5 days.

Signed and authorised by

s22
s22
Manufacturing Quality Branch
Tel: s22
Mobile: s22
E-mail: s22 @health.gov.au

DEFINITIONS

Marketing Authorisation

Compliance with regulatory requirements specified on the ARTG and any other requirements imposed by a relevant Delegate of Secretary upon product listing or registration.

Examples of regulatory requirements include but not limited to the following: compliance with registered formulations, special storage and transportation conditions, shelf life, labelling, batch release testing requirements etc.

Critical Deficiency

A deficiency in a practice or process that has produced, or may result in, a significant risk of producing a product that is harmful to the user. Also occurs when it is observed that the manufacturer has engaged in fraud, misrepresentation or falsification of products or data.

Major Deficiency

A non-critical deficiency that:

- has produced or may produce a product which does not comply with its marketing authorisation; and/or
- indicates a major deviation from the Good Manufacturing Practice; and/or
- indicates a major deviation from the terms of the manufacturing licence or GMP approval (overseas manufacturers); and/or
- indicates a failure to carry out satisfactory procedures for release of batches; and/or
- indicates a failure of the person responsible for QA/QC to fulfil his/her duties; and/or
- consists of several other deficiencies, none of which on its own may be major, but which may together represent a major deficiency and should be explained and reported as such.

Other Deficiency

A deficiency that cannot be classified as either critical or major but indicates a departure from good manufacturing practice.

A deficiency may be “other” either because it is judged as minor, or because there is insufficient information to classify it as major or critical.

One-off minor lapses or less significant issues are usually not formally reported, but are brought to the attention of the manufacturer.

Note:

1. Classification of a deficiency is based on the assessed risk level and may vary depending on the nature of products manufactured, e.g. in some circumstances an example of major deficiency may be categorised as critical.
2. A deficiency that was reported at a previous inspection and not corrected may be reported in a higher classification.

Attachment: Inspection attendance sheet

FOR OFFICIAL USE ONLY

Australian Government
Department of Health
Therapeutic Goods Administration

Manufacturing Quality Branch

Inspection attendance sheet

Manufacturer name:	GMP Pharmaceuticals Pty Limited
Manufacturer address:	7-9, s22 Amax Avenue, Girraween NSW 2145
Inspection type:	Routine Re-inspection (all sites) + Licence Variation (14 Amax Ave)
Inspection date/s:	10 – 17 February 2020
Inspector/s:	s22
Inspection standard:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products (PE009-13)

Opening meeting starting time: 10/2/2020 9.50
Closing meeting starting time: 17/2/2020 15.20

Name *(please print)*	Position *(please print)*	Opening meeting *(initials)*	Closing meeting *(initials)*
s22			

Australian Government

Department of Health

Therapeutic Goods Administration

s22

GMP Pharmaceuticals Pty Limited
7-9, s22 Amax Avenue
Girraween
NSW 2145

Ref: PH18/100422 & PH18/100426

Dear s22

RE: Inspection of GMP Pharmaceuticals Pty Ltd

Please find attached the inspection report for the inspection that took place at your Girraween, NSW sites on 20/8/2018 & 10-14/9/2018.

Your response(s) to the deficiencies reported in the post inspection letter have been evaluated and have been accepted. Effective implementation will be reviewed at the next GMP inspection.

Should you have any questions regarding the inspection, please do not hesitate to contact me.

Yours sincerely

Signed and authorised by s22
s22
Manufacturing Quality Branch
Date: 1 April 2019

Tel: s22
E-mail: s22 @health.gov.au

TGA Health Safety Regulation

Australian Government

Department of Health

Therapeutic Goods Administration

Inspection Report

Manufacturer:	GMP Pharmaceuticals Pty Limited
Inspected site/s:	7-9, s22 Amax Avenue Girraween NSW 2145
Activities carried out by manufacturer:	☑ Manufacture of finished medicinal product ☐ Manufacture of intermediate or bulk ☐ Packaging ☐ Laboratory testing ☐ Release for supply ☐ Other:
Type of inspection:	☐ Initial inspection ☑ Re-inspection ☑ Full inspection ☑ Special inspection ☐ Reduced scope inspection Applicable sections of the *Therapeutic Goods Act 1989*: ☐ section 37(2)(b) (licence application) ☐ section 40B(10)(a) (licence variation) ☑ section 40(4)(b) (re-inspection of licensed site) ☐ section 25(1)(g) (overseas in relation to registration) ☐ sections 26(1)(g), 26A(3) (overseas in relation to listing)
Scope of Inspection	As below
Inspection date/s:	20/8/2018 & 1014/9/2018
Inspector/s:	s22
Manufacturing Standard used:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products - 1 January 2017 (Referred to as GMP code in this report)

Australian Government

Department of Health

Therapeutic Goods Administration

References:	Manufacturing Licence numbers: • MI-21042005-LI-00516-1 (primary site 7-9 & all others secondary sites) • & MI-2016-LI-12063-120163-1 (primary site 14 & all others secondary sites) Trim Tracking Numbers: MI-2018-LI-08478-1 (special), MI-2018-LI-00126-1 & MI-2018-LI-0056-1 (re-inspection all sites) File reference numbers: PH18/100422 & PH18/100426

Introduction

GMP Pharmaceuticals Pty Limited (GMP) has two therapeutic licences for four manufacturing sites in Amax Ave Girraween. These sites are all within a short walking distance from each other. Sites 7-9 &s2 undertake the manufacture of therapeutic products. Sites s22 This was the first full reinspection of all four sites. Thus it was required to follow-up on the effective close-out of five previous partial TGA inspections.

A special one day unannounced inspection was conducted two weeks prior to the full re-inspection. This special inspection was to assess compliance for the use of expired raw materials for therapeutic manufacture, unsanitary conditions and the use of any unlicensed premises for steps of manufacture of therapeutic products including storage.

GMP is a contract manufacturer of listed therapeutic goods in the following dosage forms: powders, tablets, hard capsules, soft gelatine capsules, semisolids, liquids and herbal tea.

Date of previous inspection:

s22

3. s22 7-9 &s22 5-6/&/2017 (initial inspection for manufacture at site 14 licence)
4. Site 7-9,s22 &14: 5/10/2016 (special inspection to add chemical testing to site 7-9 & storage, secondary packaging & release for supply at site 14)
5. Site 7-9 &s22 1-4/3/2016 (re-inspection)

Names of inspectors involved in previous inspection:

s22

Brief report of the inspection activities undertaken

Scope of inspection

- An unannounced 1 day inspection of all 4 sites.
- Full announced reinspection of all 4 sites to cover the 2 licences and follow-up of close-outs for the previous inspections conducted on 14-15/5/2018, 3/11/2017, 5-6/7/2017, 5/10/2016 & 1-4/3/2016.

Primary Site 7-9 Amax Avenue

Manufacturing Type	Sterility	Dosage Form	Product Category	Manufacturing Step
Medicine manufacture	Non-sterile	Powder	Listed Therapeutic Good	Full Product Manufacture – excluding Microbiological Testing
Medicine manufacture	Non-sterile	Solid Unit Dosage Forms	Listed Therapeutic Good	Full Product Manufacture – excluding Microbiological Testing
Medicine manufacture	Non-sterile	Semi Solids	Listed Therapeutic Good	Full Product Manufacture – excluding Microbiological Testing
Medicine manufacture	Non-sterile	Liquids	Listed Therapeutic Good	Full Product Manufacture – excluding Microbiological Testing
Medicine manufacture	Non-sterile	Capsule, soft	Listed Therapeutic Good	Full Product Manufacture – excluding Microbiological Testing

Medicine manufacture	Non-sterile	Tea	Listed Therapeutic Good	Full Product Manufacture – excluding Microbiological Testing
Medicine manufacture	Non-sterile	All Dosage Forms	Listed Therapeutic Good	Storage

s22

Inspected areas
General areas covered at the sites included sampling, dispensing, powder blending, hard shell encapsulation, tablet compression and coating, soft gelatin capsule manufacture, primary & secondary packaging, warehousing, laboratory, heating ventilation air conditioning (HVAC), compressed air system and purified water system (PWS) utilities for the site. The secondary sites at unit 1/29 & 36 were inspected for the step of storage.

In addition, the quality system and associated records for compliance to the GMP code were reviewed. This inspection also included an assessment of corrective and preventative actions that were implemented to address the deficiencies identified in the five previous TGA inspections.

Personnel met during the inspection
Please refer to the Inspection Attendance Sheet

Inspection findings and observations

Major changes since the previous inspection:
The company advised no major changes since the previous TGA inspection.

Future Planned Changes:

s22 [redacted]

Overview of inspection findings from last inspection and the corrective action taken
The inspector noted that the company had not effectively corrected many of the deficiencies issued at the last TGA inspections.

The inspector found that the company was operating to the same standards at the unannounced inspection as the standards found at an announced routine re-inspection. GMP maintained good hygiene practices in the clean controlled manufacturing areas. There was no evidence of expired raw materials being used for the manufacture of therapeutic products. Food manufacture was outside the scope of this inspection. There was no evidence that any unlicensed sites were being used for steps of manufacture for therapeutic products.

Quality Management
GMP had implemented a pharmaceutical quality system that generally met the requirements of the GMP code. Any deficiencies noted at inspection have been recorded in this report.

The company had not yet established a Quality Manual.

GMP had established an appropriate procedure for quality risk management. The system linked to other relevant company pharmaceutical quality system processes.

The company had established an appropriate system to manage and investigate planned and unplanned deviations and non-conformances. Root causes were analysed and identified and corrective and preventative actions (CAPA) were implemented where appropriate. The inspector reviewed some examples of deviations and found that GMP had recorded and documented the investigation of issues to an appropriate depth. Company staff reviewed registers for any trends.

The change control system was not reviewed due to time constraints and should be followed up at the next inspection.

The system for conducting product quality reviews (PQRs) allowed product grouping to be undertaken. However, currently the company conducted PQRs on each product manufactured. Products manufactured at a high frequency are reviewed every three months. The PQRs covered all products manufactured in the review period and covered all the required aspects for review. The company had appropriately defined all PQR relevant responsibilities for contract manufactured products in GMP agreements.

The company had generally established a compliant system for PQRs. However, the inspector noted one issue where the PQR system would not ensure that all products were included in a review at least every two years when a small number of batches were produced (Deficiency #9).

Management reviews were not reviewed due to time constraints and should be followed up at the next inspection.

