Quality Manual Of Drug control & inspection Department

Jordan Food & Drug Administration

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Appendices

Glossary

SN	Term	Description
1	JFDA	Jordan Food & Drug Administration
2	The Department	Drug Control & Inspection Departement
3	GMP	Good Manufacturing Practice
4	GSDP	Good Storage & Distribution Practice
5	QMS	Quality Management System
7	Core Processes	The primary process which is the fundamental line of The Department
8	Support process	Processes which do not deliver value, but nessecary for mantaining core process
9	ML	Manufacturing License
10	OMCL	Official Medicines Control Laboratories
11	CAPA	Corrective and Preventive Action
12	RDU	Rational Drug Use

Introduction

1.1. General

Jordan Food & Drugs administration, since its creation by an interim law for the year 2003 and the adoption of the permanent law for the year 2008, has played a crucial role in the health care system by contributing to the economy of Jordan & the society; it is financially and administratively independent. The goal of JFDA is reflected in its vision & Mission.

JFDA Vision: To excel regionally and globally as a pioneer in the field of food, medicine and related materials, so as to enhance public health and consumer's confidence.

JFDA Mission: Ensuring food safety and quality, as well as effectiveness, quality and safety of the drug and related material through the application of controlled systems based on the scientific and international standards. Strengthen cooperation with partners and increase citizen awareness of proper handling and use of food and drug.

The partnership between JFDA and the different sectors (i.e. including the Universities, the Governmental Institutions etc.) in Jordan has allowed us to create compatible regulations and demonstrates a viable model of collaboration. Several Memorandums of Understanding were signed between JFDA and official parties inside Jordan such as; public security force, Electronic Health Solutions Co and national university. JFDA has embraced its role as a national competent authority for food and drug control and development programs through bilateral agreements with many regional and international bodies such as USAID, SFDA, Russian federal State Institute of Drugs and Good Practices (SID & GP).

JFDA regulates the quality of pharmaceuticals very carefully. The main regulatory standards for ensuring pharmaceutical quality are Jordan Good Manufacturing Practice (JFDA-GMP) & (Good Storage & distribution practice -GSDP-) regulations. JFDA enforce the compliance through national legislation enabling licensing or certification, inspections, sampling and testing of pharmaceuticals product, the empowering legislations include the following:

- Drug and Pharmacy Law No.12 of 2013
- Food and Drug Administration Law No.41 of 2008
- Public Health Law No.47 of 2008
- Pharmacist Association Law No.51" of 1972
- Accreditation of Manufacturing Site Criteria of 2016
- Narcotic Drugs and Psychotropic Substances Law No.23 of 2016

- Instruction of Accreditation of Reference Laboratories for Pharmaceutical Product Analysis of 2011
- Instructions for Testing Drugs, Medical Devices and Sterilizers" of 2017
- Instruction on Transport and Storage of Drugs, and the Technical Specifications of Transportation Vehicles of 2019
- Instructions on the Specifications of Drug Samples and Conditions of Distribution of 2017
- Criteria of Drugs Registration of 2015 and its Amendments in 2019
- Pharmacovigilance Instructions of 2016
- Bylaw of Pharmaceuticals Factories Licensing and Charged Fees No(11) of 2016

The Department carries out regular inspections of all pharmaceutical firms, depending on the nature and extent of their activities. The Department also carries out investigations and takes enforcement action against illegal activities that may impact public health.

The intent of this manual is to describe all activities/processes carried by The Department as illustrated in the scope below.

1.2. REFERENCES

This Quality Manual is based on the following normative standards and references. The content of the manual is intended to comply with the spirit and current understanding and interpretation of the referenced documents:

- PIC/S, Pharmaceutical Inspection Co-operation Scheme Recommendation on Quality System Requirements for Pharmaceutical Inspectorates, PI 002-3, September 2007.
- Compilation of community procedures on Inspection and exchange of information; EMA/572454/2014 Rev 17.
- ISO 9001:2015, Quality management systems — Requirements

1.3. Scope

The scope of this Quality Manual covers all activities that fall under the responsibility of the Drug control & Inspection Department at Jordan Food Drug Administration. The Department is responsible for insuring the compliance of Jordanian and foreign manufacturers of pharmaceuticals product with Good Manufacturing Practice (GMP) and for Jordanian warehouses with Good storage and distribution practice (GSDP) in accordance with related regulations and legislation which cover human pharmaceutical drug products such as:

- Sterile and Non-Sterile medicinal products
- Biological products (Vaccines, Sera and blood products)

- Herbal products
- Radioactive products and radiopharmaceuticals used in nuclear medicines
- Active Pharmaceutical Ingredients (APIs)

The Department maintains an up to date list of all approved drug Manufacturers & Warehouses which are inspected periodically.

