Australian Government
Department of Health
Therapeutic Goods Administration

[redacted]
Quality Assurance Manager
GMP Pharmaceuticals Pty Limited
60 Huntingwood Drive
Huntingwood NSW 2148

Dear [redacted]

RE: Initial GMP Inspection of GMP Pharmaceuticals Pty Limited

Please find attached the inspection report for the inspection that took place at your Huntingwood, NSW site on 29 – 31 January 2020.

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 and authorised by

[redacted]
Senior Inspector
Manufacturing Quality Branch
Date: 9th April 2020

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

Australian Government
Department of Health
Therapeutic Goods Administration

Inspection Report

Manufacturer:	GMP Pharmaceuticals Pty Limited
Inspected site/s:	60 Huntingwood Drive Huntingwood NSW 2148
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	Full product manufacture of non-sterile listed medicines in the form of tablets - oral disintegrating Storage of all non-sterile listed medicines dosage forms Testing of all non-sterile listed medicines dosage forms
Inspection date/s:	29 – 31 January 2020
Inspector:	s22 [redacted]
Manufacturing Standard used:	PIC/S Guide to GMP for Medicinal Products (PE-009-13)
References:	Manufacturing Licence Application Number: MI-2019-LI-01002-1 File reference number/s: PH19/50656 (inspection file), E19-518787 (licence file)

Introduction

GMP Pharmaceuticals Pty Ltd, hereafter referred to as GMP Pharmaceuticals, is a contract manufacturer of listed therapeutic goods. The company holds two licences to manufacture therapeutic goods for sites in Sydney. Medicinal product manufacture across these sites at 7-9 Amax Ave and 14 Amax Ave, Girraween NSW, include 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. The Girraween sites also manufacture food and cosmetic products.

GMP Pharmaceuticals purchased 60 Huntingwood Drive, Huntingwood NSW from Sony Corporation in mid-2018. The site is located in an industrial area 7 kilometres west of the Girraween sites. Sony had used the site for the manufacture of digital media such as CDs, DVDs and BluRay discs. The facilities have been modified to undertake the manufacture of food and pharmaceutical products.

Activities at the Huntingwood site at the time of inspection encompassed GMP Pharmaceuticals administration functions, including the company's head office, and storage of milk products for export.

The new licence application to manufacture therapeutic goods encompassed storage, microbiological testing, and chemical and physical testing of all listed medicine dosage forms; and full product manufacture of freeze-dried mouth dispersible tablets.

Other activities proposed for the site included manufacture of dry powder and liquid dairy products.

Date of previous inspection: N/A

Names of inspector involved in previous inspection: N/A

Brief report of the inspection activities undertaken

Scope of inspection

The inspection was conducted to review compliance to the PIC/S Guide to GMP for Medicinal Products (PE-009-13) for new licence application MI-2019-LI-01002-1 at GMP Pharmaceuticals Pty Limited site at 60 Huntingwood Drive, Huntingwood NSW, as below:

Manufacturing Type	Sterility	Dosage Form	Product Category	Manufacturing Step
Medicine manufacture	Non Sterile	Tablet, orally disintegrating	Listed Therapeutic Good	Finished Product Manufacture
Medicine manufacture	Non Sterile	All Dosage Forms	Listed Therapeutic Good	Storage
Medicine manufacture	Non Sterile	All Dosage Forms	Listed Therapeutic Good	Testing

The application did not encompass the manufacture of medicines listed for export that include substances at a level only permitted in medicines contained within schedules 2, 3, 4 & 8 of the Poisons Standard.

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 inspection attendance sheet.

Inspection findings and observations

Quality Management

GMP Pharmaceuticals had an established Pharmaceutical Quality System (PQS) in use at its Girraween sites that met the requirements of the PIC/S GMP to Guide. The Huntingwood site has implemented a separate PQS, based on the existing system.

A Quality Manual was available that documented the sites Quality Policy and outlined GMP Pharmaceuticals' approach to management reviews. Management

reviews were conducted twice yearly.

GMP Pharmaceuticals had a standalone quality risk management (QRM) procedure. QRM principles had also been incorporated into procedures associated with deviations, change control and complaints. The QRM procedure included tools to help assess severity and probability; however, it did not consider the detectability of identified risks when evaluating the potential impacts.

A procedure was available for the management of quality incidents and deviations. The system included impact assessment, and corrective and preventative actions (CAPA). A form and register was available to assist with the recording and investigating deviations, and CAPA effectiveness checks.

A procedure for the management of proposed changes was available. The procedure adequately addressed all cGMP requirements associated with changes including an initial assessment of likely impacts and associated risks. The inspector noted the Change Control procedure contained examples of what would constitute a major or minor change; however, some of the examples of minor changes could have a direct impact on product quality, such as changes to starting materials or new equipment introduction. The inspector discussed with staff that these would not constitute 'minor' changes.

A procedure for the preparation of product quality reviews (PQRs) was available. The procedure encompassed all cGMP requirements. The inspector noted the procedure did not ensure products with low production volumes would undergo adequate review (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.

Personnel

An organisation chart was available that demonstrated 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. These job descriptions did not encompass all cGMP responsibilities (deficiency 5).

A training program was available that included induction and GMP training, and job related development. Regular GMP refresher training was implemented. The effectiveness of training activities was evaluated by oral, written or task based evaluations and individual records were kept for all employees; however, training plans did not outline the type of training required, or the method to be used to determine effectiveness of the training (deficiency 6).

The manufacturer had implemented appropriate arrangements for personal hygiene practices, including clothing of personnel and visitors in the controlled manufacturing areas. Gowning requirements were acceptable including hairnets, facemasks, gloves, coveralls and dedicated factory shoes. Hand washing facilities were available prior to entry to the manufacturing rooms.

All employees were subjected to a medical assessment on recruitment. GMP Pharmaceuticals also had an illness policy that precluded staff from working in production areas with any infections, lesions, wounds or injuries that had not been adequately treated or dressed. These arrangements were acceptable.

Premises and Equipment

The 2.7 hectare site featured a single building, car parks and landscaped areas. The built structure was approximately 25 years old with a total floor area of 17 200 square metres. Production, warehousing and laboratory areas were situated on the ground floor and encompassed 80% of the building's floor space. Office areas occupied the remaining floor space on the first floor.

The site had appropriate warehousing facilities for the receipt and storage of

starting materials, packaging components, and storage of 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.

All storage areas were temperature monitored, and suitable controlled-temperature storage facilities were available for temperature sensitive materials. The system for monitoring and recording temperatures and humidity in all storage areas was acceptable.

A dedicated sampling area was available in Warehouse 2. The area was undergoing final fit out at the time of inspection. The inspector reviewed the construction and design of the area and found it acceptable. The sampling room will be supplied with HEPA filtered air and contained by an airlock. Documentation was available for review that detailed appropriate room qualifications, and room cleaning and sampling arrangements.

Manufacture and packaging of freeze-dried tablets was undertaken in purpose built production clean rooms, which were installed within the existing warehouse space. The production rooms were assembled from aluminium sandwich panels and were finished with epoxy coated floors, coving at all joints, and covered lights to ensure smooth internal surfaces. The production facility was divided into manufacturing and packaging areas, each with separate air lock entries.

The tablet manufacturing area featured a central corridor off which separate processing rooms were located. Freezers, and the vacuum freeze-drier, were sited in the large central corridor. Separate manufacturing rooms were accessed from the central corridor for dispensing, blending, tablet mould filling and demoulding activities.

The packaging area had separate rooms for primary and secondary packaging activities.

All production and packaging areas were suitably designed and constructed for the production of freeze-dried tablets.

The design and construction of all production and packaging equipment reviewed was suitable with inert product contact surfaces.

Personnel and material flows were appropriate for the activities undertaken on site. 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 programs and associated schedules in place that covered maintenance and calibration of equipment and utilities. Procedures associated with these activities were incorporated into the respective work instructions for each piece of equipment, and tasks are to be added to the respective schedules during the finalisation of qualification activities.

The Heating Ventilation Air Conditioning (HVAC) systems for the production clean rooms were fitted with pre-filters and final filters of an appropriate grade. The HVAC prevented the ingress of untreated air by the use of airlocks and positive pressure differentials to the outside. Appropriate pressure differentials were defined between adjacent production rooms. Staff manually monitored the HVAC during production using magnehelic gauges. Humidity was controlled and monitored in critical areas encompassed by tablet demoulding and primary packaging. The inspector reviewed documentation associated with the qualification of the HVAC system and identified some issues (deficiencies 1d & 1e).

A reverse osmosis purified water system was available, which was undergoing

qualification at the time of inspection. The design and construction of the system was acceptable for recirculating water at ambient temperature to points located within the production areas. Qualification, operation and maintenance activities, and sanitation processes, were not documented (deficiencies 1c & 3a).

There was a compressed air unit available, supplying air to the production environments. Outlets were fitted with terminal filters and underwent routine monitoring. The compressed air system had been qualified; however, no operation procedure was available (deficiency 3b).

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, secure and controlled manner.

Documentation

GMP Pharmaceuticals had systems in place that covered the generation, approval, issue and control of GMP related documents. Review periods were defined. Documentation was generally available as controlled hard copies. Virtual copies of procedures were made available to staff as pdf files via the manufacturers intranet. The inspector noted issues with the control of blank forms at site (deficiency 7).

Specifications for starting materials and finished products were available for the food products currently manufactured at site. These documented approved supplier/s, key quality attributes and acceptance criteria. Site QA and clients will review specifications for compliance with default standards prior to use in medicinal product manufacture. These arrangements were acceptable.

GMP Pharmaceuticals Technical Development staff generated master batch records (MBRs) following production trials. QA reviewed and approved these for use. Hard copy production/packaging batch documents were prepared by photocopying the MBRs. These activities were appropriately controlled via QA review prior to issue to production.

The inspector's review of production processes and batch records, which had been prepared and used for food production, indicated some issues (deficiency 9).

Records were to be retained for appropriate time periods.

Computerised systems

GMP Pharmaceuticals utilised several GMP critical computer systems. These included laboratory data acquisition systems, electronic document storage, spreadsheet registers, 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 some data management and validation requirements for computerised systems; however, some issues were identified (deficiency 2).

Production

The inspector reviewed all production activities relating to the full product manufacture of non-sterile freeze-dried tablets. Processes reviewed included dispensing, cooking/agitation, aeration, deposition, freezing, freeze-drying, sorting and unmoulding. Packaging activities were limited to packaging of tablets into alu/alu sachet blisters.

GMP Pharmaceuticals had a system in place for the assessment of suppliers of raw materials. This system included an evaluation of the material manufacturer via a desktop assessment process, and testing of initially supplied samples.

All production and packaging procedures reviewed indicated activities will be appropriately managed and controlled. Proposed in-process controls were appropriate for the products to be manufactured and packaged.

GMP Pharmaceuticals had established detailed instructions for the operation and cleaning of all manufacturing equipment. Usage and cleaning records were in place. Cleaning status labels were in use for most equipment, although, not present on some smaller equipment (deficiency 8).

Rejected goods were adequately controlled on-site.

Rework of product was restricted to packaging activities. These activities were adequately controlled by a procedure.

Returned goods could be considered for rework; however, the evaluation of the returned product did not include critical product quality events (deficiency 10).

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 control.

GMP Pharmaceuticals had a Validation Master Plan (VMP); however, the VMP did not addressed all of the requirements of the manufacturing standard (deficiency 1b).