GMP had established an appropriate system for release for supply. The Quality Assurance (QA) Manager and delegates were responsible for release. Documented procedures and checklists were utilised to cover the relevant areas, including checking the complete batch documentation package, certification that product was manufactured in compliance with the marketing authorisation and that the product quality review and on-going stability information was available.

Personnel
GMP had established position descriptions for key personnel and company organisation charts provided clear reporting and authority flows. The inspector confirmed that the heads of production and quality were independent. The inspector noted that all job descriptions were not document

controlled and one other issue regarding delegations (Deficiency #8).

The company had generally established a compliant system for training and assessment of personnel. However, the inspector reviewed the training procedures, plans and records and found several issues (Deficiency #11).

GMP had implemented a very high standard for personal hygiene practices, including clothing of personnel and visitors in the controlled manufacturing areas.

The company had implemented appropriate systems to ensure that staff with infectious diseases, or other relevant health issues could not adversely affect product quality. Medical examinations were conducted upon recruitment.

Management of consultants was not reviewed due to time constraints and should be followed up at the next inspection.

Premises and Equipment

The design for personnel and material flows were appropriate for the activities undertaken on the sites. However, the inspector found that there was inadequate capacity to store all materials appropriately and warehousing areas were not clean and tidy at the time of the inspection (Deficiency #2).

GMP had two secondary licenced sites for storage at s22 Site 7-9 contained small areas for temporary storage of materials and goods.

s22

The warehouse at site s22 was generally used for the storage of raw materials. Materials could be receipted at this site. The one manual goods received book was located at this site and staff at this site could generate starting material status labels. The sampling room was also located at this site.

s22

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The warehouse areas had separate locations for goods receipt, staging, quarantine, storage, rejected goods and returned goods. The reject area was locked and the electronic status systems added extra security and would not allow picking or use of rejected materials or goods.

The warehouse areas were not air-conditioned. The inspector noted that the acceptance criteria of a maximum temperature of 30^{0}C in warehousing areas did not ensure that all products were stored as per labelled requirements of max 25^{0}C for some products. In addition, warehouse temperature mapping reports were not available and issues with temperature monitoring were noted (Deficiency #2).

Although status was controlled electronically in the "Pronto" inventory management system, the company manually controlled status via physical location and status control labels. Starting materials used for therapeutic manufacture were labelled with a yellow status label and those for non-pharmaceutical use were labelled with an orange status label.

The inspector noted some issues in regards to status labels reflecting the correct status of some materials and in process goods shipped between the manufacturing sites (Deficiency #14).

Pallet bay storage locations were entered into Pronto for materials stored at sites s22 and RF scanners could be used at these sites to scan barcodes on the status labels. Sites 36 & 7-9 did not have this capability with Pronto.

s22

s22

There were no qualification reports available for the HVAC systems for the sampling room at site 29 (Deficiency #6).

The company maintained appropriate usage and cleaning records for the sampling area. The company ensured that sampling tools were used, cleaned and stored appropriately.

The dispensing areas were appropriately designed for the weighing activities undertaken. Staff maintained appropriate records to demonstrate an area clearance and clean after dispensing activities were completed.

Site 7-9 contained manufacturing areas on two levels. The ground floor contained the manufacturing areas for soft gelatine capsules. The first floor contained manufacturing areas for powder and solid dosage manufacture.

The soft gelatine capsule manufacturing floor contained areas for gelatine manufacture, dispensing, medicine fill mixing, encapsulation, drying, capsule sorting and a wash bay.

The area contained three soft gelatine encapsulation lines located in one large area with barriers and curtains between the lines.

The dry manufacturing area for powders and tablets and hard shell capsules contained areas for dispensing, powder blending, tablet compression, hard shell encapsulation, hard capsule sorting, and a wash bay. Manufacturing rooms were located off a main manufacturing corridor.

At the time of inspection all packaging activities had been transferred from site 7-9 to s22

s22 contained a standalone area for packaging the solid dosage forms manufactured at site7-9 and soft gelatine capsules manufactured at sites 7-9 s22 and a separate soft gelatine capsule manufacturing suite.

The soft gelatine capsule manufacturing suite contained ares for gelatine manufacture, dispensing, medicine fill mixing, encapsulation, drying, capsule sorting and a wash bay.

The area contained two soft gelatine encapsulation lines located in separate rooms.

The packaging suite had three main sections including two therapeutic packaging areas with separate rooms for primary and secondary packaging activities and a milk powder packaging area. The milk powder packaging area was outside the scope of this inspection.

Three bottle packaging lines 5, 6 & 7 were located in this area. Packaging lines extended through hatches to the secondary packaging rooms. GMP did not undertake any blister packaging at this site.

Production equipment was generally located in self-contained rooms dedicated to the specified activity. The manufacturing areas were designed for both concurrent manufacture of multiple product batches and campaign manufacture for longer runs as required. However, the inspector noted some issues in regards to ensuring all products were protected from contamination and the potential for cross contamination (Deficiency #1).

Pre-printed packaging was appropriately controlled on site. Labels were stored in a secure label room. Labels were counted upon receipt or before issue to production with a label counter. The label counters were performance checked at defined intervals.

The company had generally maintained the facility to an acceptable standard. However, the inspector noted some issues where an automatic door at s22 was not closing properly and the floor had been damaged and not repaired in several warehouse and production areas (Deficiency #1).

The company did not manufacture any highly toxic or high pharmacological activity materials

The company had established compliant maintenance and calibration systems. The inspector found that the maintenance and calibration records and SOPs reviewed demonstrated that planned schedules had been adhered to and plant equipment was appropriately managed and maintained to an appropriate standard.

The HVAC systems supplied controlled air to many different areas in the two manufacturing sites. GMP could not demonstrate that air quality was appropriately controlled. The inspector noted some issues with regards to air balancing where several pressure differentials were not meeting acceptance criteria at sites 7-9 s22 (Deficiency #1). After the unannounced inspection GMP had redesigned the pressure differential monitoring logs and modified the procedure to improve monitoring and notification of any excursions from acceptance criteria. However, the inspector still noted continuing issues at the full re-inspection.

HVAC systems had not all been qualified and where information was available several issues were noted (Deficiency #6).

The HVAC systems were described in the site master files (SMFs).

Sites 7-9 s22 contained reverse osmosis PWSs. Details of the systems were described in the SMFs.

The PWS at site 7-9 was an established system and had been in operation for four years. The system was requalified in July 2017. The inspector reviewed test data over the period Aug 2015 to July 2017, tested monthly, and found that the data supported the conclusion that the system was under appropriate control to supply water to meet the BP standard.

An interim qualification report, dated May 2018, was available for the PWS located at s22 The inspector reviewed test data over the period March 2018 to June 2018, tested daily for six months, and found that the data would support a conclusion that the system was under appropriate control to supply water to meet the BP standard. However, the inspector noted some issues with the purified water system qualification documents in regards to not covering the sanitation frequency and ensuring removal of all sanitising chemical for the system located at s22 (Deficiency #6).

Compressed air had contact with product or primary product contact surfaces. However, the company had not defined these areas. In addition, the qualification for the air compressors at s2 did not include a risk assessment and microbiological testing for worst case locations and filter changes (Deficiency #6).

GMP had generally implemented an appropriate system for pest control at all sites. The system included documented procedures, approved chemicals, device location maps, control devices for rodents and crawling and flying insects, and relevant records of activities undertaken. A contract pest control company was utilised to visit the sites at a minimum frequency of every four months or more frequently as required. However, the inspector noted that the 2 flying insect zapping lights located in the warehouse at s22 were not included on the pest control map and there were no records of these being checked. In addition, the pest control SOP did not include s22 warehouse (Deficiency #8). This issue was corrected at inspection.

The company had implemented an appropriate process for secure waste disposal that ensured products and printed packaging were unrecoverable.

Documentation

GMP had implemented a manual system for document control. The company required SOPs to be reviewed at least every 3 years to ensure that they remained current.

GMP had implemented a generally compliant system for document control. However, the inspector noted several issues (Deficiency #8).

GMP had established appropriate specifications for raw materials, packaging and finished products.

The company had prepared, checked and authorised compliant master batch records. Master batch records were generated in word. Quality staff printed out working batch records and issued these to production for use.

Production

The inspector reviewed production and packaging processes and procedures relating to the

manufacture of all therapeutic products covered under the company licence. GMP maintained appropriate in-process controls and records for the products manufactured. The inspector considered all production and packaging processes and procedures reviewed appropriate.

Bulk solid dosage forms were manufactured at site 7-9 and transferred to s22 for packaging. A deficiency raised at a previous inspection conducted in Oct 2016, for this process, had not been fully addressed (Deficiency #14). This issue was corrected at inspection.

The starting material vendors were assessed and approved to supply materials to GMP. The company had defined four categories for the status of materials suppliers including new, approved, qualified and certified.

Approved suppliers had supplied three lots of material that had been fully tested to compendia or authorised in-house specifications. Materials from approved suppliers may qualify for reduced sampling.

Qualified suppliers had returned completed supplier questionnaires, or successful on-site inspections had been conducted. Materials from qualified suppliers may qualify for reduced testing. The reduced testing system allowed for rotational testing of non-critical tests.

Certified suppliers were manufacturing sites that had been licenced or certified by the TGA.

The company had established a generally compliant supplier qualification and control system. However, the inspector noted some issues with regards to documenting an evaluation of the returned supplier questionnaire (Deficiency #15).

s22

Company staff checked receipt information against order information and packaging integrity, cleanliness, the standard name and that the materials were received from an approved supplier with a relevant certificate of analysis.

Sampling staff performed sampling activities in accordance with the company documented procedures. The inspector reviewed the sampling plans and found them acceptable. The company procedure required that identity testing was undertaken on individual samples before a maximum of ten could be combined to form a composite sample for further testing.

GMP had generally established appropriate controls over the receipt of pre-printed labels to ensure version and identity. However, the inspector noted one issue (Deficiency #13).

GMP had installed appropriate wash bays, drying rooms and clean equipment store rooms. The company had documented cleaning and sanitation instructions and records were available to demonstrate compliance. Production equipment was sanitised prior to use. Cleaning status labels were in use and generally reflected the state of the equipment at the time of inspection. However, the inspector noted some issues where powder residue was found on equipment in Dispensing Room 1& Tablet Press 1 at site 7-9 (Deficiency #1).

Although GMP had implemented an environmental monitoring program the inspector found several issues (Deficiency #12). The inspector did note that the test data available for review for viable and non-viable air particulates and contact plates and swabs appeared to support a conclusion that areas would comply with requirements for a controlled clean manufacturing facility for the production of listed therapeutic goods.