2.0 Quality System

The primary purpose of the Quality System is to ensure that adequate quality standards are maintained in all Departments' activities. The system of quality management is composed of personnel, processes, documentation, interfaces, as well as the resources we use to ensure the quality of our services. These resources are allocated by the drug director for the conduct of the processes of the QMS. The implementation of quality management means that:

- Identify and monitor the processes of the Department
- Determine criteria and methods required to ensure its effective operation and control
- Ensure availability of information needed to support and monitor its operation
- Provide monitoring, analysis and implementation, where required, of the necessary actions to achieve planned results & continuous improvement.

2.1. Quality Policy

The Quality Policy set by the Drug Director expresses a commitment to implement a system Of quality management based on continuous improvement. It is also disclosed, known and understood by all Departments' employee.

Drug Director is committed to protect the public health and fulfill their duties with professional and scientific approach.

The implementation of the quality policy is the responsibility of all staff members, with overall responsibility residing on Drug Director.

Quality Policy Statement of Drug Control & Inspection Department is" **Timely and reliable service, compliance to all applicable legislation & regulatory requirements underlie all our efforts in ensuring quality, safety & efficacy of all drugs & health care products used in Jordan through regulation & control of their production, importation & distribution."**

Quality objectives, process, system, and procedures that support this quality policy are established and reviewed periodically for continuing suitability.

3.0 Documentation System & Change Control

The Department has established, documented, and implements an effective QMS as a means of ensuring that its processes conformed to specified requirements, to foster an environment of continual improvement with an eventual goal of achieving PIC/S requirements. The Department's QMS is comprised of the Core and Support Business Processes. Control of documents maintained through QUA/01 procedure.

3.1. Core Processes

The core processes describe all the processes that are necessary for The Department to realize and deliver the desired service to its customers. The Core Processes for The Department are listed below:

Procedure Title	Documents Code
GMP Inspection Procedure	FAC/01
GMP Reporting , licensing & Certification Procedure	FAC/02
Overseas Inspection Procedure	FAC/03
GSDP Inspection Procedure	STO/01
GSDP Reporting , licensing & Certification Procedure	STO/02
Post Marketing sampling procedure	STO/03
Seizing and Destroying Pharmaceuticals Products.	STO/04
Pharmacy Inspection Procedure	STO/05
Licensing of drugs shipping vehicles	STO/06
Recall Follow-Up Procedure	STO/07
Handling Falsified Medicinal Products	STO/08
Examination of Pharmaceutical Product /Medical Sample	STO/09
Complaint Handling Procedure	QUA/06

3.2. Support Processes:

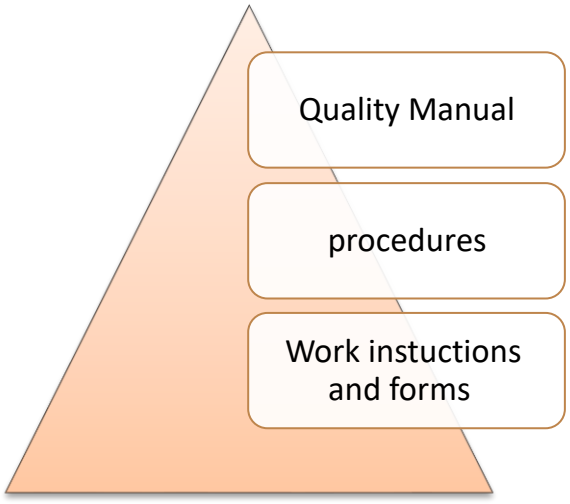
Support Processes describe all other requirements that are necessary to manage and control resources, and to perform inspection in an orderly manner. The support processes are implemented and managed in accordance with the applicable requirements of the International Standard ISO 9001.