Risk assessments included in project plans associated with implementation of medicinal product manufacture at Huntingwood identified equipment with direct product contact. The inspector's review of protocols and completed equipment qualifications indicated these activities were generally well controlled; however, some issues were noted (deficiencies 1 & 2).

A validation plan was available for process validation studies of freeze-dried tableting production processes. Studies encompassed three consecutive production batches and included critical quality attributes.

GMP Pharmaceuticals had established a cleaning validation plan that included consideration of allergens, product colourants and solubility, and microbial load. The overall philosophy for the cleaning validation studies was acceptable and included clean hold time studies.

Quality Control

GMP Pharmaceuticals planned to conduct chemical, physical and microbiological testing of all dosage forms at the Huntingwood site. At time of inspection, the laboratory fit-out in the QC and microbiological laboratories was completed and some new equipment and instrumentation was undergoing qualification. GMP Pharmaceuticals planned to transfer all QC equipment from the existing Girraween QC laboratory.

The implementation of testing activities at the Huntingwood site was appropriately controlled by well documented laboratory commissioning and project plans. The QC Laboratory had progressed to Phase II of the project, which entailed decommissioning the QC laboratory in Girraween and transferring, installing and qualifying equipment at the Huntingwood site. The Microbiological Laboratory was at Phase I, without an autoclave or biosafety cabinet. Both were purchased and planned for installation and qualification by end April 2020. Project plans outlined procedures, training, calibration, qualification and preventative maintenance requirements that needed implementation prior to commencing testing activities at site.

The QC and Microbiological laboratories were adequately separated from each other, and well separated from production areas.

The arrangements for receipt, registration and storage of samples was not

	reviewed. Appropriate storage was available for retention samples. Records or qualification protocols were available to demonstrate that most laboratory equipment was appropriately qualified, calibrated and maintained. Some issues were identified with the qualification of laboratory based computerised systems (deficiencies 1a, 2a & 2b). There were procedures in place for the investigation of out of specification (OOS) results, which included a laboratory investigation and a broader investigation in production if no assignable laboratory cause was identified. Procedures were available to control the validation and/or transfer of analytical test methods, and verification of microbiological test methods. GMP Pharmaceuticals' arrangements for on-going stability testing were summarised in a procedure. Storage and testing of stability samples was currently outsourced to contract testing laboratories; however, the manufacturer planned to move testing to the site laboratories once fully operational. The QC Laboratory demonstrated good control of laboratory reagents, volumetric solutions and chemical reference materials. No reference cultures were currently in use at the site; however, an acceptable procedure was available for maintenance of reference cultures. The Micro Laboratory initially planned to use pre-purchased plates, as no autoclave was available at site. These arrangements were acceptable. A procedure was available for the preparation and quality control of microbiological media.
Outsourced Activities	GMP Pharmaceuticals had technical agreements in place with the vendors of outsourced activities that had a potential to impact product quality. An acceptable GMP agreement was in place with the manufacturer's existing client. Preparation of GMP agreements was outlined in a procedure, which outlined the relevant responsibilities for each party.
Complaints and Product Recall	GMP Pharmaceuticals had a procedure for receiving, recording, investigating and completing client complaints. The procedure included an evaluation of risk to other batches of product; however, possible counterfeiting of product was not considered (deficiency 11). GMP Pharmaceuticals had a recall procedure in place that required reconciliation of product and confirmation of destruction; however, the procedure did not encompass all recent requirements of the Uniform Recall Procedure for Therapeutic Goods (deficiency 12).
Compliance with Marketing Authorisations	The inspector reviewed the release for supply procedure during the inspection and found it to be suitable in ensuring market authorisation of products would be met.
Self Inspection	The manufacturer had a procedure available to control self-inspections. These were to be conducted by trained personnel, or consultants, on a risk based frequency.
Specific Annexes	The Annexes of the Standard applicable to the inspection were Annexes 8, 11, 15 and 19.

O*t*her specific issues identified: None

Site Master File
GMP Pharmaceuticals provided Site Master File, SMF001, version 2, issued January 2020, 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. PH19/50656

Attachments: Inspection Attendance Sheet

List of Deficiencies observed during the inspection

Critical deficiencies:
None observed

Major deficiencies:

1. The requirements of the Principle of Annex 15 that it is a GMP requirement that manufacturers control the critical aspects of their particular operations through qualification and validation over the life cycle of the product and process were not fully met, as evidenced by the following:
    a. Qualification activities had not always considered all stages, from initial development of the user requirements specification through to the end of use of the equipment, facility, utility or system. For example, URS had not been prepared for new equipment in the QC laboratory outlining the essential elements of quality to act as a point of reference throughout the validation life cycle (Annex 15 § 3.2 & Annex 11 § 4.4).
    b. The inter-relationship between documents in complex validation projects were not clearly defined (Annex 15 § 2.3).
    c. There was no operational/performance qualification protocol available for review for the purified water system that defined the critical systems, attributes and parameters, and the associated acceptance criteria for the system to ensure it was capable of consistently delivering purified water of an acceptable quality to the distribution points within production (Annex 15 § 2.4).
    d. Validation protocols for the HVAC Performance Qualification (PQ) did not define the critical attributes and parameters, and the associated acceptance criteria. Specifically, the non-viable testing requirements outlined in PQ protocol FDUPQ001 for HVAC system at the site documented an acceptance criteria of ISO 8; however, no details of the specific attributes to be tested or sampling point locations were documented (Annex 15 § 2.4).
    e. HVAC PQ protocol FDUPQ001 contained no review or conclusion of the validation, and the results obtained were not summarised against the acceptance criteria (Annex 15 § 2.9).

2. The requirements of Annex 11 concerning computerised systems used as part of GMP regulated activities were not fully met as evidenced by the following:
    a. There was no listing of all relevant computerised systems and their GMP functionality (inventory). For critical systems (e.g. CDS) there was no up-to-date system description detailing the physical and logical arrangements, data flows and interfaces with other systems or processes, any hardware and software pre-requisites, and security measures (Annex 11 § 4.3).
    b. Documentation reviewed at inspection for Chromeleon software did not fulfil the validation documentation and report requirements of Annex 11 § 4, and did not demonstrate adequate computerised system controls that had been implemented. For example, no validation protocols, reports or procedures were documented to demonstrate the following were appropriately controlled;
        i. User levels defined, implemented and verified to ensure the system recorded the identity of operators entering, changing, confirming or deleting data (Annex 11 § 12.4).
        ii. Integrity and accuracy of backup data verified, and the restoration of data checked (Annex 11 § 7.2).

iii. Audit trails implemented and procedures available to control and document their review (Annex 11 § 9).
iv. Logical controls in place to restrict access to electronic methods to authorised persons. For example, access to chromatographic instrument/acquisition/ processing methods restricted to ensure alterations to test methods are controlled (Annex 11 § 12.1).

c. Qualification of the freeze drier did not encompass the PLC associated with the equipment. The freeze drier procedure outlined multiple access levels for the PLC; however, no evidence of appropriate test scenarios was available to demonstrate the user access levels had been verified during qualification (Annex 11 § 4.7).
d. Electronic data was not always secured by either physical or electronic means against damage. For example, Excel spreadsheets used as registers for some QA activities such as deviations, change controls and complaints were password protected; however, this did not protect GMP critical data as the password protections did not restrict, or allow tracking of, data deletion or modification.

3. The requirements of clause 4.29 that there should be written policies, procedures, protocols, reports and the associated records of actions taken or conclusions reached, where appropriate, for maintenance, cleaning and sanitation activities; and clause 4.30 that clear operating procedures should be available for major items of manufacturing and test equipment, were not fully implemented. For example;
    a. The following procedures were not available for the purified water system;
        i. Operation procedure
        ii. Sanitisation procedure
        iii. On-going monitoring procedure
    b. There was no operation procedure available for the compressed air system.

Other deficiencies:

4. The requirements of clause 1.10 that regular periodic or rolling quality reviews of all authorised medicinal products should be conducted, and such reviews should normally be conducted and documented annually, were not fully met. For example, the Product Quality Review procedure (QA0028.V01) did not ensure products with low production volumes (less than 2 batches/ year) would be subjected to review at least every two years.

5. The requirements of clause 2.3 pertaining to personnel; that people in responsible positions should have specific duties recorded in written job descriptions were not fully met. For example, job descriptions for key personnel did not encompass all cGMP responsibilities to ensure no gaps or unexplained overlaps in the responsibilities of those personnel occurred. Responsibility for activities such as qualification, validation, training and environmental monitoring were not recorded in the job descriptions for key personnel at site.

6. The requirements of clause 2.11 pertaining to training; that newly recruited personnel should receive training appropriate to the duties assigned to them, continuing training should also be given and its practical effectiveness should be periodically assessed, and training records should be kept, were not fully met. For example, the training plan did not outline the type of training required for individual staff, or the method to be used to determine effectiveness of the training i.e. a requirement for on-the-job training, and its practical assessment, for personnel conducting critical activities such as release for supply or production activities.

7. The requirements of clause 4.1 that appropriate controls for electronic documents such as templates, forms, and master documents should be implemented to ensure the integrity of the record throughout the retention period were not fulfilled, as the issue of blank forms was not uniformly controlled across the site. For example, forms used in the warehouses were not adequately controlled to allow detection of missing pages or reproduction of data.

8. The requirements of clause 5.12 that at all times during processing, all materials, bulk containers, major items of equipment and rooms used should be labelled or otherwise identified with an indication of the product or material being processed, its strength (where applicable) and batch number, and the stage of production, were not fully met. For example, clean tags/labels were not present on some smaller equipment in the production area such as tablets moulds and dispensing tools. There was no other means of identifying this equipment as clean.

9. The requirements of clause 4.20b that the Batch Processing Record should be based on the relevant parts of the currently approved Manufacturing Formula and Processing Instructions, and should contain the dates and times of commencement of significant intermediate stages, and of completion of production, were not fully implemented. For example;
    a. Batch records did not clearly record or evaluate the overall production processing time to ensure the process had been complete within the 6 hour timeframe that had been determined to ensure GMP.
    b. Clocks were not available in the production areas to ensure times were accurately recorded in batch documents. Further, there was no process available to ensure all clocks across the site displayed consistent time.

10. The requirements of clause 5.65 that products returned from the market and which have left the control of the manufacturer should be destroyed unless without doubt their quality is satisfactory; they may be considered for re-sale, re-labelling or recovery only after they have been critically assessed by the Quality Control Department, and the nature of the product, any special storage conditions it requires, its condition and history, and the time elapsed since it was issued should all be taken into account in this assessment, was not fully met. For example, the Returned Goods procedure (QA0025.V01) permitted rework of returned product; however, the evaluation of the returned product did not consider such product quality critical events as storage conditions the material had been subjected to whilst out of the control of GMP Pharmaceuticals Pty Ltd.

11. The requirement of clause 8.7 that special attention should be given to establishing whether a complaint was caused because of counterfeiting was not fully met as the Complaint procedure did not include this consideration.

12. The requirements of clause 8.10 that the written procedures used to organise any recall activity should be regularly checked and updated when necessary, were not fully met as the Recall procedure (QA0010.V01) did not encompass the most recent requirements of the Uniform Recall Procedure for Therapeutic Goods (URPTG) (V2.0, October 2017).

Summary and conclusions

Assessment of manufacturer's responses

A response to the deficiencies reported to the manufacturer was received on 6th 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 steps in manufacture, known as authorisations under section 40A of the *Therapeutic Goods Act 1989,* have been submitted to the delegate for approval:

- Full product manufacture of non-sterile listed medicines in the form of tablets - oral disintegrating
- Storage of all non-sterile listed medicines dosage forms
- Testing of all non-sterile listed medicines dosage forms.