The company appropriately managed rejected materials. The company labelled rejected materials as such and placed them into a physical reject location.

The inspector did not review the process for rework and reprocessing due to time constraints. This area should be included for review at the next inspection.

GMP had established an appropriate documented procedure to manage the return of goods. The procedure required the assessment of appropriate information relating to the traceability and control of the goods for storage and transport conditions to ensure that any goods considered for resale met the required safety, efficacy and quality criteria. No goods had been returned since the

previous inspection where this process was reviewed.

The company had documented site validation requirements in the validation master plan (VMP). The inspector reviewed this document and found that it had generally covered all relevant areas for the site. However, GMP did not maintain appropriate logs and schedules to manage current requalification and new validation project activities (Deficiency #3).

Soft Gelatine Encapsulation machine No. 9 (originally No.4) was relocated from site 7-9 s22 IQ & PQ was undertaken in April 2018 and an addendum was added to the report in May 2018.

Soft Gelatine Encapsulation machine No. 10 (originally No.6) was relocated from site 7-9 s22 . IQ & PQ was undertaken in July 2018.

The inspector noted that the wedge sealing temperature was not included as part of the control parameters in the qualification and that the worst case scenario of a slurry medicines fill had not been used as none of these products had been manufactured to-date. However, this constraint was not documented in the conclusion of the qualification documentation. GMP had not appropriately documented all equipment qualification requirements (Deficiency #5).

The inspector did not review process validation at this reinspection. This area should be included for review at the next inspection.

The inspector did not review ongoing process verification at this reinspection. This area should be included for review at the next inspection.

No cleaning validation had been conducted to demonstrate appropriate bioburden reduction and production campaign runs (Deficiency #7).

The company had not established an appropriate computer validation master plan to ensure that all relevant computer systems used for GMP activities would be validated and a risk assessment conducted for computer based systems. The company had not ensured that data integrity was maintained when using computerised systems in the warehouses and laboratory (Deficiency #4).

Quality Control

The company contained an analytical testing laboratory located at site 7-9. The laboratory was adequately equipped with modern instruments to conduct the required chemical testing of materials and products. The laboratory consisted of several testing areas including the following physical testing room; wet chemistry & ICP-OES room; UV, IR & microscope room; and GC & UHPLC room.

The company had implemented appropriate systems for the receipt, registration and storage of samples.

GMP had established appropriate specifications and test methods for raw materials, in-process materials and finished products.

The inspector did not review analytical method validation due to time constraints at this reinspection. This area should be included for review at the next inspection.

The company had generally maintained appropriate test records for starting materials, in-process and finished product tests performed. However, the inspector noted some issues (Deficiency #4).

GMP maintained appropriate controls over chemical reference standards with registers and working standards traceable to the appropriate primary standards. The company maintained reference and retention samples of starting materials and finished products under monitored storage conditions in the retention area for appropriate timeframes.

The inspector did not review on-going stability testing due to time constraints at this reinspection. This area should be included for review at the next inspection.

The company supplied records to demonstrate that generally laboratory equipment reviewed by the inspector was appropriately calibrated and maintained. However, there were no internal verification checks conducted on the laboratory disintegration unit between the external

calibrations (Deficiency #10).

GMP had not ensured that data integrity was maintained for electronic data generated on old laboratory equipment such as the AAS and UV standalone instruments. In addition, there was no description of the laboratory computer systems and the way they were used (Deficiency #4).

The company ensured that there was a sufficient number of appropriately qualified and trained staff to undertake all necessary testing functions.

The company had implemented an appropriate system for managing and investigating out of specification (OOS) and out of trend (OOT) events in the laboratory. The OOS/OOT examples reviewed by the inspector had been investigated to an appropriate depth and relevant documentation had been maintained.

GMP was able to undertake the majority of testing in-house. The company appropriately managed data received from the contract testing laboratories and had established GMP agreements defining relevant responsibilities.

The company had no microbiological testing laboratory on their sites.

Outsourced Activities

The company had established appropriate GMP agreements with service providers. The company had established appropriate GMP agreements with contract testing laboratories.

GMP had established a template for GMP agreements with raw material and packaging suppliers. The inspector advised that the TGA guidance document for Supplier Qualification was in the process of being updated and it was agreed that listed and complementary medicines manufacturers were not required to have these in place. These activities are considered as outsourced for this sector of industry.

Complaints and Product Recall

The company had established an appropriate system for receipt, recording, investigation and analysis of customer complaints. No complaints were on file since the 2016 inspection.

The inspector reviewed the system for product recalls and found it to be compliant. A mock recall to ensure that the system was effective was conducted every year, if no real recalls had been undertaken. The company had no actual market recalls for follow-up and none had been conducted to-date.

Self Inspection

The company had a generally compliant system for self-inspection. However, the inspector noted one issue (Deficiency #16).

Compliance with Marketing Authorisations

GMP had established an appropriate system to ensure that market authorisation aspects for products manufacturer for Australia were adequately covered.

Specific Annexes

The Annexes of the Standard applicable to the inspection were Annexes 7, 8, 11, 15 & 19.

Other specific issues identified

The inspector noted that no teas, semisolids or liquids had been produced for some time. This should be fold up at the next inspection. The company wanted to keep the current scope of the licence as is.

Site Master File

The company provided a copy of their 2 SMFs at inspection, these covered therapeutic activities undertaken.

s [redacted]

- Site 7-9 version 12, dated September 2018

Miscellaneous

Samples taken:
None

Distribution of Report:
Company and TGA files

Attachments:
None

List of Deficiencies observed during the inspection

Critical deficiencies:
None observed

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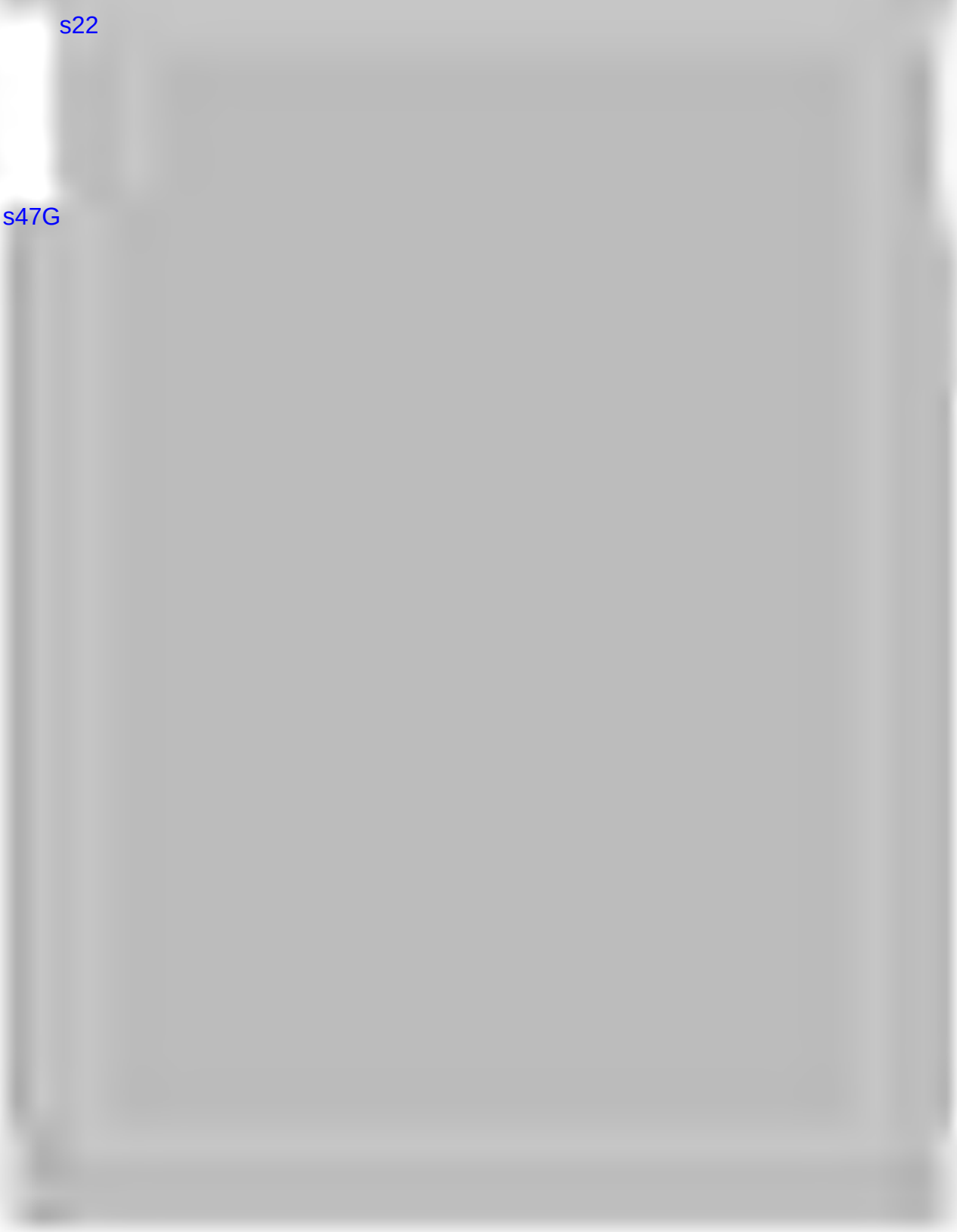