The support processes include:

Procedure Title	Documents Code
Control of Document	QUA/01
Management Review	QUA/02
Internal Audit	QUA/03
Control of Records procedure	QUA/04
Corrective & Preventive Actions (CAPA) Procedures	QUA/05
Training procedure	QUA/07
Management Responsibility procedure	QUA/08
Performance Review Procedures	QUA/09

The criteria and methods required to ensure the effective operation and control of these processes (support & Core) are defined and documented. Changes in controlled documents are reviewed and approved by relevant personnel within The Department. and result in re-issue of the document to all concerned persons with appropriate re-training (when required).

Where changes are made in a document there is a method for identifying changes from the previous version where such exists. The master copy of any superseded document is archived for a pre-determined period and all other copies are withdrawn from use in a timely and controlled manner.



The Quality Manual is a *controlled document* subjected to the requirements of standard operating procedures QUA/01.

3.3. Control of Records

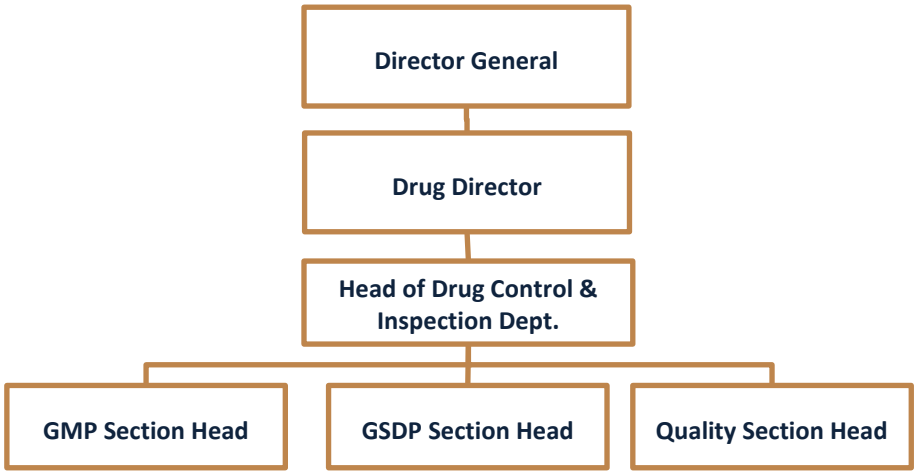
The Department maintains records to demonstrate conformance to specified requirements and the effective operation of inspection processes. Control provides for the identification, collection, indexing, filing, access, storage, maintenance, and disposition of quality records. Pertinent customer or supplier records are an element of these data.

All Department records are legible and are stored and retained in such a manner that they are readily retrievable. Control of records procedure **QUA/04** is established to assure good documentation practice and integrity of data. Retention times of quality records are established and recorded.

4.0 Administrative Structure

Drug Control & Inspection Department is a part of Drug directorate functioning reporting directly to the Drug Director. The Department basically is an enforcement department, however, it grants licenses under the Drug and Pharmacy Law No.12" of 2013 & Accreditation of Manufacturing Site Criteria" of 2016 and it is responsible for enforcement GMP & GSDP regulations in Jordan. The General Director of the Jordan Food & Drug Administration confers the ultimate legal authority for supervision of pharmaceutical facilities.

The organization chart of The Department is provided below. The Department head reports directly to Drug Director. Heads of GMP and GSDP & quality sections report directly to the The Department head



The Rational Drug Use & Pharmacovigilance Department (RDU) is responsible to obtain information during the use of a pharmaceutical product systematically. The Department continuously informed through different channels about suspected defects related to the quality of

the product and adverse drug reactions related to it. The role of RDU department extend to initiate a recalls based on notifications received/published by other competent authority/company. Pharmacovigilance Department may trigger a for cause inspections –carried out by Drug Control and Inspection department - to investigate specific aspects/ complaints related to product quality. A "for cause" inspection will focus on the particular issue related to the reported problem, but can branch out to cover unrelated elements of the manufacturer's operations. This inspection usually is initiated after reviewing manufacturer CAPA upon a joint decision made by Pharmacovigilance Department and Drug Control and Inspection department. When required RDU department may participate in such inspection. Information gained during this inspection is reported to drug director to estimate the needs of any further required action(S)

5.0 Organization and Management

The Head of Drug control & Inspection Department is responsible for the overall management of the GMP and GSDP Inspection programs and as such, for the overall management of The Department's processes. If the Department head is absent from the office for an extended period of time, responsibility for the management of The Department will be delegated to another suitably qualified member of the department. In such an event, the Acting Head will be responsible for all inspection related activities for which the Head is normally responsible.