The licence will not authorise the manufacture of medicines listed for export that include substances at a level only permitted in medicines contained within schedules 2, 3, 4 & 8 of the Poisons Standard.

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 12 months of this inspection.

5. The duration of the next inspection is estimated at this time to be 3 days.

Signed and authorised by

s22 [redacted]
Senior Inspector

Manufacturing Quality Branch

Tel: s22 [redacted]
Mobile: 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.

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:	60 Huntingwood Drive HUNTINGWOOD NSW 2148
Inspection type:	Initial Inspection
Inspection date/s:	29 – 31 January 2020
Inspector/s:	s22
Inspection standard:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products (PE009-13)

Opening meeting starting time: 29/1/2020 9.20.
Closing meeting starting time: 31/1/2020 10.40

Name *(please print)*	Position *(please print)*	Opening meeting *(initials)*	Closing meeting *(initials)*
s22	Head of Quality	s22	
	Engineering Supervisor		
	QA Manager		
	Group Chief Operating Offic		
	Site Manager		
	Production supervisor		
	QA Manager		

Australian Government
Department of Health
Therapeutic Goods Administration

s22
Quality Manager
GMP Pharmaceuticals Pty Limited
60 Huntingwood Drive
Huntingwood NSW 2148

Ref: E20-91019

Dear s22

RE: GMP Inspection of GMP Pharmaceuticals Pty Limited

Please find attached the inspection report for the inspection that took place at your Huntingwood, NSW site on 10-13th May 2021.

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 and authorised by

s22
Lead Inspector
Manufacturing Quality Branch
Date: 23rd August 2021

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

Australian Government
Department of Health
Therapeutic Goods Administration

Inspection Report

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References:	Manufacturing Licence Number: MI-2019-LI-01002-1 Licence Variation Number: MI-2020-LI-13501-1 File reference number/s: PH20/3533 (inspection file), E19-518787 (licence file)

Introduction

GMP Pharmaceuticals Pty Ltd, hereafter referred to as GMP Pharmaceuticals, is a manufacturer of listed therapeutic goods. The company holds two TGA licences to manufacture therapeutic goods for sites in Sydney. The company's main site at Girraween NSW includes 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.

GMP Pharmaceutical's Huntingwood NSW site was initially licenced in 2020 and is located in an industrial area approx. 7 kilometres west of the Girraween facility. The facilities have been commissioned for the manufacture of food and listed therapeutic goods. Initial therapeutic goods manufactured at the site were orally disintegrating tablets processed by specialised freeze drying equipment. The site continues to expand its operation to include additional solid unit dosage forms. Other activities for the site included manufacture of dry powder and liquid dairy products.

Date of previous inspection: 29 – 31 January 2020

Names of inspector involved in previous inspection: s22 [redacted]

Brief report of the inspection activities undertaken

Scope of inspection

The inspection was conducted to review compliance to the PIC/S GMP Guide Part 1 (PE009-14) for operations at GMP Pharmaceuticals Pty Ltd's Huntingwood site in relation to the licence MI-2019-LI-01002-1. The licence included the following:

- Finished product manufacture of non-sterile listed medicines in the form of tablets - oral disintegrating
- Storage of all non-sterile listed medicines dosage forms
- Testing of all non-sterile listed medicines dosage forms

In addition, the scope included licence variation application MI-2020-LI-13501-1:

Manufacturing Type	Sterility	Dosage Form	Product Code	Manufacturing Step
Medicine manufacture	Non Sterile	Powder	Listed Therapeutic Good	Finished Product Manufacture
Medicine manufacture	Non Sterile	Tablet, uncoated	Listed Therapeutic Good	Finished Product Manufacture
Medicine manufacture	Non Sterile	Tablet, chewable	Listed Therapeutic Good	Finished Product Manufacture

The application did not encompass the manufacture of medicines listed for export that include substances at a level only permitted in medicines contained within schedules 2, 3, 4 & 8 of the Poisons Standard.

Inspected areas

The inspection was conducted in accordance with an inspection plan presented to the company on site. This consisted of a review of the quality management system, warehousing, manufacturing and packaging processes, quality control, equipment calibration and maintenance, qualification and validation. All areas associated with the manufacture outlined in the scope of the inspection were reviewed.

Personnel met during the inspection

Refer to attached inspection attendance sheet.

Inspection findings and observations

Major changes since the previous inspection:

- New tablet room was built and commissioned.
- New Site Manager - s22 [redacted].
- New QA Team Leader - s22 [redacted]
- New Production Manager - s22 [redacted].
- New product introduction - s22 [redacted].

Future Planned Changes:

Significant expansion was underway with new controlled areas being constructed and equipment ordered to increase production capability at the site. Manufacturing capability to be expanded to include tablet coating and granulation processes.

Overview of inspection findings from last inspection and the corrective action taken:

The previous inspection findings were reviewed during this inspection and were found to have been satisfactory closed out with the exception of the deficiency 2 and 4, which required further corrections during this inspection.

Quality Management

GMP Pharmaceuticals had established a quality management system that generally met the requirements of the PIC/S GMP Guide. There were some deficiencies recorded against this manufacturing standard, these are noted in the relevant sections of this report.

A Quality Manual was available that documented the sites Quality Policy and outlined the site QMS and management responsibilities. Management reviews were conducted twice yearly, which incorporated senior management discussions on handling quality associated risks at the facility. Meeting minutes were formalised in the QMS and the inspector verified that minutes were maintained for the last meeting held in October 2020.

Quality risk management (QRM) activities were controlled by a procedure with individual risk assessments linked to other quality systems such as deviations and change management, where required. Risk assessments were formally documented in an associated form and the procedure outlined a systematic process for appropriate identification, assessment, evaluation and review of risks. The prominent risk assessment tool was a risk matrix approach. Evaluation of risks involved a rating process with considerations for severity and probability of the failure mode. The inspector raised an issue in relation to the definitions for risk ratings (Deficiency 5b(i)).

The manufacturer had a documented procedure for deviation management. The system was reported using Quality Incident Deviation Forms (QIDF) which were classified as critical, serious and standard after QA assessment. There were no critical deviations reported to date and only a few QIDRs had been reported due to the low level of GMP production at the site since the initial inspection. The inspector reviewed a QIDR associated with batch coding error. Root-cause analysis was effectively documented and the associated CAPA satisfactorily linked with the Quality Management System. The inspector did highlight an issue regarding the effectiveness of the deviation system (Deficiency 5a).

A procedure for the management of proposed changes was available. The procedure used the QRM process to evaluate risk of any proposed change. The inspector noted that change controls were not formally classified as major or minor but applied a risk level. Subject matter experts from relevant

departments reviewed all proposed changes prior to approval by QA. The inspector reviewed change control records associated with facility modifications, new product introductions and formulation changes. This review identified several issues with change management (Deficiency 3).

A procedure for the preparation of product quality reviews (PQRs) was available. No PQRs had been conducted since the initial inspection. The inspector noted some issues with the process (Deficiency 7).

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. No GMP batches had been released since the initial inspection.

Personnel

Key personnel were suitably experienced and effective in their roles with written job descriptions available for each position. These job descriptions did not encompass all cGMP responsibilities (Deficiency 13). The organisational chart (sighted in the Site Master File) was up-to-date and provided clear segregation between production and quality departments. The inspector checked the authorised signature of recently employed staff, which was satisfactorily maintained in records generated during employee induction.

A training program was available that included induction and GMP training, and job related development. Regular GMP refresher training was implemented. The effectiveness of training activities was evaluated by oral, written or task based evaluations and individual records were kept for all employees; however, the inspector identified some issues with the training program (Deficiency 4).

The manufacturer had implemented appropriate arrangements for personal hygiene practices, including clothing of personnel and visitors in the controlled manufacturing areas. Gowning requirements were acceptable including hairnets, facemasks, gloves, coveralls and dedicated factory shoes. Hand washing facilities were available prior to entry to the manufacturing rooms.

All employees were subjected to a medical assessment on recruitment. GMP Pharmaceuticals also had an illness policy that precluded staff from working in production areas with any infections, lesions, wounds or injuries that had not been adequately treated or dressed. These arrangements were acceptable.

Premises and Equipment

The manufacturing premises consisted of a large sized unit with total floor area of 17,200m^2 in a light industrial zone. The floor plans for this site were available and reviewed at the inspection. The design and size of the premises was adequate for the manufacturing operations performed. Production, warehousing and laboratory areas were situated on the ground floor. Further expansion of production areas were being constructed at the time of inspection.

The warehouse area was of a suitable size with multiple levels of racking installed to maximise storage capacity in the area. A total of three warehouse areas were available under the same building. The warehouse area was temperature monitored to <30°C by monitors at pre-defined locations. The general housekeeping in the warehouse was acceptable.

Secure areas were available for pre-printed packaging and returned goods. There was a rejected goods area in the Warehouse 2 that was empty at the time of inspection. The inspector noted an issue with this arrangement (Deficiency 14).

A dedicated sampling area was available in Warehouse 2. The sampling area was supplied with HEPA filtered air and contained a material airlock and gowning room. The gowning area into the sampling room was appropriately equipped and the sampling booth was adequate for the materials being handled. Stainless steel utensils were used during sampling of raw materials. There was a separate sampling room used for packaging components. Warehouse 3 was temperature controlled for storage of temperature sensitive materials where required. There was also a 0-4°C cool room and -18°C freezers but these was currently used for food products only.

The controlled manufacturing areas were located within the main production building. The entry to the controlled area had an appropriate hand-washing and gowning facility. The manufacturing rooms maintained negative air pressure (>5Pa) to the manufacturing corridor to prevent cross contamination. Suitably sized airlocks were available for the transfer of material between controlled and uncontrolled areas. The inspector did not an issue on the monitoring program for some airlocks (Deficiency 6a).

The production rooms were assembled from aluminium sandwich panels and were finished with epoxy coated floors, coving at all joints, and covered lights to ensure smooth internal surfaces. The production facility was divided into manufacturing and packaging areas, each with separate air lock entries.

A common corridor led to the various manufacturing rooms. There was a dedicated dispensary room with suitably calibrated weighing equipment. Daily performance checks were conducted to verify balance accuracy. The blending room was adjacent to the dispensary and was equipped with rotary bin blending equipment (500L).

The wash bay area was well maintained and provided sufficient cleaning facilities for production equipment. The wash bay had an automated mould washer and compressed air for equipment drying. An equipment drying/storage room was available next to the wash bay, where the inspector observed appropriate storage of cleaned items.

There was a formulation room for the mixing and cooking of starting materials. Specialised solid/liquid mixers were connected to stainless steel vessels. The formulation equipment included 2 x missing vessels, 1 x CIP vessel and a holding vessel. The holding vessel was hard piped to the filling line in an adjacent room.

Filling operations for orally disintegrating tablets was conducted in a dedicated room. The line was operated via PLC and had a single pass-through cooling system. Product was filled into silicon moulds with fill weight checks conducted.

A -40°C walk-in freezer and two vacuum freeze-driers were available in the large central corridor. The transfer of moulds between each area was facilitated by ceiling rails. The two freeze-dryers were similar models with automated programs defined for each product. To date, only Vmores Sleep had been validated for the freeze-drying process.

Tablet compression equipment was available in a dedicated manufacturing room. The equipment was vacuum fed and had metal detection capability. Tablet testing equipment such as a balance, hardness tester, disintegration and friability apparatus were available.