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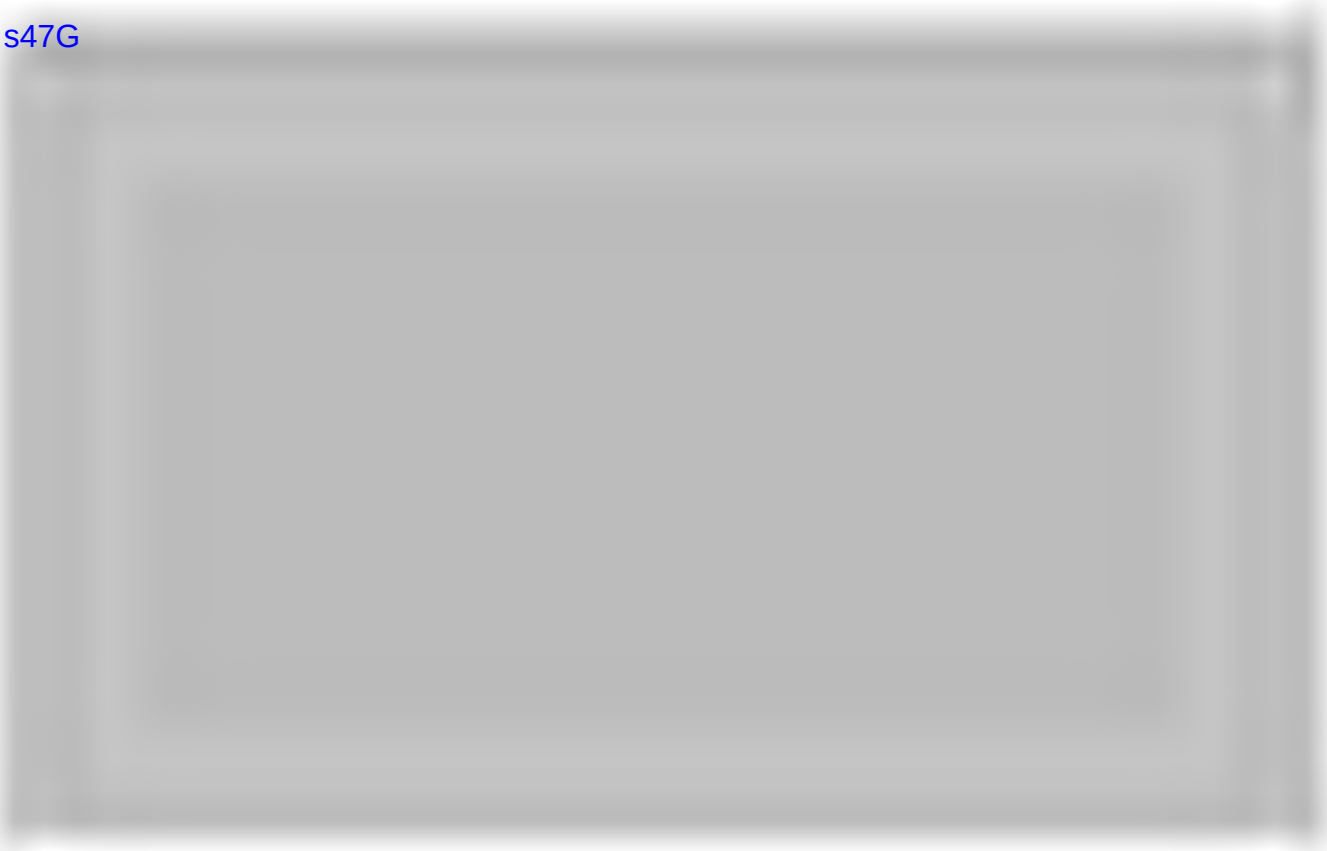

Comments
Any comments made to the company, in reference to their response to correct deficiencies raised at the inspection, during the closeout process can be found in the close out record.

Summary and conclusions

Assessment of manufacturer's responses
A response to the deficiencies reported to the manufacturer was received on 13/12/2018.

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.

Final evaluation and recommendations:

1. The manufacturer operates in accordance with the relevant GMP requirements.
2. TGA records have been updated to show a final compliance rating of your facility of A3: basic compliance with the manufacturing standard established under the *Therapeutic Goods Act 1989*.
3. The next re inspection is expected to be performed within 18 months from the dates of inspection.
4. The duration of the next inspection is estimated at this time to be 5 days for 1 inspector.

Signed and authorised by Lead Inspector
s22
Manufacturing Quality Branch
Date: 1 April 2019

Tel: s22
E-mail: s22 @health.gov.au

DEFINITIONS

Marketing Authorisation

Compliance with regulatory requirements specified in the ARTG and any other requirements imposed by a relevant Delegate of the Secretary, upon product listing or registration.

Examples of regulatory requirements include but not limited to the following: compliance with registered formulations, special storage and transportation conditions, shelf life, labelling, batch release testing requirements etc.

Critical Deficiency

A deficiency in a practice or process that has produced, or may result in, a significant risk of producing a product that is harmful to the user. Also occurs when it is observed that the manufacturer has engaged in fraud, misrepresentation or falsification of products or data.

Major Deficiency

A non-critical deficiency that:

- has produced or may produce a product which does not comply with its marketing authorisation; and/or
- indicates a major deviation from the Good Manufacturing Practice; and/or
- indicates a major deviation from the terms of the manufacturing licence or GMP approval (overseas manufacturers); and/or
- indicates a failure to carry out satisfactory procedures for release of batches; and/or
- indicates a failure of the person responsible for QA/QC to fulfil his/her duties; and/or
- consists of several other deficiencies, none of which on its own may be major, but which may together represent a major deficiency and should be explained and reported as such.

Other Deficiency

A deficiency that cannot be classified as either critical or major, but indicates a departure from good manufacturing practice.

A deficiency may be "other" either because it is judged as minor, or because there is insufficient information to classify it as major or critical.

One-off minor lapses or less significant issues are usually not formally reported, but are brought to the attention of the manufacturer.

Note:

1. Classification of a deficiency is based on the assessed risk level and may vary depending on the nature of products manufactured, e.g. in some circumstances an example of major deficiency may be categorised as critical.
2. A deficiency that was reported at a previous inspection and not corrected may be reported in a higher classification.

Australian Government

Department of Health

Therapeutic Goods Administration

s22

GMP Pharmaceuticals Pty Ltd
7-9 Amax Ave
Girraween, NSW 2145

Dear s22

RE: Inspection of GMP Pharmaceuticals Pty Ltd

Please find attached the inspection report for the inspection that took place at your Girraween site on 01-04 March 2016.

Your responses to the deficiencies reported in the post inspection letter have been evaluated and have been accepted. Effective implementation will be reviewed at the next GMP inspection.

Should you have any questions regarding the inspection, please do not hesitate to contact me.

Yours sincerely

(Signed electronically; contains no visible signature)

s22
s22
Manufacturing Quality Branch
Date: 21st September 2016
Tel: s22
E-mail: s22 @tga.gov.au

Australian Government

Department of Health

Therapeutic Goods Administration

Manufacturer:	GMP Pharmaceuticals Pty Ltd
Inspected site/s:	Primary Site: 7-9 Amax Ave Girraween, NSW 2145 s22
Activities carried out by manufacturer:	☑ Manufacture of finished medicinal product ☐ Manufacture of intermediate or bulk ☐ Packaging ☐ Laboratory testing ☐ Release for supply ☑ Other: Testing activities are restricted to physical testing
Type of inspection:	☐ Initial inspection ☑ Re-inspection ☑ Full inspection ☐ Special inspection Applicable sections of the *Therapeutic Goods Act 1989*: ☐ section 37(2)(b) (licence application) ☐ section 40B(10)(a) (licence variation) ☑ section 40(4)(b) (re-inspection of licensed site) ☐ section 25(1)(g) (overseas in relation to registration) ☐ sections 26(1)(g), 26A(3) (overseas in relation to listing)
Scope of Inspection	Full product manufacture, excluding testing, of non-sterile listed therapeutic goods in the form of solid unit dose forms, soft gel capsules, liquids, herbal teas and semi solids. Physical testing of all dosage forms. Full product manufacture, excluding chemical and microbiological testing, of veterinary chemical products in the form of tablets, pellets, capsules (hard shell & soft gelatine), creams/lotions, ointments, pastes, powders, sprays and liquids.
Inspection dates:	01- 04 March 2016
Inspector/s:	s22

Australian Government

Department of Health

Therapeutic Goods Administration

Manufacturing Standard used:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products - 15 January 2009
References:	Manufacturing Licence number: MI-21042005-LI-000516-1 File reference number/s: PH14/11942 (inspection file), 2014/012527 (licence file)

Introduction

GMP Pharmaceuticals Pty Ltd, hereafter referred to as GMP Pharmaceuticals, is a contract manufacturer of listed therapeutic goods, with core business being soft gel capsule production. Other dosage forms are produced on site including tablets, herbal teas, hard shell capsules, powders and liquids. The facility is equipped for primary and secondary packaging but products are also supplied in bulk for packaging by third parties.

The manufacturer currently employs approximately 100 people and manufactures human and veterinary medicines, as well as food products. In addition to their TGA licence, the site holds a manufacturing licence from the APVMA and HACCP certification. Approximately 75% of the products manufactured at the Girraween site are for therapeutic use.

Manufacture of veterinary chemical products is conducted under an APVMA licence number 2205. These activities were included in the scope of this TGA inspection.

Date of previous inspection: 26-28 June 2013

Names of inspectors involved in previous inspection: Lynda Linhart and Carl Kelly

Major changes since the previous inspection: GMP Pharmaceuticals had installed a new capsule counting line and tabletting press. Daniel Xu is Head of Production.

Brief report of the inspection activities undertaken

Scope of inspection

- Full product manufacture, excluding testing, of non-sterile listed therapeutic goods in the form of solid unit dose forms, soft gel capsules, liquids, herbal teas and semi solids. Physical testing of all dosage forms.
- Full product manufacture, excluding chemical and microbiological testing, of veterinary chemical products in the form of tablets, pellets, capsules (hard shell & soft gelatine), creams/lotions, ointments, pastes, powders, sprays and liquids.

The inspection was conducted to review compliance to the PIC/S Guide to Good Manufacturing Practice (GMP) for Medicinal Products - 15th January 2009 for these operations at GMP Pharmaceuticals. Food products manufactured at GMP Pharmaceuticals were excluded from the scope of this inspection.

This inspection also included an assessment of corrective and preventative actions that were implemented to address the deficiencies identified in the last inspection of these facilities in June 2013.

Inspected areas

The inspection reviewed all activities and areas related to the scope of the inspection for compliance to the PIC/S Guide to GMP for Medicinal Products - 15 January 2009.

Personnel met during the inspection

Refer to attached meeting attendance record.

Inspection findings and observations

Quality Management

GMP Pharmaceuticals had an established quality management system that generally met the requirements of the PIC/S GMP Guide. Quality risk management (QRM) activities were documented in a procedure "Risk Management Master File" which was reinforced by HACCP certification. The inspector reviewed a risk assessment relating to product packaging for compliance with over-arching policies which was deemed satisfactory. However, the inspector observed that the QRM was not appropriately linked to several procedures including those

associated with deviations, non-conformances, internal audits, reworks and reprocesses where selected examples were lacking in risk assessment (Deficiency 7).