Based on his / her professional discretion, the Head of department/sections May delegate responsibility for specific activities to other Inspectorate personnel. The responsibilities and authority of The Department personnel are described in written job descriptions for each position in The Department Job descriptions are signed by the staff and by Drug Director, indicating that they are both aware and agree to the scope of activities described therein. Job descriptions are filed in each staff member's personal file held by the human resource department.

The Department personnel must have appropriate educational qualification, training and experience or suitable combination of these factors to enable them to perform their duties.

Minimum educational requirements for inspectors are an academic degree in pharmacy in accordance with Drug and Pharmacy Law No.12 of 2013.

Practical experience in the pharmaceutical or related industry at a management level is considered an advantage although is not necessarily a pre-requisite for employment in the department. The Department is currently staffed by 14 inspectors (9 GMP inspectors, 5 GSDP and Pharmacies) including: the Head The Department, GMP section head, GSDP section head & QA section head.

The responsibilities of Drug directors. Include but are not limited to:

- Ensuring the availability of adequate resources for implementation and maintenance of Drug control & Inspection Department quality System
- Intervening and assisting in resolving ongoing compliance issues where resolution between the Inspectorate and industry has not reached an acceptable conclusion
- Liaison with industry representatives and bodies where appropriate

The responsibilities of the Department Head include but limited to:

- Ensuring the existence of and implementation of an annual training plan
- Arranging, planning and conducting inspections program
- Ensuring impartiality of the inspection
- Handling complaints lodged by public.
- Review and approval of SOPs and other documentation related to the activities of the Department as appropriate.
- Ensuring the performance of management reviews and providing solutions to problems as necessary
- Liaison with other regulatory and certification bodies
- Participating on committees or panels as necessary.

The responsibilities of the GMP section head, GSDP section head shall include:

- Overall management of the GMP & GSDP Compliance inspection program.
- Form inspection team
- Analyze inspectors gap to identify weakness and recommend appropriate training to lever inspectors performance
- Establishing and monitoring performance metrics regarding the effectiveness of inspection process.

The responsibilities of the Quality section head shall include:

- Establishing and maintaining the Inspectorate's Quality System.
- Establishing and maintaining an internal audit program.
- Establishing and monitoring Quality metrics regarding the effectiveness of the Quality System & continuous improvement.
- Liaison with other regulatory and certification bodies, including PIC/S
- Establishing, maintaining and monitoring CAPA program.
- Prepare Initial draft of the management review documents.

5.1. Code of Ethics & Professional Conduct

The Code of Ethics and Conduct sets forth legal and ethical standards of conduct for JFDA inspectors. It is intended to deter wrongdoing and to promote the conduct of all activities in accordance with high standards. All inspectors required to declare the absence of conflict of interest by signing code of ethics and conducts policy.

Inspections are not compromised by conflict of interest or improper influence. JFDA has no financial dependence on those institutions that are inspected. Inspectors are required to comply with the official conduct and ethics requirements of the Civil Service Bureau by law. Drug control & Inspection Department may make use of technical expert to cover the scope and the objectives of inspection based on Drug Director Decision..

When selecting inspectors or technical expert to inspect manufacturers/ warehouse where there may be a real or perceived conflict of interest. An inspector cannot:

- have been employed by the manufacturer
- have a commercial or financial interest in the manufacturer
- be a significant shareholder in the manufacturer or the manufacturer's industry
- have been engaged by the manufacturer as a consultant

The decisions on whether or not to issue a manufacturer's license and/or GMP,GSDP certificates are based solely on documented, professional considerations resulting from observations and / or other evidence collected during the performance of the inspection process.