All of the rooms and equipment within the manufacturing areas were clean with good housekeeping observed. Batches of product currently under manufacture were identified on status boards or tags.

The packaging areas were adjacent to the manufacturing zone and accommodated an automated sachet packing line for freeze-dried products and a powder filling line. There was equipment available for vacuum leak testing used for integrity checks on the sealed foil packs. Secondary packaging of freeze-dried products was conducted by hand into plastic bottles. Both the powder and freeze-dried tablet packaging lines were equipped with x-ray detectors.

The design and construction of packaging and ancillary equipment was generally acceptable with predominantly inert product contact surfaces and appropriate capacities for the production processes undertaken on site.

GMP Pharmaceuticals had programs and associated schedules in place that covered maintenance and calibration of equipment and utilities. Procedures associated with these activities were incorporated into the respective work instructions for each piece of equipment, and tasks are to be added to the respective schedules during the finalisation of qualification activities.

The HVAC system in the manufacturing building had four air handling units (AHUs) supplying suitably filtered air to controlled areas. Each AHU was fitted with a G4 pre-filter, F8 intermediate filters and HEPA filters were installed for final filtration into the manufacturing areas. The inspector reviewed the qualification of the HVAC for the new tabletting area that was conducted in 2020/21, which was well documented and demonstrated the suitability of the air supply. The manufacturing areas were tested annually by a suitable external service provider. Records for non-viable particles demonstrated that ISO-8 limits were met and room pressures were also verified during annual certification.

A reverse osmosis (RO) water system provided the manufacturing area with purified water (PW). The sanitisation of the distribution system was performed weekly by an automated ozone treatment. Routine monitoring of the PW was conducted in accordance with the relevant BP monograph with additional monitoring for Pseudomonas, Coliforms and E coli. The 2020 PQ Phase 3 summary report for PW was available for review. The inspector noted that the system was in control based on the data from the monitoring program. The inspector highlighted an issue with the PW monitoring (Deficiency 6c-f).

The compressed air system was used in various machine operations with product contact surfaces impacted during product filling and bottle blowing prior to filling. The three compressors supporting the system were oil-free and appropriately maintained. The filtration design on the system was appropriate for its intended use. On-line 0.01µm filtration was installed at the point of use. The system had been qualified to demonstrate the quality of the air was suitable and was part of the monthly EM program.

There was a suitable pest control program in place and there was no evidence of pest infestation in any area of the facility. Ecolab, an external service provider, conducted monthly visits to support the pest control program and issued quarterly reports.

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

Documentation

Document control was performed according to an appropriate procedure and GMP related documents were effectively controlled by Quality Assurance using a paper-based system.

A comprehensive set of documentation including specifications, procedures, work instructions, methods, validation documentation, forms and batch manufacturing/packaging records was established. The writing, approval, issuing, distribution and revision of documents were performed in accordance with approved procedures. Controlled hard copies were issued for production areas where required.

SOP's and associated forms were required to be reviewed every three years. These reviews had been conducted as scheduled, or earlier if changes were required. The document register was adequately maintained by QA. Document updates were managed under the change control system.

There were appropriate specifications in place for all raw materials, packaging components and finished products. Test methods were available for the testing of these materials.

GMP Pharmaceuticals had defined periods for the retention of critical documentation. The inspector noted an inconsistency in the retention periods (Deficiency 9a).

The Technical Development staff generated master work orders following new product introduction. QA reviewed and approved these for use. Hard copy production/packaging batch documents were prepared by photocopying the work orders. There records were appropriate and included sufficient space for operators to record all required operations. Completed batch documents were formally reviewed by production and QA as part of the batch review process.

GMP Pharmaceuticals utilised GMP critical computer systems. These included laboratory data acquisition systems, electronic document storage, spreadsheet registers, 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 some data management and validation requirements for computerised systems; however, an issue with the control of computerised systems was highlighted (Deficiency 8b).

Production

The inspector reviewed all production activities relating to the full product manufacture of non-sterile freeze-dried tablets, powders and uncoated tablets. The operations of the facility were designed for manufacturing and packaging of solid unit dosage forms. The manufacturing processes were documented in procedures and batch documents that were appropriately controlled and were available in the production areas for completion at the time of operation.

Suppliers of starting materials were subjected to assessment with each new material requiring evaluation by the QA team at the GMP Pharmaceuticals Girraween site. A supplier qualification register was available on a controlled document. Initial qualification included questionnaires and a review of quality certificates, with the outcome of the vendor performance recorded by the QA team. The inspector identified some issues with the evaluation program (Deficiency 1a-f).

Material specifications were generated and TSE/BSE certification obtained prior to initial ordering of new materials. Where justified, reduced sampling and skip lot/rotational testing was implemented for starting materials. Records demonstrated that the sampling plans and testing requirements were not fully compliant (Deficiency 1g-i). All incoming lots were subject to critical tests with non-critical testing performed periodically.

The manufacturer had a program for the receipt, inspection and sampling of starting materials. Warehouse personnel checked starting material containers on receipt for seal integrity and damage prior to receipt into the inventory control system, Pronto. Identification of materials was controlled by labelling relevant details onto individual containers. A goods inwards number (GIN) was issued for each incoming material. The material status was appropriately managed through physical labelling of containers and segregated storage in the warehouse. Product labels were checked with the master record during receipt and samples retained as a reference. Label counts were verified at receipt. An issue with the label counter was noted (Deficiency 11).

Entry into the manufacturing area was appropriately managed with airlocks and gowning rooms that led to production corridors. Dispensing of starting materials was controlled by the manufacturing work orders and verified by a 2nd operator. Materials checked prior to dispensing to ensure they were the correct material and after weighing individual dispensing labels were assigned to the material. A review of records by the inspector demonstrated that the dispensary area was appropriately cleaned between each batch of dispensed material. Powders were dispensed into LDPE bags prior to blending.

Formulation of the freeze-dried products was conducted in large room with fixed equipment for the preparation (known as cooking) of product formulations. Critical process parameters were controlled via work orders. Vessels were cleaned using RO water on CIP programs.

After mixing, the bulk liquid for freeze fried products was transferred to a holding vessel that supplied the filling machine in the adjacent room. A start-up process was required to verify the fill weights prior to progressing to production of the filled moulds. Filled moulds were transferred to -40°C walk-in freezer for 5 hours prior to freeze drying. The inspector noted an issue with this process (Deficiency 6b). Once freeze-drying was completed, bulk tablets were manually removed from moulds in a dedicated room. Freeze dried products were packaged into aluminium foil sachets. Hourly seal integrity testing was conducted on the automated sachet packaging line to verify foil closure. Individual packs were check weighed after primary packaging.

The inspector observed packaging operations of milk products (non TGA) on a bottling line with 2 fill head configuration. An air knife was installed for cleaning of incoming empty bottles. The line was automated with x-ray, labelling and batch coding capability. Routine allergy monitoring was conducted on the line due to the dairy products being processed. Introduction of TGA products was planned for this area in the future.

Production processes and procedures were of an acceptable standard with appropriate batch records (work orders) available. Batch documentation incorporated essential activities such as batch reconciliation, line clearance and in-process checks. Room status and usage logs were clearly visible at the entry doors. Instructions were available for the operation, usage, and cleaning of major production equipment.

Limited manufacturing processes were in progress and observed by the inspector due to the low level of production since initial licencing and covid-19 restrictions. Adequate equipment was in-site for dispensing, blending, cooking,

freeze-drying, tablet compression and packaging. Each manufacturing activity was performed in dedicated rooms.

GMP Pharmaceuticals had established instructions for the operation and cleaning of all manufacturing equipment. Usage and cleaning records were in place.

Rejected goods were adequately controlled on-site. Rework of product was restricted to packaging activities. These activities were not adequately detailed by a procedure (Deficiency 9b).

Returned goods had not been received at the site to date. Adequate procedures were in place for handling returned goods if required.

An environmental monitoring program was in place for the controlled areas of the facility and the inspector observed from EM data that an appropriate level of control was being maintained. Microbial monitoring of the air was performed using settle plate and active air method. Microbial swabs were performed on surfaces in controlled areas. EM media (TSA) was supplied by a TGA licenced laboratory and they also performed the incubation/reading of samples. A monthly sampling regime was conducted to ensure all rooms were sampled on a regular basis. Appropriate action limits were applied to each sample type and any excursions were managed through the OOS system. The inspector identified some issues with the EM program was (Deficiency 6c-e).

There was an approved Validation Master Plan (VMP) available. The VMP detailed the manufacturer's approach to validation and addressed the validation of equipment, utilities, computer systems, test methods, cleaning and processes. The inspector highlighted some issues with the VMP (Deficiency 2a and 2b).

The inspector reviewed the equipment validation for the new tablet compression production line. Tablet compression equipment had been qualified to IQ/OQ status. PQ of the equipment was scheduled for process validation of products to be transferred from the Girraween site. No issues were noted with the equipment validation.

The validation studies for freeze-dried tableting production processes had been completed since the initial inspection. Studies encompassed three consecutive production batches and included critical quality attributes. The process was validated with three representative batches and included mixing times, critical quality attributes and inclusion of cleaning validation in the study. No issues were identified during this review. The inspector reviewed the cleaning validation of the 1000L cooking tank, which included visual inspection, bioburden, allergens and analysis of detergent residues. An issue was noted with the validation record (Deficiency 2e).

The inspector reviewed the validation of a selection of temperature controlled equipment including the freeze dryers. Some issues were highlighted during this review (Deficiency 2c-d).

Quality Control

GMP Pharmaceuticals had chemistry and microbiology laboratories on site engaged in testing starting materials, intermediates, bulk, and finished products. The laboratories were adequately segregated from production areas.

<u>Chemistry Laboratory</u>

The chemistry laboratory was designed with sample preparation benches and instrument areas. The laboratory was equipped with modern instruments suitable for the analysis required.

The laboratory managed sample receipts using a sample logbook, and samples were allocated to staff for testing following an electronic register. Laboratory staff analysed the samples in accordance with approved specifications and validated methods. Analysts recorded test results in work sheets that were adequately controlled.

All specifications and methods regarding the materials for this inspection were available for Vmores Sleep. Where in-house method was used, method validation was conducted. An in depth review of key methods identified an issue with method validation (Deficiency 2f).

Primary standards were purchased from reputable sources from which working standards were appropriately managed for routine use. A spreadsheet was in use to manage standards receipt, use, and expiry.

The laboratory was appropriately staffed and equipped for the operations being performed. Analytical equipment available included HPLCs, GCs, UV/Vis, IR, ICP, Karl Fischer, Sartorius PW system, along with other analytical instruments such as balances and pH meters. Some issues were observed with laboratory instruments (Deficiency 12).

The laboratory had usage logs and operation procedures for instruments. Chromeleon 7 was used for HPLC systems and was examined by the inspector for user management and the audit trail records. The inspector's review of system configuration identified some issues with the integrity of data (Deficiency 8a).

Instrument calibrations and maintenance were conducted internally and by external calibration services and vendors as required following the instrument calibration and maintenance schedule. The inspector reviewed selected instruments and noted that these had calibration status labels and were up to date for maintenance.

GMP Pharmaceuticals had an on-going stability program that was typically product specific but considered a grouping strategy to assess stability of finished products. The inspector reviewed the on-going stability SOP and current stability program for Vmores Sleep. The stability testing was outsourced to a contract laboratory including 25°C/60%RH product storage. The inspector noted an issue with on-going stability (Deficiency #9c).

A procedure regarding the management of out-of-specification (OOS) results was available. The procedure specified details in relation to the retesting and repeat testing of samples, and the basis for invalidating chemistry results was specified.