GMP Pharmaceuticals had written procedure for handling of deviations QA0020d. This procedure was reviewed in accordance with the overall QMS. The system excluded all issues relating to out of specification (OOS) laboratory investigations. The inspector reviewed examples of completed deviation and non-conformance reports e.g. 00628, 00629 and 00631 and some issues were identified (Deficiency 2).

An acceptable change control procedure was available, along with a corresponding form and register. Quality Assurance (QA) assessed and approved all changes, with appropriate consideration given to areas which may be impacted by the proposed change.

GMP Pharmaceuticals had a suitable procedure for product quality reviews (PQR), QA005d. GMP Pharmaceuticals did not apply a product grouping strategy and had completed PQRs for each product on a two year frequency. The parameters monitored and summarised were consistent with the PIC/S Guide. An appraisal of a recent product quality review showed this area of the quality system to be adequately documented and controlled.

There was an appropriate procedure in place for the release of bulk and finished products. Batch release was restricted to QA Manager or delegate authorised to release for supply and were suitably trained for this task. The release for supply process effectively ensured that finished products complied with the marketing authorisation

Systems were in place to ensure that products released to the market were in accordance with the relevant marketing authorisations.

Personnel

Key personnel were defined and their responsibilities were documented in job descriptions. The inspector reviewed a number of job descriptions and identified some issues (Deficiency 3 and 4). The organisational chart (sighted in the Site Master File) demonstrated clear separation between Production and QA. Appropriate medical checks were performed for employees to ensure that staff with infectious diseases, or other relevant health issues could not adversely affect product quality.

Requirements for training were documented in a procedure and the system was managed via individual training plans showing training needs, completed training and competency levels achieved. A system was in place to provide retraining in connection with procedural changes along with annual GMP refresher training provided by paper-based modules. The inspector reviewed a selection of training material and identified several documentation issues with these records (Deficiency 11b and 11c). The signature register was also reviewed for compliance.

Gowning requirements were appropriate. Personnel entering the therapeutic packaging area wore hairnets, gloves, shoe covers and over garments. Adequate hand washing and sanitising facilities were provided.

Premises and Equipment

Primary manufacturing operations were undertaken in the main building on the 7-9 Amax Avenue site which consisted of material staging, manufacturing, packaging and quality control areas. Thes[redacted]

s22 [redacted] . s22 [redacted]

The manufacturing facility at 7-9 Amax Ave site consisted of two main areas: the upper level for the manufacture of tablets and hard capsules, and the lower level for the manufacture of soft-gel capsules and liquids. The ground floor of 7 Amax Ave was primarily a packaging area with ancillary office and storage areas. It was suitably constructed with sealed floors, smooth walls and ceilings, covered lights and coving at all joints. The packaging area was fit for purpose, with appropriate materials of construction used and adequate space provided. The design and construction of equipment was acceptable with predominately inert product contact surfaces and appropriate capacities for the production processes undertaken on site.

The dry material dispensary was located on the mezzanine floor of the upper level at 9 Amax Ave. Powder blending, tablet compression and hard shell encapsulation also took place on this level. The rooms were equipped with suitable equipment and dust extraction. Pressure differential readings were reviewed by the inspector and the blending rooms' pressures were below the specification required (Deficiency 6b). This was immediately resolved by the maintenance team and confirmed by the inspector.

Materials for soft-gel capsule production were dispensed in a dedicated room within the ground floor at 9 Amax Ave. Liquid ingredients were weighed directly before mixing in the liquid manufacturing room. All soft-gel capsule and liquid manufacture and packaging activities were performed in the lower level area. Generally, there were individual rooms for each activity accessed via common corridors. The inspector observed that the status of both the liquid filling room and liquid manufacturing room was not visible, which, was adequately addressed during the inspection (Deficiency 13). Equipment inspected was labelled appropriately and the physical condition matched the status indicated.

The solid dose packaging area was located on the ground floor at 7 Amax Ave. The area was accessed via a gowning room and contained three packaging rooms designated to bottle filling and secondary packaging. A smaller room was dedicated to blistering.

Key production equipment included mixing vessels, hard shell encapsulators, soft gel encapsulators, tablet presses, a blister packer, tablet counter, and liquid filler. Equipment inspected was labelled appropriately and the physical condition matched the status indicated. A program of preventative maintenance was in place. The inspector observed that the system was well managed, with equipment maintenance checks occurring at the specified intervals.

A system was in place to ensure equipment was calibrated at the defined intervals. Records for balances were reviewed and some issues were identified with the methodology for the calibration and performance verification of this equipment (Deficiency 12).

There was a HVAC system supplying filtered air to sampling, manufacturing and packaging areas. A procedure for monitoring of air handing units (AHU's) was available which specified the monthly monitoring of pressure differential across filters with documented acceptance criteria. The HVAC system had undergone requalification in the last 2 years with some issues raised in relation to the number of air changes in the Soft Gel Mixing Room (Deficiency 6a). HEPA filtration was utilised in the air supply to the processing areas with dehumidifying units in place for the dry manufacturing area. GMP Pharmaceuticals appropriately maintained the independent AHUs and other system components of the HVAC system.

Reverse osmosis was used in the generation of purified water. The quality of the purified water was monitored on a monthly basis and specifications were in line with current BP requirements.

An external contractor managed pest control across the facility. The inspector found the program and records satisfactorily controlled.

The company had implemented an appropriate system for secure waste disposal.

In general, the facilities were maintained to an acceptable standard and good housekeeping was evident throughout both sites. The inspector noted that some areas may require attention as rust on legs of liquid filling machine was observed and dry production corridor was congested with equipment.

Documentation

A document control system was in place to administer the generation, approval, issue and review of GMP related documents. Controlled, paper-based versions of all necessary documents were available at the point of use. Adequate records of distribution of these hard copy documents were maintained. Superseded and obsolete documents were appropriately managed within this system. GMP documents are stored for a minimum of 6 years after expiration has been reached.

Procedures reviewed during the inspection were generally found current and under control. The review period on all SOPs was 3 years which was confirmed by the inspector on procedures reviewed. Appropriate specifications were available for all packaging materials, bulk and finished products. Development, approval and review of these specifications were adequately controlled.

The inspector reviewed a range of GMP records through the course of the inspection and a number of issues with documentation practice were identified (Deficiency 11b, c, d, e). Manufacturing batch documents were reviewed by QA prior to issue to production. The inspector reviewed a limited selection of batch records and found similar documentation issues as highlighted previously (Deficiency 11c).

A selection of external documents was reviewed and highlighted non-compliance in the appropriate control of contract laboratory data and calibration certification (Deficiency 11a).

Production

GMP Pharmaceuticals had a procedure in place for the assessment of suppliers which was considered a suitable approach to supplier approval and a register of approved suppliers was maintained. The manufacturer had a program for the sampling and testing of starting materials. Warehouse personnel checked starting material containers on receipt for seal integrity and damage prior to entering into a goods receipt logbook and Pronto – a computerised inventory control system. A unique good inwards number (GIN) was assigned from the manual system. The GIN was printed along with other identifying details on quarantine labels, which were subsequently affixed to the goods. Upon release, the materials were labelled with green approved stickers such that the original quarantine status was covered but other key information on the label remained visible. The inspector observed that pre-printed labels were processed before entering delivery into the GIN register and issuance of a GIN by label store supervisor (Deficiency 15).

GMP Pharmaceuticals permitted the extension of retest dates on raw materials based on satisfactory QC analysis at the time of expiry. On review, the inspector observed incomplete documentation to support the 2 year extension of GIN 27901. There was a lack of justification on the period for which raw material retest dates could be extended (Deficiency 1).

An environmental monitoring program was in place which was performed on a six-monthly schedule. Samples were taken using settle plates, contact plates and surface swabs through a contract laboratory service. GMP Pharmaceuticals had appropriate limits in place (equivalent to Grade D classification) and QA reviewed test records. Environmental reports demonstrated that the monitored areas were under control with no excursions reported in 2015-2016 period.

Manufacturing processes included dispensing, mixing, compression, gel cooking, encapsulation, drying, and sorting. These were performed in accordance with written procedures and batch document instructions.

Packaging was conducted with the use of both manual and semi-automatic packing processes. Specific packing instructions for each product were available, along with SOPs for equipment operation. Appropriate checks were recorded during production; including area/line clearance, cleaning, identity of starting materials, equipment performance tests, and material reconciliation. The inspector reviewed the line clearance procedure and highlighted that adequate control of products or labels from the previous batch was not considered (Deficiency 14). Records showed that printed packaging components were controlled in accordance with the procedures. Most labels were back numbered and a label counter was used when required. Appropriate calibration using test rolls was regularly performed (monthly) on the label counter.

Cleaning and sanitation procedures for processing rooms and equipment were in place, with appropriate records of these activities maintained. Wash bays were available in both the wet and dry manufacturing areas for cleaning of equipment. Approved cleaning agents were prepared and labelled correctly and cleaning equipment was stored in an appropriate manner.

A procedure for rework and reprocessing was in place (QA0128a) and specified that a batch instruction with QA approval was required for the process. The inspector identified some issues with the detail in the rework procedure (Deficiency 8a). Rework root cause investigation and corrective actions were not appropriately controlled and documented in the selected rework reports reviewed by the inspector (Deficiency 8b).

GMP Pharmaceuticals had established an appropriate documented procedure to manage the return of goods (SOP QA0103e). The manufacturer would only re-release goods returned from clients if the products were appropriately stored and controlled during the returns process.

There was an appropriate Validation Master Plan/File (VMP) available. The VMP detailing GMP Pharmaceuticals approach to validation was in place that addressed the validation of equipment, cleaning and processes. The inspector reviewed selected equipment qualification for Countec Tablet Counter and Zhejiang YDF-50 liquid filler which were found to be acceptable.

The Pronto computerised inventory control system was only used to manage inventory which had password protection and access controls. Computer validation was not covered in detail during this inspection.

GMP Pharmaceuticals appropriately managed rejected materials via the use of reject labels, secure storage in an exclusive area and use of a rejected goods log. The reject goods form included an area to document the return or secure destruction of rejected materials.

Quality Control

The manufacturer used contract laboratories for all release and stability testing of finished products. External contract laboratory services were also scheduled to conduct routine environmental monitoring. The contract laboratories were TGA licenced and were covered by appropriate agreements with the manufacturer. Quality control testing on site was limited to physical tests such as uniformity of weight, disintegration, friability and hardness. Equipment was subject to regular calibration and instruments displayed appropriate calibration labels.