6.0 Inspection Procedures

Local manufacturers are regularly inspected by us using a risk-based approach to ensure compliance with GMP requirements .

The risk-based approach is used to determine the frequency at which a manufacturer should be inspected. The inspection frequency of local manufacturer are determined taking into account the following:

- Intrinsic risks associated with the product and manufacturing process
- Manufacturer compliance history.

Overseas manufacturers who supply pharmaceutical products to Jordan are also required to manufacture pharmaceuticals to the same high standard. Where a recognized international regulator has approved a manufacturer, it may not be necessary for JFDA Inspectors to inspect the manufacturing site. GMP Inspection procedure FAC/01 details planning and conducting GMP inspection for local and foreign manufacturer

Following on-site inspection, the inspection team is responsible for preparing a report which includes the inspection findings and a summary of the overall compliance of the manufacturer's operations against GMP requirements.

Deficiencies identified during Inspections are classified as critical, major or other based on the internationally harmonized definitions provided by the Pharmaceutical Inspection Co-operation Scheme (PIC/S) in their document PI013-3. GMP procedure FAC/02 details reporting, certification and licensing mechanism

6.1. Pre-Inspection

Prior to the inspection, a pre-inspection meeting for inspection team shall be made to review manufacturer documents, previous manufacturer inspection report and other related documents as illustrated in GMP inspection procedure FAC/01. A notification is given by sending email contain inspection plan that details the inspection program. At the start of the inspection, the Lead Inspector will hold an opening meeting to discuss details of the inspection including:

- The purpose of the inspection.
- The scope and duration of the inspection;
- The inspection process
- Related guidelines to be used as inspection reference.
- Any required documents to be reviewed.

During the inspection, Inspectors will review the Quality Management System, areas to be inspected and personnel involved in the manufacturing process/supply chain process . The team will ask questions and request to see evidence that demonstrates compliance with the relevant GMP/GSDP standards. If an inspector identifies areas of non-compliance (called deficiencies), these will be discussed during the inspection and additional evidence may be requested by the inspector.

At the end of the inspection, the Lead Inspector will conduct a closing meeting during which a verbal summary of main deficiencies is presented to the manufacturer/warehouse for discussion.

6.2. Inspection duration

The duration of an inspection depends on the nature and complexity of the processes that need to be covered. Where a manufacturer is new an initial inspection is conducted. It is important that the

initial inspection be thorough and comprehensive, involving a detailed examination of the operations & premises. The duration of inspections of manufacturers will be determined taking into account:

- The previous inspection recommendation
- the level of compliance at the last inspection
- the product and process risk factors
- Any other relevant information that is available to the JFDA.
- Significant changes since the last inspection

6.3. Inspection Reporting

Following the on-site inspection, inspection team shall prepare an inspection report within 21 working days of inspection date (report subjected to internal review). Inspection team shall classified all deficiencies in accordance to GMP Reporting, licensing & Certification Procedure FAC/02 & PIC\S PI 040-1`-1: PIC/S Guidance on Classification of GMP Deficiency

The manufacturer/warehouse is provided with a list of deficiencies identified during the inspection. Upon receipt of the list, manufacturers/warehouses should response within two weeks , the response must contain:

- Corrective and preventative action (CAPA) plan for all deficiencies, this plan must include:
  - Investigation of the root cause.
  - Detail of the corrective action(s) taken to address the root cause
  - Detail of the preventative action(s) taken to address the root cause
  - Corrections taken to address the deficiency including objective evidence
  - Due dates for completion of all actions.

The response is viewed as the manufacturers'/warehouses commitment to resolve the identified deficiencies inspection team may uses the response in consultation with team leader to determine whether compliance has/will be achieved in a timely and effective manner. In consultation with department and section head Inspection team leader shall provide manufacturer/warehouse with a cover letter indicating any legal action taken (warning letter, alert letter, suspension of production line, revoke of ML, oblige manufacturer/warehouse to conduct recall).

Once the manufacturer's response is accepted, it is expected that the manufacturer implements the actions as described. Manufacturers are normally required to provide objective evidence in responses to deficiencies/non-conformances. When required section head may decide to plan on-site inspection to verify the effectiveness of CAPA.