Microbiology Laboratory

The microbiology laboratory was limited in size and outsourced a number of tests to a contract laboratory. In-house microbiological function was generally limited to sampling of water and environmental samples, bioburden analysis of finished product and media preparation. The laboratory consisted of an autoclave, range of incubators, Elix purified water system and bioburden testing suite with 2 x LAF cabinets.

Microbiological media used by the laboratory was purchased from reputable vendors. The media was suitably prepared, stored and labelled. There was an approved procedure for the QC of microbiological media (growth promotion) which was being adhered to. The inspector noted that a production autoclave room was routinely used for the sterilisation of laboratory media and test items. There was an issue with this process (Deficiency 9d & 9f).

Temperature controlled equipment was available for all conditions required for the routine microbiology tests performed in the laboratory. The arrangements

for receipt, registration and storage of samples was reviewed. The inspector identified an issue with this arrangement (Deficiency 8c).

Procedures were available to control the method verification of microbiological test methods. The inspector reviewed the microbiology test method validation for Vmores Sleep and an issue was observed (Deficiency 2g).

Outsourced Activities

GMP Pharmaceuticals had a procedure in place for the management of outsourced activities. The procedure stated that such out-sourcing had to be covered by a written contract. The inspector noted agreements were in place for GMP service providers such as the contract laboratory (ALS) used for chemical and microbiological testing. The GMP agreements reviewed were appropriately controlled and reviewed periodically.

The inspector reviewed arrangements that were in place with product sponsors and other contract manufacturers. There was a GMP agreement in place with the main site at Girraween. Some issues were noted with this arrangement (Deficiency 1a).

Complaints and Product Recall

A procedure and corresponding form was in place for the recording and investigation of customer complaints, which were directed through product sponsors. Complaints were entered into the complaints register with no complaints reported as product had not been released to market. The inspector noted a minor issue with the complaint procedure (Deficiency 5bii).

GMP Pharmaceuticals had a recall procedure in place that appropriately identified responsible personnel and requirements for investigation of the product recalls. As a contract manufacturer, this process only covered stock held at the manufacturing site with distributed stock managed by the relevant sponsor. The procedure required that the effectiveness of the system was evaluated via mock recalls. The inspector identified some issues with the recall process (Deficiency 9c and 10).

Self Inspection

The manufacturer had a documented system to manage the self-inspection of the facility and GMP operations. Self inspections were conducted annually in accordance with a pre-approved inspection schedule. The scope of the audits was sufficient to cover systems and areas associated with the manufacture of medicinal products. A 2021 inspection schedule had been implemented and was in compliance with the procedure. The inspection program of critical outsourced activities such as contract laboratory testing was on a two-year schedule.

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. A review of formulations for compliance with market authorisation requirements was conducted during the inspection for Vmores Sleep AUSTL 353140. The manufacturing documentation and specifications were consistent with the current ARTG entries for the products reviewed.

Specific Annexes

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

Other specific issues identified:
There was no evidence to support the manufacture of granules or film coated tablets (licence variation application MI-2020-LI-13501-1) at the time of inspection. Significant expansion was underway with new controlled areas being commissioned and equipment ordered to increase production capability at the site. The manufacturer agreed to modify the MI-2020-LI-13501-1 application to vary the existing licence to include powder, uncoated and chewable tablet dosage forms only.

Site Master File
GMP Pharmaceuticals provided Site Master File SMF001 (version 3, issued February 2021) 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. PH20/3533

Attachments: Inspection Attendance Sheet

List of Deficiencies observed during the inspection

Critical deficiencies:
None observed

Major deficiencies:

1. The requirements of Clause 5.27 that the selection, qualification, approval and maintenance of suppliers of starting materials, together with their purchase and acceptance, should be documented as part of the pharmaceutical quality system, the level of supervision should be proportionate to the risks posed by the individual materials, taking account of their source, manufacturing process, supply chain complexity and the final use to which the material is put in the medicinal product. The supporting evidence for each supplier/material approval should be maintained was not fully met as evidenced by:
    a. The Huntingwood site relied on supplier approval program conducted at their sister site (Girraween) but this was not covered by the GMP agreement between the sites (Also refer to Clause 7.1).
    b. The periodic review of key suppliers in SOP QA0026 was not defined.
    c. The Approved Supplier List (ASL) was not up-to-date or adequately controlled in the QMS. In addition, the supplier & manufacturer's address was not stated in the ASL to fully identify the approved supply chain.
    d. For Jiaherb supplier; the questionnaire was reviewed by the Girraween site but there was no evidence that this had been accepted by the Huntingwood QMS.
    e. For Euromed; the supplier was currently being used for active ingredients (Passion Flower) without the completed questionnaire as required by SOP QA0038.
    f. For Magnesium Citrate, only the supplier (Redox) had answered the questionnaire. There was no assessment available for the manufacturer VASA Pharm.
    g. $\sqrt{n+1}$ was permitted for sampling containers of active materials from unqualified suppliers in SOP QA0038 (Also refer to Annex 8 §2).
    h. SOP QA0038 required full testing on the first three deliveries of new raw materials but did not specify for three different lots to ensure qualification testing covered lot-to-lot variability.
    i. Sampling of all containers (for ID) was not observed for the unqualified supply of the active ingredients Chamomile and Passion Flower from Jiaherb and Euromed respectively (Also refer to Annex 8 §2).

2. The requirements of Annex 15 §1.1 that all qualification and validation activities should be planned and take the life cycle of facilities, equipment, utilities, process and product into consideration were not fully met*. For example:
    a. Validation Master Plan VAL001 had not been updated for manufacture of tablets and powders.
    b. There was no VAL001 Appendix B available for process validation grouping.
    c. There was no protocol for the temperature mapping conducted in the warehouse in February 2021 (Also refer to Annex 15 §2.4).
    d. The -40°C walk-in freezer had not been considered for mapping studies to demonstrate uniformity of temperature throughout the unit (Also refer to Annex 15 §5.9).
    e. The Clean in Place (CIP) program was not referenced or defined in the Cleaning Study conducted on the 1000L cooking tank (Also refer to Annex 15 §10.4).
    f. Test method validation for Magnesium Content by ICP-OES (HW-AMVP-011) was performed on a hard shell capsule product (Dr Nature) with no justification for how this validated the Vmores Sleep product testing (Also refer to Clause 6.15).
    g. Microbiology method validation (V-MIC-PDT-0052) was conducted on a Vmores Sleep placebo product that did not include herbal components (Also refer to Clause 6.15).

    **A similar deficiency was observed in the previous inspection.*

3. The requirements of Annex 15 §11.4 that quality risk management should be used to evaluate planned changes to determine the potential impact on product quality, pharmaceutical quality systems, documentation, validation, regulatory status, calibration, maintenance and on any other system to avoid unintended consequences and to plan for any necessary process validation, verification or requalification efforts were not fully met as evidenced by the following:
    a. Change controls were not fully effective in detailing the actions required in order to control the implementation of change:
        i. CC20035 for the facility expansion did not state if change was major/minor. There was no implementation plan available in the change control. This was a significant site expansion project for new production lines/areas, which was in progress at the time of inspection. In addition, there was no risk assessment conducted to determine any impact on current production activity at the site.
        ii. CC20043 for the introduction of Vmores Sleep did not include the validation, stability, documents and training activity required to support the product introduction.
        iii. CC21020 for the Vmores Sleep formulation change did not have QA approval for implementation.
    b. Target dates were not assigned to action items or change controls to manage the progression and completion of changes.

Other deficiencies:

4. The requirements of Clause 2.11 that newly recruited personnel should receive training appropriate to the duties assigned to them, continuing training should also be given, and its practical effectiveness should be periodically assessed and that training programmes should be available, approved by either the head of Production or the head of Quality Control, as appropriate was not fully met as evidenced by*:
    a. The training program for release for supply qualification was not outlined in the Quality Management System. Training was limited to reading of the QA0029 SOP with no consideration of conducting an associated test or assessment of trainees' ability to perform RFS of all relevant dosage forms etc.
    b. The training system did not adequately cover practical effectiveness of training activity. For example, there was no practical training provided for the Freeze-Drying equipment and training was limited to procedural training by QA who were not the subject matter experts for this equipment/process.

c. There was no timeframe stated for the completion of induction training of new employees.

**A similar deficiency was observed in the previous inspection.*

5. The requirements of the Clause 1.4 (xiv) that a Pharmaceutical Quality System appropriate for the manufacture of medicinal products should ensure that appropriate level of root cause analysis should be applied during the investigation of deviations, suspected product defects and other problems and appropriate corrective actions and/or preventive actions (CAPAs) should be identified and taken in response to investigations, with the effectiveness of such actions monitored and assessed were not fully met as evidenced by:
    a. In relation to the Quality Incident Deviation Report (QIDR) system:
        i. The rejected batch of Vmores Sleep (H00603) was not subject to a formal investigation/QIDR. There were no actions recorded to show root cause analysis and CAPA to address the formulation issues that resulted in the batch rejection.
        ii. SOP QA0006 did not clearly reference the QIDR register (R4).
        iii. QA0006 did not adequately describe the planned and unplanned deviation process. The QIDF did not differentiate between these deviation types.
    b. In relation to the complaint investigation process SOP QA0013:
        i. There was an inconsistent approach for risk assessment of customer complaints. Critical, major and minor complaints were defined in QA0013 but did not occur in risk matrix, which used low, medium, high and extreme levels of risk. It was not clear how the risk levels aligned with the complaint categories.
        ii. The timelines for actions and closure of complaint investigations were not defined (Also refer to Clause 8.14).

6. The requirements of Clause 4.29 that there should be written policies, procedures, protocols, reports and the associated records of actions taken or conclusions reached, where appropriate, for environmental monitoring were not fully met. For example;
    a. Pressure differentials from the warehouse to material transfer airlock interface were not routinely monitored.
    b. The control parameter of temperature was not recorded in the batch record (MWO) for the -40°C freezer step.
    c. There were no alert limits established for water or environmental monitoring programs.
    d. There was no requirement to heighten the monitoring of water or the environment in the event of an Out of Specification (OOS).
    e. Microbial identification was not required for OOS reported on water or environmental monitoring.
    f. The trend reporting of water and environmental data was not formalised by procedure.

7. The requirements of Clause 1.10 and 1.11 pertaining to product quality reviews; that such reviews should normally be conducted and documented annually and quality reviews may be Pharmaceutical Quality System grouped by product type e.g. solid dosage forms, liquid dosage forms, sterile products, etc. where scientifically justified, were not fully met. For example:
    a. There were no timelines associated with the completion of Periodic Product Reviews (PQRs) in SOP QA0028.
    b. There was no grouping strategy for the PQRs. It was unclear if PQRs were required for each product.

8. The requirements of Clause 4.1 that complex systems need to be understood, well documented, validated, and adequate controls should be in place were not fully met. For example:
    a. The administration SOP-QC-0023 for this computerised system did not adequately define the users and their management in the laboratory (Also refer to Annex 11 §12).
    b. The computerised systems register did not include the version number of the GxP systems.

c. The Microbiology Lab used MSTEAMs for access to controlled forms. There was no evidence this system was validated and analysts could print multiple copies of test forms, which were not traceable.