The procedures for sample receipt and despatch to the relevant contract laboratories were adequately controlled. Certificates of analysis for the specified testing were reviewed by QA and used in consideration for the batch release. Where applicable, compendial test methods were employed. Test method validation was the responsibility of the contract laboratories but the inspector observed the appropriate method validation was not available for non-compendial methodology (Deficiency 10).

Retention samples of raw materials and finished products were stored in accordance with GMP requirements.

Specifications were available for all starting materials, in process materials and finished products. Specifications for raw materials were based on BP monographs where applicable. An out-of-specification result required investigation by the relevant contract laboratory and procedures were in place to perform retesting and/or resampling if appropriate. The management of out of specification (OOS) results was controlled by the non-conformance procedures discussed earlier (Deficiency 2b).

GMP Pharmaceuticals had a procedure available that detailed arrangements for on-going stability testing of some finished products. Representative samples were taken for stability purposes and stored in appropriate conditions. A selection of stability programs were reviewed by the inspector and were deemed satisfactory. Where applicable, it was the sponsor's responsibility to manage stability testing of their products which was included in the GMP agreement with GMP Pharmaceuticals.

Contract Manufacture and Analysis	Current GMP agreements were in place with all sponsors, vendors and contract testing laboratories. The inspector reviewed a selection of agreement documents which were considered appropriate for contract arrangements in place. Both agreements were current and had five year validity.
Complaints and Product Recall	A suitable procedure and corresponding form was in place for the recording and investigation of customer complaints. Investigation and tracking of complaints was performed by QA. GMP Pharmaceuticals had a recall procedure, SOP QA 0127a, in place that appropriately identified responsible personnel and requirements for investigation. This inspector identified an issue with the recall process that needs to be addressed (Deficiency 9). GMP Pharmaceuticals had not been involved with any recall activities since the last inspection. The inspector reviewed the recall rehearsal report which was deemed satisfactory.
Self Inspection	The manufacturer had a documented system for self-inspection conducted by QA personnel. A pre-approved inspection schedule was available and an inspection report was reviewed for compliance. QA conducted inspections of their areas of responsibility and there was no procedural requirement for independence of auditors (Deficiency 5a). The procedure did not consider appropriate timelines for action times relating to deficiencies observed (Deficiency 5b).
Compliance with Marketing Authorisations	A system was established to ensure that products met the requirements of the marketing authorisation at the time of product introduction. Thereafter, compliance was verified during routine release for supply. Product sponsors were required to supply a copy of the ARTG listing.
Specific Annexes	The Annexes of the Standard applicable to the inspection were Annexes 7, 8, 9, 15 and 19.

Areas/processes not inspected: None

Other specific issues identified: None

Site Master File
GMP Pharmaceuticals provided Site Master File version 011, issued June 2015, for review. The document covered all aspects of the site and was acceptable.

Miscellaneous

Samples taken: None

Distribution of Report: GMP Pharmaceuticals Pty Ltd, TGA electronic file no. PH14/11942

Attachments: None

List of Deficiencies observed during the inspection

Critical deficiencies:
None observed

s47G

s47G

Comments

The inspection was performed by s22 . The final report was written by s22 based on the inspection notes taken on 01-04 March 2016.

A review of the inspection documentations indicated that a licence variation application, MI-2015-LI-03934-1, was received prior to the inspection. This variation was for the inclusion of the following steps in manufacturer;

- Chemical testing of non-sterile listed therapeutic goods in the form of all dosage forms at GMP Pharmaceuticals primary site, 7 – 9 Amax Ave, Girraween.
- Storage & secondary packaging only of non-sterile listed therapeutic goods in the form of all dosage forms at an additional site at s22

s22 inspection notes did not include adequate evidence to support this licence variation application. The notes did not contain any mention of the suitability of the warehouse at 14 Amax Ave, Girraween, nor did they contain any reference to GMP Pharmaceuticals ability to conduct chemical testing activities.

An additional on-site inspection, restricted to the steps in manufacturer encompassed by licence variation application, MI-2015-LI-03934-1, will be required.

Summary and conclusions

Assessment of manufacturer's responses

A response to the deficiencies reported to the manufacturer was received on 5th June 2016. Following requests for further information, a final satisfactory response was received on 16th September 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.

Final evaluation and recommendations:

1. The manufacturer operates in accordance with the relevant GMP requirements.

2. TGA records have been updated to show a final compliance rating of your facility of A2: basic compliance with the manufacturing standard established under the Therapeutic Goods Act *1989*.

3. The next re-inspection is expected to be performed within 20 months.

(Signed electronically; contains no visible signature)

s22
Manufacturing Quality Branch
Date: 21st September 2016
Tel: s22
@tga.gov.au

DEFINITIONS

Marketing Authorisation

Compliance with regulatory requirements specified on the ARTG and any other requirements imposed by a relevant Delegate of Secretary upon product listing or registration.

Examples of regulatory requirements include but not limited to the following: compliance with registered formulations, special storage and transportation conditions, shelf life, labelling, batch release testing requirements etc.

Critical Deficiency

A deficiency in a practice or process that has produced, or may result in, a significant risk of producing a product that is harmful to the user. Also occurs when it is observed that the manufacturer has engaged in fraud, misrepresentation or falsification of products or data.

Major Deficiency

A non-critical deficiency that:

- has produced or may produce a product which does not comply with its marketing authorisation; and/or
- indicates a major deviation from the Good Manufacturing Practice; and/or
- indicates a major deviation from the terms of the manufacturing licence or GMP approval (overseas manufacturers); and/or
- indicates a failure to carry out satisfactory procedures for release of batches; and/or
- indicates a failure of the person responsible for QA/QC to fulfil his/her duties; and/or
- consists of several other deficiencies, none of which on its own may be major, but which may together represent a major deficiency and should be explained and reported as such.

Other Deficiency

A deficiency that cannot be classified as either critical or major, but indicates a departure from good manufacturing practice.

A deficiency may be "other" either because it is judged as minor, or because there is insufficient information to classify it as major or critical.

One-off minor lapses or less significant issues are usually not formally reported, but are brought to the attention of the manufacturer.

Note:

1. Classification of a deficiency is based on the assessed risk level and may vary depending on the nature of products manufactured, e.g. in some circumstances an example of major deficiency may be categorised as critical.
2. A deficiency that was reported at a previous inspection and not corrected may be reported in a higher classification.

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Australian Government
Department of Health
Therapeutic Goods Administration

Manufacturing Quality Branch

Inspection attendance sheet

Manufacturer name:	GMP Pharmaceuticals
Manufacturer address:	7-9 Amax Avenue, Girraween NSW 2145
Inspection type:	Re-inspection
Inspection date/s:	1-4/03/2016
Inspector/s:	s22
Inspection standard:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products - 15 January 2009

Opening meeting starting time:
Closing meeting starting time:

Name *(please print)*	Position *(please print)*	Opening meeting *(initials)*	Closing meeting *(initials)*
s22			

Australian Government

Department of Health
Therapeutic Goods Administration

s22

GMP Pharmaceuticals Pty Ltd
7-9 Amax Ave
Girraween, NSW 2145

Ref: Trim 2016/025070.

s22

RE: SPECIAL GMP INSPECTION of GMP Pharmaceutical Pty Ltd

Please find attached the inspection report for the inspection that took s22 , Girraween NSW site on 12 December 2016 .

Should you have any questions regarding the inspection, please do not hesitate to contact me.

Yours sincerely

(Signed electronically; contains no visible signature)

s22

Manufacturing Quality Branch
Date: 23/12/2016

Tel: s22
@tga.gov.au

Australian Government

Department of Health
Therapeutic Goods Administration

Manufacturer:	GMP Pharmaceuticals Pty Ltd
Inspected site/s:	Primary Site: 7-9 Amax Ave, Girraween, NSW 2145 Secondary site: s22
Activities carried out by manufacturer:	☑ Manufacture of finished medicinal product ☐ Manufacture of intermediate or bulk ☐ Packaging ☐ Laboratory testing ☐ Release for supply ☐ Other:
Type of inspection:	☐ Initial inspection ☐ Re-inspection ☐ Full inspection ☑ Special inspection Applicable sections of the *Therapeutic Goods Act 1989*: ☐ section 37(2)(b) (licence application) ☐ section 40B(10)(a) (licence variation) ☑ section 40(4)(b) (re-inspection of licensed site) ☐ section 25(1)(g) (overseas in relation to registration) ☐ sections 26(1)(g), 26A(3) (overseas in relation to listing)
Scope of Inspection	Inspection of batch s47G Bio Island s47G capsules and associated retention sample and records
Inspection date/s:	12 December 2016
Inspector/s:	s22
Manufacturing Standard used:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products - 15 January 2009
References:	Manufacturing Licence number: MI-2015-03934-1 MIS number: MI-2016-LI-08420-1 File reference number/s: 2016/025070

Introduction

GMP Pharmaceuticals Pty Ltd, hereafter referred to as GMP Pharmaceuticals, is a contract manufacturer of listed therapeutic goods, with core business being soft gel capsule production. Other dosage forms are produced on site including tablets, herbal teas, hard shell capsules, powders and liquids. The facility is equipped for primary and secondary packaging but products are also supplied in bulk for packaging by third parties.

The manufacturer currently employs approximately 100 people and manufactures human and veterinary medicines, as well as food products. In addition to their TGA licence, the site holds a manufacturing licence from the APVMA and HACCP certification. Approximately 75% of the products manufactured at the Girraween site are for therapeutic use.

Date of previous inspection: 5/10/2016 Special inspection and 01-04 March 2016 Re-inspection

Names of inspectors involved in previous inspections: 5/10/2016 s22), 01-04 March 2016 s22)

Brief report of the inspection activities undertaken

Scope of inspection

The scope of the inspection was to review packed batch s47G Bio Island s47G capsules s47G , bulk batches used in the packed batch, and batch retention samples

Inspected areas

Batch document review of Bio Island s47G capsules s47G including quality control and retention samples inspection.

Personnel met during the inspection

Refer to the attached attendance record

Inspection findings and observations

Major changes since the previous inspection: No changes since last inspection

Future Planned Changes: s22 s22

Action taken since the last inspection: working on correction of last inspection

Quality Management	Not inspected
Personnel	Not inspected
Premises and Equipment	s22
Documentation	A review of batch s47G Bio Island s47G softgel noted no issues with the completion of documents and batch release. Related bulk batch documents were

additionally reviewed, bulk batches s47G through to s47G and no issues were found. The inspectors suggested improvements to the bill of materials design so to accommodate multiple lot numbers of each item.