Any significant changes or delays to implementation should be discussed with the relevant Lead Inspector & section head. Failure to implement actions to address deficiencies will be identified at the next re inspection and may affect the manufacturer's risk rating and inspection frequency, however when serious situation requires immediate resolution and require regulatory action the department may carry out an urgent follow up inspection.

Following the inspection, inspection team required to enter manufacturer inspection outcomes in the integrated inspection system. The system will assign company compliance level and intrinsic risk to evaluate over all company risk level and determine the frequency of inspection

6.4. Appeals

- If a manufacturer is unsatisfied with an inspector's conclusions and related decision, the management of the inspected site have a right to appeal the inspection decision to the appeal committee within one calendar month from the date of inspection decision official letter. Such appeals should be addressed, in writing and submitted to appeal committee secretary. The appeal committee formed by director general and the member of the committee shall be independent of the persons making the decision that have led to the appeal. according to drug pharmacy law the committee headed by director general and with the membership of:
    1. An internist.
    2. A pharmacist specializing in pharmacology or clinical pharmacology.
    3. A pharmacist specializing in pharmacology.
    4. Specialist in pharmaceutical economics.
    5. Legal advisor in the institution.

6.5. Complaint

Complaints against the JFDA inspectors can be submitted by any party associated with inspection. Irrespective of the means by which it was communicated (telephone, fax, e-mail or letter) through JFDA complain management system. All complains will be handled with strict confidentiality and investigated in reasonable time under Drug director supervision in accordance with Economic activity control and inspection law of 2017 and civil bureau regulations

7.0 Inspection Resources

The Department has a sufficient number of permanent personnel with the necessary expertise to carry out the volume and range of work demanded by its defined functions and duties. Personnel responsible for inspection must have appropriate qualifications, training, experience and knowledge of GMP &GSDP requirements, guidelines and expectations to enable them to perform the inspection. Personnel must understand and be fully conversant with the consequences of deviations that occur or may occur during the production, distribution or use of these products.

Inspectors have the ability to make professional judgments as to conformity with the requirements based on inspectional findings and to prepare detailed reports based on those findings. Inspectors are provided with on-the-job training including participating in training courses provided by experts.

All inspectors undergo a probationary period for 3 months during which they are trained by senior inspector and are gradually permitted to be more active in the conduct of an inspection until the senior is satisfied that they are competent to perform the inspection unaided. all inspections program are performed by two inspectors at least.

Inspectors must have relevant knowledge of the manufacturing technologies and product processes for the types of products being inspected, including understanding of potential defects that may arise as a result of poor quality (safety and / or efficacy). Training procedure QUA/07 illustrate training and qualification of inspectors

The inspectorate has a documented training system to ensure that the training of its personnel, in the technical and administrative aspects of the work in which they will be involved is kept up to date in accordance with its policy. The training required is tailored to the ability, prior work experience and qualifications of the individual. Stages of training include:

- Induction training.
- Supervised working period with experienced inspectors.
- Refresh training.
- On-going training and continuing professional development

The professional requirements for the Inspectors are stated in the: 1) "Accreditation of Manufacturing Site Criteria" of 2016, Appendix 11. According to the Instructions inspectors are classified three levels:

- Inspection Team Leader (lead) : Pharmacist: Bachelor’s degree minimum, at least 5 years of experience in pharmaceutical inspection, trained on GMP, deliver at least two lectures in JFDA

- Inspector Level 1(Senior): Pharmacist, Bachelor's degree minimum, at least 3 years of experience in pharmaceutical inspection, participated in GMP training, still participating in drug inspection (not less than 5 inspections/year)
- Inspector Level 2 (Junior): Pharmacist, Bachelor's degree minimum, at least 1 year of experience in pharmaceutical inspection, participated in GMP training, still participating in drug inspection (not less than 10 inspections/year)

Furthermore, the department have a consolidated training procedure to determine training needs based on competencies gap analysis. New hired inspectors (trainee) shall be trained and observe inspection for at least one year before participating in inspection.

The Department has suitable and adequate facilities and equipment to facilitate to perform inspection. Where computers are used there are procedures to ensure that the software is suitable for use. User manuals are in place to protect data integrity and to ensure that there are routine and regular back-ups of data.