9. The requirements of Clause 1.8 (iv) that instructions and procedures are written in an instructional form in clear and unambiguous language, specifically applicable to the facilities provided was not fully met as evidenced by:
    a. The Quality Manual stated that GMP documents were retained for 6 years. This conflicted with the retention times cited in QA0001 for Document Control i.e. 5 years.
    b. The rework procedure SOP QA0024 did not clearly define what processes were eligible for rework i.e. freeze-dried bulk product could not be reprocessed once freeze drying had occurred.
    c. The mock recall form QAF011 was not clearly linked to the SOP QA0010.
    d. The media preparation sheet (QCF) in the Microbiology laboratory incorrectly referenced SOP-MIC-0016.
    e. The stability program did not state the frequency of stability testing i.e. minimum of 1 batch per year (Also refer to Clause 6.32).
    f. The autoclave programs for media sterilisation in the Microbiology laboratory were not clearly defined in the associated SOP-MIC-0047.

10. The requirement of Clause 8.30 that the effectiveness of the arrangements in place for recalls should be periodically evaluated to confirm that they remain robust and fit for use was not fully met as the mock recall conducted in 2020 did not incorporate stock reconciliation of the recalled product.

11. The requirement of Clause 5.57 that checks should be made to ensure that any electronic code readers, label counters or similar devices are operating correctly was not fully met as the performance checks on the label counter were limited to annual calibration only.

12. The requirement of Clause 5.13 that labels applied to containers, equipment or premises should be clear, unambiguous and in the company's agreed format was not fully met as evidenced by:
    a. The QC balances external calibration labels did not align with the annual requirement in SOP QC 0032.
    b. There was no status label affixed to the 'unqualified' water activity meter in the QC laboratory.

13. The requirements of Clause 2.8(i) that the head of Quality Control generally has the following responsibilities; to approve or reject, as he/she sees fit, starting materials, packaging materials, intermediate, bulk and finished products was not met in the job description for QA Team Leader (draft), which, was proposed as the head of Quality Control.

14. The requirement of Clause 5.66 that rejected materials and products should be clearly marked as such and stored separately in restricted areas was not fully met as the rejected materials and returned goods section of the warehouse were not restricted access.

Summary and conclusions

Assessment of manufacturer's responses

A response to the deficiencies reported to the manufacturer was received on 16/07/2021. Following requests for further information, a final satisfactory response was received on 13/08/2021.

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, 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 with the addition of the following authorisations:

Manufacturing Type	Sterility	Dosage Form	Product Code	Manufacturing Step
Medicine manufacture	Non Sterile	Powder	Listed Therapeutic Good	Finished Product Manufacture
Medicine manufacture	Non Sterile	Tablet, uncoated	Listed Therapeutic Good	Finished Product Manufacture
Medicine manufacture	Non Sterile	Tablet, chewable	Listed Therapeutic Good	Finished Product Manufacture

   - Update the Head of QC to s22 [redacted].

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 of this inspection.

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

Signed and authorised by

s22 [redacted]
Lead Inspector

Manufacturing Quality Branch
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.

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:	60 Huntingwood Drive, Huntingwood, NSW 2148
Inspection type:	Re-Inspection & Licence Variation
Inspection date/s:	10 – 13 May 2021
Inspector/s	s22 [redacted]
Inspection standard:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products (PE009-14)

Opening meeting starting time: 09:25
Closing meeting starting time: 15:00

Name *(please print)*	Position *(please print)*	Opening meeting *(initials)*	Closing meeting *(initials)*
s22 [redacted]	Quality Manager	s22 [redacted]	
	Snr. QA Associate		
	QA Team Leader		
	Site Manager		

Australian Government
Department of Health
Therapeutic Goods Administration

s22
Quality Manager
GMP Pharmaceuticals Pty Limited
60 Huntingwood Drive
Huntingwood NSW 2148

Ref: E21-407636

Dear s22

RE: GMP Inspection of GMP Pharmaceuticals Pty Limited

Please find attached the inspection report for the special inspection that took place at your Huntingwood, NSW site on 5-6th May 2022.

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 and authorised by

s22
Lead Inspector
Manufacturing Quality Branch
Date: 4th July 2022

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

Australian Government
Department of Health
Therapeutic Goods Administration

Inspection Report

Manufacturer:	GMP Pharmaceuticals Pty Limited
Inspected site/s:	60 Huntingwood Drive, Huntingwood NSW 2148
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	Full product manufacture of non-sterile listed medicines in the form of granules, coated tablets and hard-shell capsules.
Inspection date/s:	5-6 May 2022
Inspector:	s22 [redacted]
Manufacturing Standard used:	PIC/S Guide to GMP for Medicinal Products (PE-009-14)
References:	Manufacturing Licence Number: MI-2019-LI-01002-1 Licence Variation Number: MI-2021-LI-10110-1 File reference number/s: PH21/4609 (inspection file), E19-518787 (licence file)

Introduction

GMP Pharmaceuticals Pty Ltd, hereafter referred to as GMP Pharmaceuticals, is a manufacturer of listed therapeutic goods. The company holds two TGA licences to manufacture therapeutic goods for sites in Sydney. The company's main site at Girraween NSW is approx. 7 kilometres from the Huntingwood facility.

GMP Pharmaceutical's Huntingwood NSW site was initially licenced in 2020 and is located in an industrial area. The facilities have been commissioned for the manufacture of food and listed therapeutic goods. Initial therapeutic goods manufactured at the site were orally disintegrating tablets processed by specialised freeze drying equipment. Since initial licencing the site has been developed to include additional solid unit dosage forms. This inspection was focussed on the introduction of coated tablets, granulation and hard-shell encapsulation. Other activities for the site included manufacture of dry powder and liquid dairy products.

Date of previous inspection: 10-13th May 2021

Names of inspector involved in previous inspection: s22 [redacted]

Brief report of the inspection activities undertaken

Scope of inspection

The special inspection was conducted to review compliance to the PIC/S GMP Guide Part 1 (PE009-14) for operations at GMP Pharmaceuticals Pty Ltd's Huntingwood site in relation to the Variation Application MI-2021-LI-10110-1, which included the following:

- Finished product manufacture of non-sterile listed medicines in the form of tablets - group
- Finished product manufacture of non-sterile listed medicines in the form of granules
- Finished product manufacture of non-sterile listed medicines in the form of hard-shell capsules

The application did not encompass the manufacture of medicines listed for export that include substances at a level only permitted in medicines contained within schedules 2, 3, 4 & 8 of the Poisons Standard.

Inspected areas

The inspection was conducted in accordance with an inspection plan presented to the company on site. This consisted of a review of the quality management system, manufacturing and packaging processes, qualification and validation in relation to the variation application MI-2021-LI-10110-1. All areas associated with the manufacture outlined in the scope of the inspection were reviewed. On-site inspection conducted on 5th May followed by close-out via MSTEAMs on 6th May.

Personnel met during the inspection

Refer to attached inspection attendance sheet.

Inspection findings and observations

Major changes since the previous inspection:

- Commissioning of new manufacturing and packaging areas
- Installation and qualification of tablet coating
- New dispensary area
- Installation and qualification of granulator
- Installation and qualification of encapsulation equipment
- RO water system upgrade

Future Planned Changes:

Transfer of products from Girraween site.

Overview of inspection findings from last inspection and the corrective action taken:

This was a special inspection only with limited scope on licence variation application. This did not include a review of previous inspection findings.

Quality Management

GMP Pharmaceuticals had established a quality management system that generally met the requirements of the PIC/S GMP Guide. There were some deficiencies recorded against this manufacturing standard, these are noted in the relevant sections of this report.

Quality risk management (QRM) activities were controlled by a procedure with individual risk assessments linked to other quality systems such as deviations and change management, where required. Risk assessments were formally documented in an associated form and the procedure outlined a systematic process for appropriate identification, assessment, evaluation and review of risks. The prominent risk assessment tool was a risk matrix approach. Evaluation of risks involved a rating process with considerations for severity and probability of the failure mode.

The manufacturer had a documented procedure for deviation management. The system was reported using Quality Incident Deviation Forms (QIDF) which were classified as critical, serious and standard after QA assessment. This inspection did not fully review the deviation system as only validation deviations associated with the new licence application covered.

A procedure for the management of proposed changes was available. The procedure used the QRM process to evaluate risk of any proposed change. Subject matter experts from relevant departments reviewed all proposed changes prior to approval by QA. The inspector reviewed change control records associated with facility modifications, new equipment and activities required to support the licence variation application. This review identified several issues with change management (Deficiency 1).

A procedure for the preparation of product quality reviews (PQRs) was available but this was not covered during this inspection.

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.

Personnel

Key personnel were suitably experienced and effective in their roles with written job descriptions available for each position. The organisational chart (sighted in the Site Master File) was up-to-date and provided segregation between production and quality departments. The inspector's review of personnel was focussed on the resourcing required to effectively manage the licence update to expand manufacturing authorisations at the site.

A training program was available that included induction and GMP training, and job-related development. The effectiveness of training activities was evaluated by oral, written or task-based evaluations and individual records were kept trained staff. Review of training was limited to new equipment introduced as part of the licence variation.

The manufacturer had implemented appropriate arrangements for personal hygiene practices, including clothing of personnel and visitors in the controlled manufacturing areas. Gowning requirements were acceptable including hairnets, facemasks, gloves, coveralls and dedicated factory shoes. Hand washing facilities were available prior to entry to the manufacturing rooms.

All employees were subjected to a medical assessment on recruitment. GMP Pharmaceuticals also had an illness policy that precluded staff from working in production areas with any infections, lesions, wounds or injuries that had not been adequately treated or dressed. These arrangements were acceptable.

Premises and Equipment

The manufacturing premises consisted of a large sized unit with total floor area of 17,200m^2 in a light industrial zone. The floor plans for this site were available and reviewed at the inspection. The design and size of the premises was adequate for the manufacturing operations performed. This inspection was limited to the site expansion which included the dry manufacturing area on the ground floor and tablet dispensary on the mezzanine floor.

The existing warehouse and dedicated materials sampling area was not included in the scope of this inspection.

The controlled manufacturing areas were located within the main production building. The entry to the controlled area had an appropriate hand-washing and gowning facility. The production rooms were assembled from expanded polystyrene panels and were finished with sealed floors, coving at all joints, and covered lights to ensure smooth internal surfaces.

A separate change area was available for the tablet dispensary on the mezzanine floor. This large dispensary area included a central corridor with two adjacent dispensary rooms with segregated wash bay and an equipment storage room. There was a material airlock that provided access to the warehouse area. There was also an initial processing room with calibrated weighing equipment. Daily performance checks were conducted to verify balance accuracy. The inspector noted some issues with this equipment (Deficiency 3). The dispensary rooms had sieving equipment and gravity feed to the lower-level floor.

The dry manufacturing area on the ground floor consisted of a wet granulation room, blending areas equipped with stainless steel IBC rotators, multiple tablet compression and hard-shell encapsulation rooms, two tablet coating rooms, wash bay, IPC testing room and packaging hall. The suites were supplied with filtered, temperature-controlled air and with appropriate room pressure design.

During the facility tour, equipment had been installed but not operational for production use. In-process test laboratories were located adjacent to manufacturing suites. The laboratories were equipped with balances, hardness testers, friability and disintegration apparatus.

The granulation system consisted of a rapid dry mixer and fluid bed dryer. This system was fully automated with HMI and SCADA controls. Critical utilities such as purified water was hard-piped for processing and CIP capability. The inspector noted an issue with this area (Deficiency 4).

New coating equipment which was fully automated with CIP had been installed. Other equipment such as rotary table press and hard shell encapsulation had been transferred from the manufacturer's Girraween site.

The design and construction of production and ancillary equipment was generally acceptable with predominantly inert product contact surfaces and appropriate capacities for the production processes undertaken on site.