Production	Not inspected
Quality Control	Quality control records in relation to batch s47G were reviewed and no issues were recorded. The retention samples of Bio island s47G bulk batches s47G through to s47G and those for the finished product batch s47G were inspected for any damages and contamination. No defects were found with the samples. However, the inspector noted that the air conditioning was switched off in the room. The company stated that this was an error as the light switch was adjacent to the air-conditioning switch. A work order would be raised to change the switch location to avoid this error from reoccurring.
Contract Manufacture and Analysis	Not inspected
Complaints and Product Recall	Not inspected
Self Inspection	Not inspected
Compliance with Marketing Authorisations	Not inspected
Specific Annexes	No Annexes of the Standard were applicable to this inspection

s22

[redacted]

Site Master File
Not reviewed at this inspection

Miscellaneous

Samples taken:
None

Distribution of Report: GMP Pharmaceuticals and TGA Trim file2016/025070.

Attachments:

Attendance records

List of Deficiencies observed during the inspection
None

Comments

Summary and conclusions

Assessment of manufacturer's responses
Not applicable

Final evaluation and recommendations:

With respect to this special inspection regarding Bio Island batch s47G , there were no issues noted.

(Signed electronically; contains no visible signature)

s22

Manufacturing Quality Branch
Date: 23/12/2016

Tel: s22
E-mail: tga.gov.au

DEFINITIONS

Marketing Authorisation

Compliance with regulatory requirements specified on the ARTG and any other requirements imposed by a relevant Delegate of Secretary upon product listing or registration.

Examples of regulatory requirements include but not limited to the following: compliance with registered formulations, special storage and transportation conditions, shelf life, labelling, batch release testing requirements etc.

Critical Deficiency

A deficiency in a practice or process that has produced, or may result in, a significant risk of producing a product that is harmful to the user. Also occurs when it is observed that the manufacturer has engaged in fraud, misrepresentation or falsification of products or data.

Major Deficiency

A non-critical deficiency that:

- has produced or may produce a product which does not comply with its marketing authorisation; and/or
- indicates a major deviation from the Good Manufacturing Practice; and/or
- indicates a major deviation from the terms of the manufacturing licence or GMP approval (overseas manufacturers); and/or
- indicates a failure to carry out satisfactory procedures for release of batches; and/or
- indicates a failure of the person responsible for QA/QC to fulfil his/her duties; and/or
- consists of several other deficiencies, none of which on its own may be major, but which may together represent a major deficiency and should be explained and reported as such.

Other Deficiency

A deficiency that cannot be classified as either critical or major, but indicates a departure from good manufacturing practice.

A deficiency may be "other" either because it is judged as minor, or because there is insufficient information to classify it as major or critical.

One-off minor lapses or less significant issues are usually not formally reported, but are brought to the attention of the manufacturer.

Note:

1. Classification of a deficiency is based on the assessed risk level and may vary depending on the nature of products manufactured, e.g. in some circumstances an example of major deficiency may be categorised as critical.
2. A deficiency that was reported at a previous inspection and not corrected may be reported in a higher classification.

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Department of Health
Therapeutic Goods Administration

Manufacturing Quality Branch

Inspection attendance sheet

Manufacturer name:	GMP Pharmaceuticals Pty Ltd
Manufacturer address:	Primary Site 1: 7-9 Amax Avenue, Girraween NSW 2145
	Secondary Site: s22
	Site under review/application received: s22
Inspection type:	Special Inspection
Inspection date/s:	~~5-8 December 2016~~ 12 DECEMBER 2016
Inspector/s:	s22
Inspection standard:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products - 15 January 2009

Opening meeting starting time: 9:30 AM
Closing meeting starting time: 16:40 PM

Name *(please print)*	Position *(please print)*	Opening meeting *(initials)*	Closing meeting *(initials)*
s22			

Australian Government

Department of Health

Therapeutic Goods Administration

s22
s22
GMP Pharmaceuticals Pty Ltd
7-9 Amax Ave
Girraween, NSW 2145

Dear s22

RE: Inspection of GMP Pharmaceuticals Pty Ltd Manufacturer's Tracking Number: MI-2015-LI-03934-1

Please find attached the inspection report for the inspection that took place at your Girraween site on 05th October 2016.

Your responses to the deficiencies reported in the post inspection letter have been evaluated and have been accepted. Effective implementation will be reviewed at the next GMP inspection.

Should you have any questions regarding the inspection, please do not hesitate to contact me.

Yours sincerely

(Signed electronically; contains no visible signature)

s22
GMP Inspector
Manufacturing Quality Branch
Date: 18th January 2017

Tel: s22
Mobile: s22
E-mail: s22 @tga.gov.au

Manufacturer:	GMP Pharmaceuticals Pty Ltd
Inspected site/s:	Primary Site: 7-9 Amax Ave Girraween, NSW 2145 Secondary site 1: s22 [redacted]
Activities carried out by manufacturer:	☑ Manufacture of finished medicinal product ☐ Manufacture of intermediate or bulk ☐ Packaging ☐ Laboratory testing ☐ Release for supply ☑ Other: Laboratory activities are restricted to physical and chemical testing
Type of inspection:	☐ Initial inspection ☐ Re-inspection ☐ Full inspection ☑ Special inspection Applicable sections of the Therapeutic Goods Act 1989: ☐ section 37(2)(b) (licence application) ☑ section 40B(10)(a) (licence variation) ☐ section 40(4)(b) (re-inspection of licensed site) ☐ section 25(1)(g) (overseas in relation to registration) ☐ sections 26(1)(g), 26A(3) (overseas in relation to listing)
Scope of Inspection	• Chemical testing, in addition to physical testing, of listed therapeutic goods in all dosage forms at the primary site located at 7-9 Amax Ave, Girraween, NSW 2145. • Storage, secondary packaging, and release for supply of s22 [redacted]
Inspection date/s:	05 October 2016
Inspector/s:	s22 [redacted] and s22 [redacted]
Manufacturing Standard used:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products - 15 January 2009
References:	Manufacturing Licence number: MI-21042005-LI-000516-1 Variation Application number: MI-2015-LI-03934-1 File reference number/s: PH16/4333 (inspection file), 2014/012527 (licence file)

Introduction

GMP Pharmaceuticals Pty Ltd, hereafter referred to as GMP Pharmaceuticals, is a contract manufacturer of listed therapeutic goods, with core business being soft gel capsule production. Other dosage forms are produced on site including tablets, herbal teas, hard shell capsules, powders and liquids. The facility is equipped for primary and secondary packaging but products are also supplied in bulk for packaging by third parties.

The primary manufacturing site is located at 7-9 Amax Avenue with secondary site Unit 1/29 Amax Avenue used for storage of all dosage forms of therapeutic goods.

In addition to their TGA licence, the site holds a manufacturing licence from the APVMA and HACCP certification. Manufacture of veterinary chemical products is conducted under APVMA licence number 2205. These activities were not included in the scope of this special inspection.

Date of previous inspection: 01 – 04 March 2016

Names of inspector involved in previous inspection: s22

Major changes since the previous inspection: GMP Pharmaceuticals has acquired equipment and personnel with the capability of chemistry testing of finished product. An additional secondary site at Unit 1, 2 and 3/14 Amax Avenue has been developed to add to the existing manufacturing licence.

Brief report of the inspection activities undertaken

Scope of inspection

The inspection was conducted to review compliance to the PIC/S GMP Guide for current operations at GMP Pharmaceuticals under licence variation application MI-2015-LI-03934-1:

- Chemical testing, in addition to physical testing, of listed therapeutic goods in all dosage forms at the primary site located at 7-9 Amax Ave, Girraween, NSW 2145.
- s22
- Change dosage form Dried Herbs to Tea.
- Update Head of Production to Daniel Xu and site contact to John Peverill.

Inspected areas

The inspection reviewed all activities and areas related to the scope of the inspection for compliance to the PIC/S Guide to GMP for Medicinal Products - 15 January 2009.

s22 at 7-9 Amax Avenue were the specific areas inspected.

Personnel met during the inspection

Refer to attached meeting attendance record.

Inspection findings and observations

Quality Management

GMP Pharmaceuticals had an established quality management system (QMS) that generally met the requirements of the PIC/S GMP Guide as evidenced during routine inspection MI-2015-LI-03739-1. It was confirmed with the manufacturer that the previously inspected QMS at 7-9 Amax Avenue will be adopted for the s22 The QMS was not inspected in its entirety during this special inspection. s22

s22

This was highlighted as a major breach of GMP compliance (Deficiency 1).

Although an acceptable change control procedure was available, along with a corresponding form and register there were issues identified relating to change management (Deficiency 2).

s22 atch release was restricted to QA Manager or delegate authorised to release for supply and were suitably trained for this task. The release for supply process was not covered in detail during this inspection.

Personnel

The key personnel remain the same for GMP Pharmaceuticals with the senior management team at 7-9 Amax Avenue responsible for activities at 14 Amax Avenue. There was no significant change in organisational structure as this is not site specific. A new QC laboratory supervisor had been employed to manage the introduction of chemistry testing at 7-9 Amax Avenue. The training program for new laboratory analysts will consist of SOP training combined with on-the-job training. It was discussed with the Quality Manager that the evidence of results should be incorporated into the training records for the laboratory.

Gowning requirements were appropriate in the controlled area of the 14 Amax Avenue facility. Personnel entering the therapeutic packaging area wore hairnets, shoe covers and over garments. Adequate hand washing and sanitising facilities were provided.

Premises and Equipment

s22

s22

s22

In general, the warehouse area was well maintained and materials within were stored in an orderly manner.

s22 [redacted]

An external contractor (Ecolab) managed pest control across the 14 Amax Avenue facility in a similar program as 7-9 Amax Avenue. The pest control system included rodent bait stations (external and internal) and spraying with approved pesticides. The procedure required inspections of devices and checks for ingress every month. Records were available to demonstrate that pest control services were conducted. The inspectors observed evidence of opening to the facility (open windows, poor door seals), which could allow for pest infestations (Deficiency 4b and 4c).

The company used a similar system for secure waste disposal as 7-9 Amax Avenue s22 [redacted]

Documentation

The document control system from 7-9 Amax Avenue was in place to administer the generation, approval, issue and review of GMP related documents at the s22 [redacted] Controlled, paper-based versions of all necessary documents were available at the point of use in the inspected areas; however, the inspector identified issues with some documentation requirements (Deficiency 4a and 5).

