Australian Government

Department of Health
Therapeutic Goods Administration

s22
Senior QA Manager
Sandoz Pty Ltd
Level 15, 100 Pacific Highway
North Sydney, NSW 2060

s47G

Dear s22

RE: GMP INSPECTION Sandoz Pty Ltd, Tracking Number s47G

Please find attached the inspection report for the remote inspection that took place for your North Sydney, NSW site on the s47G

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

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

Yours sincerely

Signed and authorised by

s22
s22
Manufacturing Quality Branch
Date: s47G

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

Australian Government
Department of Health
Therapeutic Goods Administration

Inspection Report

Manufacturer:	Sandoz Pty Ltd
Inspected site/s:	Level 15, 100 Pacific Highway North Sydney, NSW 2060
Activities carried out by manufacturer:	☐ Manufacture of finished medicinal product ☐ Manufacture of intermediate or bulk ☐ Packaging ☐ Laboratory testing ☑ Release for supply ☐ Other:
Type of inspection:	☑ Initial inspection ☐ Re-inspection ☑ Full inspection ☐ Special inspection ☐ Reduced scope inspection Applicable sections of the *Therapeutic Goods Act 1989*: ☑ section 37(2)(b) (licence application) ☐ section 40B(10)(a) (licence variation) ☐ section 40(4)(b) (re-inspection of licensed site) ☐ section 25(1)(g) (overseas in relation to registration) ☐ sections 26(1)(g), 26A(3) (overseas in relation to listing)
Scope of Inspection	The release for supply of sterile and non-sterile registered dosage forms.
Inspection date/s:	s47G
Inspector/s:	s22
Manufacturing Standard used:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products – Part 1 (1 May 2021)
References:	Inspection Tracking Number s47G File reference number/s: s47G (inspection file), s47G (licence/certification file)

Introduction

Sandoz is a multinational, generic pharmaceutical group headquartered in Switzerland. s47G Sandoz Pty Ltd, the Australian entity of the multinational group, imports products into the Australian market. Approximately s47 of the products are imported s47

Sandoz Pty Ltd performs release for supply of these products in accordance with the GMP contract agreement. Sandoz Pty Ltd may also perform release for supply for products that are imported under quarantine status. This initial inspection was conducted for the new office relocation due to the spin-oof from Novartis. Previous Sandoz Pty Ltd licencing for release for supply was held under s47G

Date of previous inspection (for licence s47G
Names of inspectors involved in previous inspection: s22

Brief report of the inspection activities undertaken

Scope of inspection

This initial inspection was conducted to review compliance to the PIC/S GMP Guide (PE 009-15) for the release for supply of sterile and non-sterile registered therapeutic goods. The scope also included the release for supply activity of the current licence s47G held at s47G

Inspected areas

The inspection was conducted remotely in accordance with a written plan and covered all areas of the quality system in relation to the release for supply of medicinal products. The application was limited to release for supply so there was no manufacturing facility inspected.

Key Personnel met during the inspection (via MSTEAMS)

See Attachment

Inspection findings and observations

Major changes since the previous inspection:

- New QA staff joined the local Sandoz team including the Senior Quality Manager s22
- s47G including move to new office at North Sydney
- Implementation of change from s47 warehousing (3PL)
- Change management system for s47G, and reversion back to s47G
- Adoption of s47G for eQMS modules - complaint and deviation management.

Future Planned Changes:

- s47

Overview of inspection findings from last inspection and the corrective action taken	A review of the actions taken by Sandoz Pty Ltd to address the previous inspection findings (from s47G licence) was conducted and no issues were identified.

Quality Management

The manufacturer had implemented a pharmaceutical quality system (PQS) that was designed to meet the requirements of the PIC/S Guide to Good Manufacturing Practice (GMP). A review of the system demonstrated that the system was appropriately designed and effectively implemented.

The manufacturer had written and developed a procedure relating to quality risk management (QRM), and this document included the assessment of risks of the overall business operations, throughout the lifecycle of the event or item. Risk management was used to assess significant changes, deviations, the repackaging and re-release of goods. A review of QRM systems was conducted by the inspector and no issues identified.

A Sandoz Global Quality Manual was available that described Sandoz quality systems and objectives including management review. The QM adequately described the various aspects of the quality systems and how they contributed to ensure that therapeutic goods were of the required standards. At a local level, quality management review meetings were held quarterly for topics related to regulatory and quality systems. A quality management review was reported annually.

A written and authorised procedure for the management of deviations had been implemented by the manufacturer. The procedure outlined the process for the recording, investigation, correction and prevention of the issue, and s47G was used to capture and record relevant details of each event. The level of risk to product quality determined the classification of deviation i.e. critical, major and minor. Investigations into deviations were required through the s47G with a structured approach to root cause analysis. A selection of investigation records were reviewed which generally complied with the procedure. This inspector identified some issues with deviation management s47

Changes were managed in accordance with a written change control procedure a global change control procedure was used that managed changes performed on a global level. The local change control system was managed within s47G and required authorisation from a QA Evaluator and the QA Manager was a requirement before a change control can be initiated. A review of several change control records demonstrated that the system was not full effective particularly relating to the s47G s47

Annual Product Quality Reviews (PQRs) were conducted according to defined procedures, which covered all elements required by cGMP. There was a PQR schedule in place detailing the products (SKUs) to be reviewed within the year. The inspector reviewed the s47 PQR for s47 which contained all the relevant information to support product quality. Bulk product reports were issued by the contract manufacturer with complaints management, regulatory review and finalisation by Sandoz at a global level (EOS). PQRs were made available to the local team via the s47G system.