The wash bay area was well maintained and provided sufficient cleaning facilities for production equipment. The wash bay had RO water supply and compressed air for equipment drying.

The packaging area was limited to a large room with benches to accommodate manually packing activity.

GMP Pharmaceuticals had programs and associated schedules in place that covered maintenance and calibration of equipment and utilities. Procedures associated with these activities were incorporated into the respective work instructions for each piece of equipment, and tasks are to be added to the respective schedules during the finalisation of qualification activities.

The HVAC system in the manufacturing building had four air handling units (AHUs) supplying suitably filtered air to controlled areas. Each AHU was fitted with a G4 pre-filter, F8 intermediate filters and HEPA filters were installed for final filtration into the manufacturing areas. The inspector reviewed the qualification of the HVAC for the new manufacturing area that was conducted in 2021/2, which was well documented and demonstrated the suitability of the air supply. OQ studies included airflow visualisation and room pressure verification. PQ studies verified environmental conditions with microbial and non-viable air monitoring. Non-viable particles demonstrated that ISO-8 limits were met. The inspector highlighted an issue with the HVAC studies (Deficiency 2c).

A reverse osmosis (RO) water system provided the manufacturing area with purified water (PW). The RO system had been modified to service the new manufacturing areas. Full IQ/OQ/PQ had been conducted to support the system upgrade. This included validation of the removal of the ozone used in routine sanitisation. The PQ incorporated microbial, oxidisable substances, conductivity and nitrates on a 4-week study. Data indicated the quality of the RO water was acceptable. The inspector did identify an issue with the routine monitoring program (Deficiency 8).

The compressed air system was used in various machine operations with product contact surfaces impacted during product filling and bottle blowing prior to filling. The compressors supporting the system were oil-free and appropriately maintained. The system had been qualified to demonstrate the quality of the air was suitable and was part of the monthly EM program. The inspector highlighted an issue with the compressed air monitoring (Deficiency 2d).

There was a suitable pest control program in place and there was no evidence of pest infestation in any area of the facility. This was not reviewed during this inspection.

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

Documentation

Document control was performed according to an appropriate procedure and GMP related documents were effectively controlled by Quality Assurance using a paper-based system.

The document management system was not reviewed in detail during this inspection. The inspector noted that the system was capable of managing the new manufacturing authorisations and template batch manufacturing records were available for the new dosage forms being introduced at the site.

The Technical Development staff generated master work orders following new product introduction. QA reviewed and approved these for use. Hard copy

production/packaging batch documents were prepared by photocopying the work orders. There records were appropriate and included sufficient space for operators to record all required operations. Completed batch documents were formally reviewed by production and QA as part of the batch review process.

GMP Pharmaceuticals utilised GMP critical computer systems. These included laboratory data acquisition systems, electronic document storage, spreadsheet registers, and PLC controllers for production equipment. GMP Pharmaceuticals had implemented some data management and validation requirements for computerised systems; however, some issues with the control of computerised systems was highlighted (Deficiency 2e, 6 and 7).

Production

The inspector reviewed the production areas relating to granulation, tablets, and hard-shell capsules. The operations of the facility were designed for manufacturing and packaging of solid unit dosage forms.

Suppliers of starting materials were subjected to assessment with each new material requiring evaluation by the QA team at the GMP Pharmaceuticals Girraween site. A supplier qualification register was available on a controlled document. This are was not reviewed in detail in this inspection.

All incoming lots were subject to critical tests with non-critical testing performed periodically.

The manufacturer had a program for the receipt, inspection and sampling of starting materials. Warehouse personnel checked starting material containers on receipt for seal integrity and damage prior to receipt into the inventory control system, Pronto. This area was unchanged for the licence variation and not reviewed during this inspection.

Entry into the manufacturing area was appropriately managed with airlocks and gowning rooms that led to production corridors. Dispensing of starting materials was controlled by the manufacturing work orders and verified by a 2nd operator. Materials checked prior to dispensing to ensure they were the correct material and after weighing individual dispensing labels were assigned to the material.

Production processes and procedures were of an acceptable standard with appropriate batch records (work orders) available. Batch documentation incorporated essential activities such as batch reconciliation, line clearance and in-process checks. Room status and usage logs were clearly visible at the entry doors. Instructions were available for the operation, usage, and cleaning of major production equipment.

There were no manufacturing processes in progress as the new production area had not been licenced for manufacturing. Various manufacturing equipment had been adequately installed for dispensing, blending, wet granulation, tablet compression and coating, encapsulation and packaging. Each manufacturing activity was performed in dedicated rooms with appropriate environmental controls.

Rejected goods were adequately controlled on-site. Rework of product was restricted to packaging activities.

Returned goods was not reviewed as part of this inspection.

Cleaning and sanitation procedures for manufacturing rooms and equipment were in place, with appropriate records to log these activities available. Approved cleaning agents were prepared and labelled appropriately, and cleaning implements were stored in a satisfactory manner. 70% alcohol from an

	approved supplier was used for room and equipment sanitisation. The inspector noted an issue with the cleaning program (Deficiency 5). An environmental monitoring program was in place for the controlled areas of the facility and the inspector observed from EM data that an appropriate level of control was being maintained. Microbial monitoring of the air was performed using settle plate and active air method. Microbial swabs were performed on surfaces in controlled areas. EM media (TSA) was supplied by a TGA licenced laboratory and they also performed the incubation/reading of samples. A monthly sampling regime was conducted to ensure all rooms were sampled on a regular basis. There was an approved Validation Master Plan (VMP) available. The VMP detailed the manufacturer's approach to validation and addressed the validation of equipment, utilities, computer systems, test methods, cleaning and processes. The inspector highlighted some issues with the VMP (Deficiency 2a and 2b). The inspector reviewed the validation of new equipment including the rapid mixer granulator and tablet coating machine. In general, equipment validation was well documented and performed to a high standard. DQ/IQ and OQ studies had been successfully completed. Draft protocols were available for performance qualification. SOP creation and operator training were incorporated into OQ studies. Separate validation studies were available for equipment software and WIP systems. Equipment transferred from the Girraween site had been requalified to an appropriate standard. The validation studies for new equipment incorporated cleaning verification of CIP program with conductivity testing of rinse samples and visual inspection of cleaned surfaces. Formal cleaning validation had not commenced and this was planned for process validation during 'worst-case' conditions.
Quality Control	GMP Pharmaceuticals had chemistry and microbiology laboratories on site engaged in testing starting materials, intermediates, bulk, and finished products. The laboratories were adequately segregated from production areas. The QC laboratories were not reviewed during this special inspection.
Outsourced Activities	This area was not reviewed during this special inspection.
Complaints and Product Recall	This area was not reviewed during this special inspection
Self Inspection	This area was not reviewed during this special inspection
Compliance with Marketing Authorisations	This area was not reviewed during this special inspection
Specific Annexes	The Annexes of the Standard applicable to the inspection were Annexes 8, 11, 15 and 19.

Other specific issues identified:
None

Site Master File
GMP Pharmaceuticals provided Site Master File SMF001 (version 5) 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. PH21/4609

Attachments: Inspection Attendance Sheet

List of Deficiencies observed during the inspection

Critical deficiencies:
None observed

Major deficiencies:

1. The requirements of Annex 15 §11.4 that quality risk management should be used to evaluate planned changes to determine the potential impact on product quality, pharmaceutical quality systems, documentation, validation, regulatory status, calibration, maintenance and on any other system to avoid unintended consequences and to plan for any necessary process validation, verification or requalification efforts were not fully met as evidenced by the following:
    a. Change Control, CC21065 for the introduction of new processes i.e. tablet coating, wet granulation and hard shell capsules, was not appropriately managed as required actions were not adequately recorded or controlled:
        i. The approval to proceed on 14/01/2022 was retrospective as facility expansion, equipment purchase/delivery and validation preparation were in progress at that time.
        ii. There was no link or reference to CC20035 for the facility expansion that was previously approved for implementation.
        iii. CC21065 was limited to equipment qualification and training and did not adequately consider upgrades to critical utilities, QMS requirements and the GMP licence updates required for this change.
    b. There was ineffective management for change controls as target dates were not always assigned to action items or change controls to manage the completion of changes. For example, CC21028 for compressed air upgrade and CC21029 for RO Water upgrade had been raised in May 2021 but had not been progressed even though both systems had been upgraded and requalified.

Other deficiencies:

2. The requirements of Annex 15 §1.1 that all qualification and validation activities should be planned and take the life cycle of facilities, equipment, utilities, process and product into consideration were not fully met. For example:
    a. The VMP (v4) had not been updated for hard shell capsule and granule dosage forms.
    b. The VMP did not outline the process for handling deviations that occurred during validation.
    c. There was no methodology or acceptance criteria outlined for active air and swab sampling conducted for the HVAC PQ in the tablet manufacturing area. The protocol did not reference the routine SOP for environmental monitoring.
    d. The action limit 1000cfu/m^3 applied to compressed air monitoring in PQ testing was not justified in relation to direct product contact zones.
    e. The computerised system validation for the coating machine did not adequately test the following critical attributes:

i. User security such as locking of system following unauthorised login attempts. In addition, SOP PTB0009 for the coating machine did not outline administration of the system i.e. control of users (Also Annex 11 §12).
ii. Audit trail verification. Furthermore, SOP PTB0009 did not outline the use of audit trail (Also Annex 11 §9).
iii. Data storage/back-up (Also Annex 11 §7).

3. The requirement of Clause 3.41 that measuring, weighing, recording and control equipment should be calibrated and checked at defined intervals by appropriate methods, and adequate records of such tests should be maintained, was not fully met as evidenced by:
   a. There was no calibration label on the dispensary scales CAL620
   b. The bubble level was not centred for weighing equipment CAL620 in the in-process testing room.

4. The requirement of Clause 3.42 that fixed pipework should be clearly labelled to indicate the contents and, where applicable, the direction of flow was not fully met as pipework (water etc.) in the wet granulation area was not labelled to signify direction of material flow.

5. The requirement of Clause 4.29 that there should be written policies, procedures, protocols, reports and the associated records of actions taken or conclusions reached for maintenance, cleaning and sanitation was not fully met as there was no procedure for cleaning of some product contact equipment i.e. cleaning of transfer chute in dispensing from sieving to IBC.

6. The requirement of Annex 11 §4.3 that an up to date listing of all relevant systems and their GMP functionality (inventory) should be available was not fully met as there was no register for GMP computerised systems used at the site.

7. The requirement of Annex 11 §13 that all incidents, not only system failures and data errors, should be reported and assessed; and the root cause of a critical incident should be identified and should form the basis of corrective and preventive actions, was not fully met as SOP PTB0009 for the coating machine did not outline handling of equipment failure or alarms.

8. The requirements of Annex 15 §4.1 that equipment, facilities, utilities and systems should be evaluated at an appropriate frequency to confirm that they remain in a state of control was not fully met as routine sampling of the purified water system was monthly but this frequency was not justified given the recent qualification and lack of historical data available.

Summary and conclusions

Assessment of manufacturer's responses

A response to the deficiencies reported to the manufacturer was received on 27/05/2022. Following requests for further information, a final satisfactory response was received on 24/06/2022.