Production

s22 [redacted]
release for supply as a secondary site to 7-9 Amax Avenue. The warehouse at 1/29 Amax Avenue receives starting material, packaging materials, intermediate and bulk products which were entered into a goods receipt logbook and Pronto – a computerised inventory control system.s22 [redacted]

s22 [redacted] s22 [redacted]

Secondary packaging was conducted with the use of both manual and semi-automatic packing processes. Specific packing instructions for each product, along with SOPs for equipment operation will be adopted from 7-9 Amax Avenue ensuring appropriate checks are recorded during production; including area/line clearance, cleaning, identity of starting materials, equipment performance tests, and material reconciliation.s22 [redacted]

All bulk manufacturing and primary packaging was performed at 7-9 Amax Avenue which was not covered during this inspection.s22 [redacted]

s22 [redacted]

The Pronto computerised inventory control system was only used to manage inventory which had password protection and access controls. Computer validation was not covered during this inspection.

GMP Pharmaceuticals managed rejected materials via the use of reject labels, secure storage in an exclusive area and use of a rejected goods log. The reject goods form included an area to document the return or secure destruction of rejected materials.

Quality Control

Quality control testing on site was limited to physical tests such as uniformity of weight, disintegration, friability and hardness. As part of this inspection, the capability for 'in-house' chemistry analysis was reviewed. The main laboratory had been modified with additional work-benches and a purified water system to support wet chemistry testing. The purified water system was subject to regular calibration and maintenance records were up-to-date.

A dedicated instrument room had an HPLC, GC, AA, FTIR, UV/Vis, pH meters, analytical balances and a Karl Fisher titrator all of which was suitably calibrated and maintained. There were operational SOP's and usage logs for each piece of equipment. The GC and HPLC were new instruments that were installed by the vendor (Agilent). Appropriate equipment qualification was conducted and documented with support provided by the vendor. The inspector reviewed the GC qualification report, which was appropriately documented with no deviations recorded during execution. System suitability is performed for each test run.

Method development was on-going and validation test data will be compared with routine tests being performed at the contract laboratories. A suitable procedure for test method validation was approved for use in the laboratory. There was no completed method validation at the time of the inspection.

Finished products were sampled by the production department during the production activities. A QC sample number was generated and samples were stored appropriately in the laboratory and kept for a 1 month period after testing has been completed. Reference standards were stored according to the required conditions. Working standards were generated from a batch with at least 1 year expiry remaining and handled in accordance to an approved procedure. No herbal standards were available as this product type is tested at a contract laboratory.

Most of the automated equipment e.g. GC and HPLC, had software and data storage systems, which were controlled on networked computers. The data management associated with these systems was the responsibility of the QC laboratory manager. There was no formalised procedure or policy to ensure that electronic data relating to QC analysis was handled in accordance with GMP requirements (Deficiency 8). This was discussed at length with the Quality Manager and QC Laboratory supervisor.

Where applicable test data is entered into laboratory notebooks, which was peer-reviewed prior to result entry into batch records. Certificates of Analysis from contract laboratories were also reviewed prior to entering data into batch records, which was the current system for chemistry testing. The inspector

checked a soft gel capsule batch record for compliance of this system with no issues identified.

There was no change required for specifications, which were available for starting materials, in process materials and finished products. This area was not covered during this inspection.

An out-of-specification (OOS) procedure with investigation report from was reviewed by the inspection team. The investigation system guided the laboratory to perform appropriate actions in the event of an OOS result being reported.

Self Inspection The manufacturer had a documented system for self-inspection conducted by QA personnel. A recent facility inspection report (Sep 2016) was reviewed by the inspector. The report was a checklist of the condition on a number of facility items. There were poor conditions recorded for the HVAC system with no actions to address the poor condition. This was discussed with the Quality Manager and concluded that the condition was acceptable but pressure differentials were at the lower end of the allowable specification.

Specific Annexes The Annexes of the Standard applicable to the inspection were Annexes 8, 11 and 15.

Areas/processes not inspected: Manufacturing activity at 7-9 Amax Avenue and s22 .

Other specific issues identified: None

Site Master File
GMP Pharmaceuticals provided Site Master File version 011, issued June 2015, for review. The document covered all aspects of the site and was acceptable.

Miscellaneous

Samples taken: None

Distribution of Report: GMP Pharmaceuticals Pty Ltd, TGA electronic file no. PH16/4333

Attachments: Inspection Attendance Sheet

List of Deficiencies observed during the inspection

Critical deficiencies:
None observed

s47G

s22

s47G

s22

s47G

s47G

a. s22

s47G

5. s47G

b. s22

d. s47G

s47G [redacted]

b. s22 [redacted]

7. s47G [redacted] s22 .

8. s47G [redacted]

Comments

None

Summary and conclusions

Assessment of manufacturer's responses

A response to the deficiencies reported to the manufacturer was received on 2nd November 2016. Following requests for further action, a final satisfactory response was received on 9th December 2016. During special inspection of GMP Pharmaceuticals MI-2016-LI-08420-1 on 12th December 2016, corrective actions relating to storage of therapeutic goods at 14 Amax Avenue were not evidenced at the facility. Further actions, including risk assessment, were requested from the manufacturer to ensure corrective actions were implemented effectively. This information was received on 12th January 2017.

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.

Final evaluation and recommendations:

1. The manufacturer operates in accordance with the relevant GMP requirements.

2. TGA records have been updated to show a final compliance rating of your facility of A2: satisfactory compliance with the manufacturing standard established under the *Therapeutic Goods Act 1989.*

3. As discussed during the inspection and throughout the close out process, the following variations to your Licence for approved steps in manufacture, known as authorisations under section 40A of the Therapeutic Goods Act 1989, or variations to conditions under section 40 of the Therapeutic Goods Act 1989, have been submitted to the delegate for approval:

For the Primary Site 7-9 Amax Ave:

No	Manufacturing Type	Sterility	Manufacturing Class	Dosage Form	Product Code	Manufacturing Step
1	Medicine manufacture	Non Sterile	Multiple manufacturing steps/Multiple products	Powder	Listed Therapeutic Good	Full Product Manufacture - excluding Microbiological Testing
2	Medicine manufacture	Non Sterile	Multiple manufacturing steps/Multiple products	Solid Unit Dosage Forms	Listed Therapeutic Good	Full Product Manufacture - excluding Microbiological Testing
3	Medicine manufacture	Non Sterile	Multiple manufacturing steps/Multiple products	Semi Solids	Listed Therapeutic Good	Full Product Manufacture - excluding Microbiological Testing
4	Medicine manufacture	Non Sterile	Multiple manufacturing steps/Multiple products	Liquids	Listed Therapeutic Good	Full Product Manufacture - excluding Microbiological Testing
5	Medicine manufacture	Non Sterile	Multiple manufacturing steps/Multiple products	Capsule, soft	Listed Therapeutic Good	Full Product Manufacture - excluding Microbiological Testing
6	Medicine manufacture	Non Sterile	Multiple manufacturing steps/Multiple products	Tea	Listed Therapeutic Good	Full Product Manufacture - excluding Microbiological Testing

Addition of Secondary Site Unit 1, 2, 3/14 Amax Ave:

No	Manufacturing Type	Sterility	Manufacturing Class	Dosage Form	Product Code	Manufacturing Step
1	Medicine manufacture	Non Sterile	Multiple manufacturing steps/Multiple products	All Dosage Forms	Listed Therapeutic Good	Secondary packaging
2	Medicine manufacture	Non Sterile	Multiple manufacturing steps/Multiple products	All Dosage Forms	Listed Therapeutic Good	Storage
3	Medicine manufacture	Non Sterile	Multiple manufacturing steps/Multiple products	All Dosage Forms	Listed Therapeutic Good	Release for supply

If approved, the Licence will be re-issued with these amendments.

4. The next re-inspection is expected to be performed within 6 months. This heightened inspection frequency is due to repeated deficiencies observed during special inspection MI-2016-LI-08420-1 conducted on 12th December 2016.

(Signed electronically; contains no visible signature)

s22
s22
Manufacturing Quality Branch
Date: 18th January 2017

Tel: s22
Mobile: s22
E-mail: s22 @tga.gov.au

DEFINITIONS

Marketing Authorisation

Compliance with regulatory requirements specified on the ARTG and any other requirements imposed by a relevant Delegate of Secretary upon product listing or registration.

Examples of regulatory requirements include but not limited to the following: compliance with registered formulations, special storage and transportation conditions, shelf life, labelling, batch release testing requirements etc.

Critical Deficiency

A deficiency in a practice or process that has produced, or may result in, a significant risk of producing a product that is harmful to the user. Also occurs when it is observed that the manufacturer has engaged in fraud, misrepresentation or falsification of products or data.

Major Deficiency

A non-critical deficiency that:

- has produced or may produce a product which does not comply with its marketing authorisation; and/or
- indicates a major deviation from the Good Manufacturing Practice; and/or
- indicates a major deviation from the terms of the manufacturing licence or GMP approval (overseas manufacturers); and/or
- indicates a failure to carry out satisfactory procedures for release of batches; and/or
- indicates a failure of the person responsible for QA/QC to fulfil his/her duties; and/or
- consists of several other deficiencies, none of which on its own may be major, but which may together represent a major deficiency and should be explained and reported as such.

Other Deficiency

A deficiency that cannot be classified as either critical or major, but indicates a departure from good manufacturing practice.

A deficiency may be “other” either because it is judged as minor, or because there is insufficient information to classify it as major or critical.

One-off minor lapses or less significant issues are usually not formally reported, but are brought to the attention of the manufacturer.

Note:

1. Classification of a deficiency is based on the assessed risk level and may vary depending on the nature of products manufactured, e.g. in some circumstances an example of major deficiency may be categorised as critical.
2. A deficiency that was reported at a previous inspection and not corrected may be reported in a higher classification.

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Australian Government
Department of Health
Therapeutic Goods Administration

Manufacturing Quality Branch

Inspection attendance sheet

Manufacturer name:	GMP Pharmaceuticals
Manufacturer address:	7-9 Amax Avenue, Girraween NSW 2145
Inspection type:	Special inspection
Inspection date/s:	05th October 2018
Inspector/s:	s22
Inspection standard:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products - 15 January 2009

Opening meeting starting time: 9:10
Closing meeting starting time: 16:15

Name (please print)	Position (please print)	Opening meeting (initials)	Closing meeting (initials)
s22			