Sandoz had implemented a controlled, written procedure for the release for supply of products. The release process followed a logical review of batch related documentation, quality control certificates and certificates of conformance against product profile specifications. Arrangements were in place for the collection of retention samples that were initially evaluated by Sandoz QA before being stored at the third party s47 warehouse. Release forms were used for each batch and pertinent details were recorded and checked during the release process. s47

Personnel

Position descriptions were available, and all persons interviewed appeared to be appropriately trained and experienced to perform the licensable activities. The delegation of release for supply was adequately controlled within the quality team structure and job descriptions.

The manufacturer's arrangements for training were outlined by procedure at both a global and national level. The SOP for training indicated a process for the initial training of staff (on-boarding) and job-specific training. s47G was used as a learning management system and maintained records for training. GxP was performed as part of on-boarding but an issue was raised for refresher training s47 s47 Overall, training systems were well managed but the inspector noted a minor issue s47

Premises and Equipment

Not applicable. The site at North Sydney was office space only and was not visited during this remote inspection. Manufacturing operations were limited to the release for supply of products and this action was performed by a dedicated team located within the premises.

The primary manufacture of dosage forms, and the packaging and testing of dosage forms was performed under contract by suitably qualified and authorised contract manufacturers. s47

Documentation

GMP related documents and records were generated and controlled in accordance with a written procedure; and electronic portable document formats were accessed via the s47G platform. Several approved SOPs were available that covered the range of Sandoz activities.

SOPs were issued with defined review periods and mechanisms to capture the review and re-issue of documents were in place via s47G Records were retained for periods that met GMP requirements.

The manufacturer had implemented a system for the generation and control of finished product specifications. A selection of available specifications was reviewed by the inspector and no issues identified.

Certificates of compliance and GMP declarations were observed for these products manufactured under contract. Batch approval records relating to the products released by the site were reviewed and retained by the manufacturer. The records included certificates of compliance, certificates of analysis, transport conditions and GMP declarations by the primary manufacturer.

Procedures were in place for the management of validation, and these procedures addressed the computerised systems in use at the site. Computerised System Validation (CSV) was generally managed and supported by s47 . There was an up-to-date list of GxP computerised systems used at Sandoz.

Production

Production of therapeutic goods was conducted by TGA licensed/certified manufacturing sites. Refer to outsourced activities for more details.

All finished products requiring release for supply were physically held at licensed warehouse premises in s47 under quarantine prior to release by Sandoz.

The manufacturer utilised a number of electronic systems within the business. These systems were located on remote servers and were supported and maintained by both local and remotely located IT teams, underpinned by both global and local VMPs for GxP systems.

An electronic Enterprise Resource Planning system, s47G was used to control the status of materials released by the manufacturer and track the distribution of materials at the s47 s47G was interfaced with s47 warehouse management system; the validation required for the computer system interface was performed by the global IT support team.

Quality Control

Not applicable. Refer to outsourced activities for more details.

Outsourced Activities

A system for the identification, evaluation and management of outsourced activities was in place. Quality agreements were in place between Sandoz, external manufacturers, contract packaging sites and warehousing in the product supply chain. The inspector reviewed the agreement with s47 The agreement reviewed met GMP requirements and clearly included the responsibilities relating to product release, PQRs, retention samples, product stability and recalls. Quality audits were performed at defined frequencies for external manufacturers and periodic audits were conducted at s47 by the Sandoz global audit team.

Complaints and Product Recall

Complaints relating to marketed products were managed in accordance with documented systems. Procedures were available that outlined the systematic approach taken to documenting and reviewing complaints, which included reviews of trends, batch records, retention samples and relevant deviations. Sandoz handled complaints through a centralised systems known as the s47G. Complaints were received by the patient safety team and were forwarded to QA for review if product quality related. s47G was in place for the management of complaints. Complaints were categorised based on their significance – critical, major and minor. A review of the system and a selection of complaint records highlighted some issues s47 Quarterly trend reports were made available to the local Sandoz team.

The manufacturer had implemented a system for product recalls, which was in line with PIC/S GMP and URPTG requirements. The inspector reviewed a recall of product that had been performed in s47 ,s47G which had been reported to the TGA and reconciled appropriately. The recall was in relation to missing information on the s47 which was not noted as a recurring issue.

Self Inspection

The manufacturer had implemented a system for the conduct of self inspections; however, these were not reviewed in detail. QA consultants had historically been used for self inspections and the global audit team also conducted inspections as per the global audit program.