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, 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 with the addition of the following authorisations:

Manufacturing Type	Sterility	Dosage Form	Product Code	Manufacturing Step
Medicine manufacture	Non Sterile	All Dosage Forms	Listed Therapeutic Good	Storage
Medicine manufacture	Non Sterile	All Dosage Forms	Listed Therapeutic Good	Testing
Medicine manufacture	Non Sterile	Powders and Granules Group	Listed Therapeutic Good	Finished Product Manufacture
Medicine manufacture	Non Sterile	Solid Unit Dosage Forms - Tablet	Listed Therapeutic Good	Finished Product Manufacture
Medicine manufacture	Non Sterile	Capsules, hard	Listed Therapeutic Good	Finished Product Manufacture

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*.

Signed and authorised by

s22 [redacted]
Lead Inspector

Manufacturing Quality Branch
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.

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:	60 Huntingwood Drive, Huntingwood, NSW 2148
Inspection type:	Licence Variation
Inspection date/s:	5 - 6 May 2022
Inspector/s	s22 [redacted]
Inspection standard:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products (PE009-14)

Opening meeting starting time: 9:20
Closing meeting starting time: 13:30

Name *(please print)*	Position *(please print)*	Opening meeting *(initials)*	Closing meeting *(initials)*
s22 [redacted]	QA Manager	s22 [redacted]	
	QA Supervisor		
	Snr. QA Associate		
	Site Manager		

* Closing Meeting conducted via MS Teams s22 6/05/2022

Australian Government
Department of Health and Aged Care
Therapeutic Goods Administration

s22
Quality Manager
GMP Pharmaceuticals Pty Limited
60 Huntingwood Drive
Huntingwood
NSW 2148

Our Reference: PH23/20896

Dear s22

Subject: GMP Surveillance Inspection of GMP Pharmaceuticals Pty Limited

Please find attached the inspection report for the surveillance inspection that took place at GMP Pharmaceuticals Pty Limited's Huntingwood facility on 3 – 4 April 2025.

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.

You should note that assessments made during Surveillance Inspections are based on a random and limited examination and verification of the manufacturer's documents. This inspection report does not therefore claim to be a complete evaluation of all manufacturing operations performed at your site, and does not release you from the obligation to rectify deficiencies that have not been identified or stated herein.

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

Yours sincerely

Signed and authorised by

s22
Senior GMP Inspector
Manufacturing Quality Branch

Date: 30 May 2025
Tel: s22
E-mail: s22 health.gov.au

Surveillance Inspection Report

Manufacturer:	GMP Pharmaceuticals Pty Limited
Inspected site/s:	60 Huntingwood Drive, Huntingwood NSW 2148
Manufacturer information:	GMP Pharmaceuticals Pty Ltd (GMPP) is a manufacturer of listed therapeutic goods. GMPP holds 3 TGA licences to manufacture listed therapeutic goods. All licenced sites are located in western Sydney, in the suburbs of Girraween and Huntingwood. The facilities have been commissioned for the manufacture of both food and listed therapeutic goods. The Huntingwood site is in a light industrial area approximately 7 kilometres west of the Girraween complex and has held a TGA licence since 2020. The Huntingwood site continues to expand its portfolio of medicinal products, primarily with additional solid unit dosage form products. The manufacture food products was excluded from the scope of this insepction.
Activities carried out by manufacturer:	☑ Manufacture of finished medicinal product ☐ Manufacture of intermediate or bulk ☐ Packaging ☐ Laboratory testing ☐ Release for supply ☐ Manufacture of Active Pharmaceutical Ingredient ☐ Other:
Type of inspection:	☑ Re-inspection ☑ Surveillance inspection ☐ Remote inspection ☐ Hybrid inspection Applicable sections of the *Therapeutic Goods Act 1989*: ☑ 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	Finished product manufacture of listed medicine in powder, granule, tablet and hard shell capsule dosage forms. Packaging, labelling and release for supply of listed medicine in soft gel capsule dosage form. Storage and testing of listed medicine in all dosage forms.
Inspection date/s:	3 – 4 April 2025
Inspector:	s22 [redacted]

Manufacturing Standard used:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products, Part I (PE 009-16)
References:	Manufacturing Licence number: MI-2019-LI-01002-1 Inspection tracking number: MI-2023-LI-03211-1 File reference number/s: PH22/23917 (inspection file), E19-540033 (licence file)

Personnel met during the inspection

s22 [redacted] QA Manager
Quality & Compliance Manager

Inspected areas, findings and observations

Refer to Site Master File, SMF001 version 8, effective December 2025, for information of site activities.

Major changes since the previous inspection:

- Multiple new products introduced to site
- Changes to key personnel at Huntington; replaced by suitably experienced staff from GMP Pharmaceuticals' Girraween complex
- Upgrade or replacement to some ancillary production and laboratory equipment

Future Planned Changes: None discussed

Quality Management	
Subject area inspected	**Compliance outcome / comments**
Review of actions taken since previous inspection	Deficiencies 1 & 2 recorded at this inspection were similar to deficiencies recorded at the previous routine re-inspections of May 2021.
Product Quality Reviews	Refer to deficiency 1. A similar deficiency was recorded at the previous routine re-inspection conducted in May 2021.
Change Management	Refer to deficiency 4
Complaints management	No deficiencies identified
Deviation, non-conformance and CAPA management	No deficiencies identified
Internal Audits	No deficiencies identified
Batch Record Review and Batch Release	No deficiencies identified
Training	Refer to deficiency 2. A similar deficiency was recorded concerning on-the-job training at previous routine re-inspections, including that conducted in May 2021.

Materials Management	
Subject area inspected	**Compliance outcome / comments**
Warehousing	Refer to deficiency 5
Starting Materials	No deficiencies identified
Production System	
Subject area inspected	**Compliance outcome / comments**
Production - Formulation Areas	Refer to deficiency 6
Production - Manufacture/Filling	No deficiencies identified
Production – Labelling/ Packaging	No deficiencies identified
Validation/Qualification	
Subject area inspected	**Compliance outcome / comments**
Process Validation	Refer to deficiency 4a
Cleaning Validation	Refer to deficiency 3
Computer System Validation	No deficiencies identified
Facilities and Equipment	
Subject area inspected	**Compliance outcome / comments**
HVAC	Refer to deficiency 7
Water Systems	No deficiencies identified
Quality Control	
Subject area inspected	**Compliance outcome / comments**
Chemistry Laboratory	No deficiencies identified
Control of OOS results	No deficiencies identified

List of Deficiencies observed during the inspection

Critical deficiencies:

None observed

Major deficiencies:

1. The requirement of Clause 1.10 that regular periodic or rolling quality reviews of all authorised medicinal products, including export only products, should be conducted with the objective of verifying the consistency of the existing process, the appropriateness of current specifications for both starting materials and finished product, to highlight any trends and to identify product and process improvements; and these product quality reviews (PQRs) should normally be conducted and documented annually, were not fully met. For example, there were no formal processes in place to ensure PQRs were available for all authorised medicinal products manufactured at site, and to ensure PQRs were conducted annually (or every 2 years for low volume products). The inspector noted that the available PQRs may represent the full product range; however, GMP Pharmaceuticals approved process was to conduct individual, product based PQRs, rather than using a grouped product approach.

2. The requirements of Clause 2.11 that newly recruited personnel should receive training appropriate to the duties assigned to them, continuing training should also be given, and its practical effectiveness should be periodically assessed, were not fully met. For example, processes for recording the effectiveness of on-the-job training had been formalised into procedures; however, the planned checklists for recording on-the-job training activities were still being developed and no records of on-the-job training were available.

Other deficiencies:

3. The requirements of Annex 15 §10.9 that where campaign manufacture is carried out, the impact on the ease of cleaning at the end of the campaign should be considered and the maximum length of a campaign (in time and/or number of batches) should be the basis for cleaning validation exercises was not fully met. For example, cleaning validation protocols associated with the extension of campaign manufacturing activities, outlined in Quality Incident report, QID 24124, did not specify hard to clean locations on equipment, which could be impacted by the extended campaign length, to ensure these were reviewed for visual cleanliness and microbiological build-up.

4. The requirements of Annex 15 §11.4 concerning change control, that quality risk management should be used to evaluate planned changes to determine the potential impact on product quality, pharmaceutical quality systems, documentation, validation, regulatory status, calibration, maintenance and on any other system to avoid unintended consequences, and to plan for any necessary process validation, verification or requalification efforts, had not been fully implemented. For example, new product introduction processes did not consistently evaluate the need for process validation, nor formally evaluate whether the new product should be included in the site's on-going stability program. For example, regarding Change Control CC24163 for the transfer of Wonderland Capsules from GMP Pharmaceuticals Girraween site to the Huntingwood site,
    a. CC24163 did not identify process validation as a requirement, nor was there an evaluation recorded to ensure the new product was represented by the existing process validation product groups.
    b. CC24163 did not evaluate the need for an on-going stability study for the new product. It is acknowledged that on-going stability for this product was underway at the Girraween site; however, this was not documented in the change control and it was unclear whether manufacturing processes at the Huntingwood site would be comparable to those used at the Girraween site.

5. The requirements of clause 3.19 that storage areas should be designed or adapted to ensure good storage conditions, [. . .] they should be clean and dry and maintained within acceptable temperature limits, and where special storage conditions are required (e.g. temperature, humidity) these should be provided, checked and monitored, were not fully met. For example, the warehouse temperature in the locations used for storage of gelatine capsule shells were not specifically monitored. The warehouse temperatures were monitored at the 'worst case' locations and temperature excursions were only actioned when temperatures were above 30 °C. There was no evidence available to demonstrate the storage locations for gelatine capsule shells would remain at or below 25 °C, as required by the special storage conditions of the material. The temperature records indicated the 'worst case' locations were above 25 °C (and below 30 °C) on multiple occasions during January and February 2025.

6. The requirements of clause 5.19 that cross-contamination should be prevented by attention to design of the premises and equipment as described in Chapter 3 of the PIC/S Guide, and this should be supported by attention to process design and implementation of any relevant technical or organizational measures, including effective and reproducible cleaning processes to control risk of cross-contamination, were not fully met. For example, wash bays on both the mezzanine level and ground floors of the Tableting/Dry Powder Suite were noted to have black residue on some horizontal surfaces within the wet areas of the wash bay. The residue was present in/on sealant between wall panels and floor coving, and upon multiple horizontal ledges around the wash bay enclosures.

7. The requirements of clause 5.21 regarding technical measures required to control risks for cross-contamination were not fully met as evidenced by the following,
    a. Appropriate use of air-locks and pressure cascade to confine potential airborne contaminant within a specified area were not effectively implemented (clause 5.21 (x) Technical Measures). For example, the pressure gauge reading for the wash bay on the mezzanine level of the Tableting/Dry Powder Suite indicated the pressure differential of the wash bay was positive to the central staging area of the mezzanine. This was not compliant with the facility design.
    b. On-going monitoring and preventative maintenance of the HVAC did not minimise the risks of contamination caused by recirculation or re-entry of untreated or insufficiently treated air (clause 5.21 (xi) Technical Measures). For example, confirmation of HEPA filter integrity in AHUs across the facility were limited to visual checks; however, this was not adequate to determine whether the HEPA filters had been perforated. HEPA filter integrity was a critical component of the sites HVAC design as the on-going monitoring program of room pressure differentials had no upper pressure limits, and AHUs had no pressure monitoring across their filter banks.

Comments
None

Summary and conclusions

Assessment of manufacturer's responses
A response to the deficiencies reported to the manufacturer was received on 5 May 2025. 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. The next re inspection is expected to be performed within 30 months.

4. The duration of the next inspection is estimated at this time to be 4 days and will be conducted as a Full Inspection.

Signed and authorised by

s22
Senior Inspector
Manufacturing Quality Branch

Date: 30 May 2025
Mobile: s22
E-mail: s22 health.gov.au