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. The authorised persons responsible for product release had full oversight on the relevant market authorisations and ensured product specifications were appropriately

aligned. A review of formulations for compliance with market authorisation requirements was conducted during the inspection but some issues were noted due to the change in site address of the RFS office.

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

Other specific issues identified

Shared quality system procedures such as deviation handling s47G , product quality review s47G , GxP Document Lifecycle Management s47G , QA Product Recall s47G Training of GxP personnel s47G Batch Certification and Release for Distribution, etc. had been cloned but not updated to remove s47 descriptors and terminology. A position paper was presented to address this approach and commitment to update/remove references to s47 at the next SOP revision(s).

Site Master File

A copy of the Site Master File, s47G , was received prior to the inspection and was found to be an accurate reflection of the activities of the business.

Miscellaneous

Samples taken: None

Distribution of Report: Sandoz Pty Ltd and TGA inspection file s47G

Attachments: None

List of Deficiencies observed during the inspection

Critical deficiencies:
None observed

Major deficiencies:

1. The requirements of Clause 1.4 (xii) that arrangements are in place for the prospective evaluation of planned changes s47
   a. s47G
      i. The change control did not require an action item to obtain a new GMP licence to allow release for supply to be conducted under the correct licence reflecting Sandoz's new site address. s47 (also refer to Clause 1.4xv). *It is acknowledged that most products released by Sandoz are released for distribution whereby the release for supply step has been conducted by 3rd parties.*
      ii. The nominated Sandoz release for supply site on associated Marketing Authorisations (MA) was still referencing the vacated s47 and it was not clear if all relevant MA holders had been notified of the site address change.
   b. For the change control related to s47 warehousing, s47G :
      i. The computerised system validation for SAP configuration/interface at s47 was not adequately captured. The "IT" go-live date stated in s47G ' of 1

s47 and follow-up actions from s47 validation were not managed in the change control or local quality system.

ii. ARTG entries s47 were not updated to include s47 as a nominated manufacturing site. *It is acknowledged that these ARTG products are not currently marketed in Australia.*

Other deficiencies:

2. The requirements of Clause 1.4 (xiv) that an appropriate level of root cause analysis should be applied during the investigation of deviations, suspected product defects and other problems; where human error is suspected or identified as the cause, this should be justified having taken care to ensure that process, procedural or system based errors or problems have not been overlooked, if present; appropriate corrective actions and/or preventive actions (CAPAs) should be identified and taken in response to investigations were not fully met. For example:
   a. s47 relating to s47 observed on product by wholesalers was inappropriately handled as deviation investigation even though the product defect was observed at wholesale level which was outside the control of Sandoz i.e. this was/should have been handled as complaint(s). *It is acknowledged that the first reporting of this issue was raised as a complaint but subsequent occurrences investigated as deviations.*
   b. s47 for the missing temperature data logger on s47 shipment:
      i. The deviation assumed the single data logger read available was representative of 'worst-case' on the shipment and, therefore, negated the missing data from the 2nd data logger. It was unclear if the 24.2°C temperature reported was a maximum or average reading on the shipment.
      ii. The investigation did not assess the storage controls available for that shipment type to maintain <25°C i.e. enviro-container.
      iii. Historical shipping for this product/transport route was not evaluated or discussed during the investigation.

3. The requirements of Clauses 2.11 that besides the basic training on the theory and practice of the Pharmaceutical Quality System and Good Manufacturing Practice, newly recruited personnel should receive training appropriate to the duties assigned to them and continuing training should also be given, s47 and practice of the Pharmaceutical Quality System and Good Manufacturing Practice (PIC/S) and s47

4. The requirement of Clause 8.9 (ii) that when a quality defect investigation is initiated, procedures should be in place to address the determination of the extent of the quality defect and the checking or testing of reference and/or retention samples should be considered as part of this was not fully met. For example:
   a. s47 investigation related to s47 did not perform a s47 of retention samples for cloudiness. The root cause of the s47 on the complaint sample had not been established in order to dismiss a batch related event for the s47 .
   b. s47 for the expired blister pack of s47 did not include an investigation into the retention samples to verify correct packaging occurred during packaging.

Summary and conclusions

Assessment of manufacturer's responses

A satisfactory response to the deficiencies reported to the manufacturer was received on s47

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:

No	Manufacturing Type	Sterility	Manufacturing Class	Dosage Form	Product Code	Manufacturing Step
1	Medicine manufacture	Sterile & Non Sterile	Not Applicable	All Dosage Forms	Registered Therapeutic Good	Release for supply

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 s47G

5. The duration of the next inspection is estimated at this time to be s47G

Yours sincerely

Signed (electronically) and authorised by

s22
s22
Manufacturing Quality Branch

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

DEFINITIONS

Marketing Authorisation

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

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

Critical Deficiency

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

Major Deficiency

A non-critical deficiency that:

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

Other Deficiency

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

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

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

Note:

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

Attachment 1:

Name	Role
s22	Senior QA Manager
s22	Senior QA Associate
s22	QA Associate
s22	QA Specialist
s22	QA Associate
s22	QA Associate