8.0 Internal audit

The Department conducts periodic internal audits, or schedules equivalent audits by other departments. The purpose of the internal audit is to determine whether the department's QMS:

- Conforms to the requirements of the Standard.
- Is being effectively implemented and maintained.

Internal quality audits are planned and scheduled on the basis of the status and importance of the activity to be audited. Audits are performed at least annually under the supervision of Quality section Head. Trained personnel independent of those having direct responsibility for the activity being audited carry out the audits, thus ensuring that auditors do not audit their own work.

Since The Department is small that independence cannot always be fully assured, the department may arrange for the internal audit function to be performed by other qualified parties. Examples of other qualified parties include qualified internal auditors from other departments of JFDA.

On issuance of the report the Head of the inspection section must provide a written response with corrective actions. The results of the internal audits are documented and brought to the attention of the personnel having responsibility for the area audited.

Follow-up activities verify and record the implementation of the corrective action, report the verification results, and close out the audit. CAPA are submitted for management review. Internal Audit QUA/03 & Corrective & Preventive Actions (CAPA) Procedures QUA/05 are followed to perform internal audit and follow-up CAPA.

9.0 Continuous Quality Improvement and CAPA

The Department have established and maintain a system of key performance indicators, organized and defined in an approved Standard Operating Procedure QUA/09 In particular these indicators address but not necessarily limited to: timeframes for performing inspections, for issuance of reports, for review of submitted information, complaints resolving time, etc. Management review meetings will include a review of key performance indicators.

Head of Quality section is responsible for maintaining a Corrective and Preventive Action (CAPA) program in accordance with the relevant standard operating procedure QUA/05. The procedure requires entering any CAPA item into a CAPA register form with a target date for implementation of the required actions and an assigned staff member responsible for the implementation.

Annual Management review meeting will include a review of recurrent CAPA items – those deviations that apparently have not been adequately resolved so that permanent solutions can be put forward and implemented.

10.0 Licensing of Authorization Process

Jordanian pharmaceutical manufacturers are required to obtain licenses of authorization to manufacture pharmaceutical products (according to Bylaw of Pharmaceuticals Factories Licensing and Charged Fees No.11 of 2016). The purpose of licensing is to assure the adequacy of manufacturer location and infrastructure to comply with specifics regulatory requirements.

The following sequence/steps applied when manufacturer require license of authorization:

1. Submit licensing application along with required document as mentioned in instruction of Pharmaceuticals Factories Licensing for 2018 to drug inspection and control department
2. Review of the application by the Committee of licensing
3. Member of the Committee will observe the site/location to assure compliance to the Bylaw of Pharmaceuticals Factories Licensing and Charged Fees No.11
4. The Director-General shall make his recommendation on the licensing application to the Minister of health to make the appropriate decision thereof, provided that such decision shall be made within 30 days from the date of examination.

11.0 Manufacturer Licensing & GMP certification

After the manufacturer obtains the license of authorization, the manufacturer shall obtain GMP and ML certificates. The following sequence/steps applied:

1. submit application (product file and manufacturing site file as illustrated in Criteria of Manufacturing Sites Accreditation) to drug registration department in drug directorate
2. The accreditation committee will review the application of drug manufacturing site and inform the applicant with its decision by formal letter and acknowledge Drug inspection and control department through a copy of the letter
3. If the application is successful, the company shall submit an official request to drug inspection and control department requesting to arrange for inspection, the company required to submit the request within six month of committee decision.
4. Inspection department will schedule the inspection and perform the inspection based on GMP inspection procedures

11.1. On-site inspection

The purpose of the inspection is to establish whether a manufacturer has implemented management systems and practices that comply with the relevant code, quality management system standard and regulations. This will be done by examining actual practices, documentation and records and comparing them against the manufacturer's policies and procedures and the relevant Code or QMS Standard requirements, which can be found in the Manufacturing Principles.

For further details regarding the on-site inspection, refer to the section 'Inspection Procedures' of this document. The Department maintains and follows as stet of standard operating procedure to perform and report inspections:

- GMP Inspection Procedure FAC/01
- GMP Reporting & Certification Procedure FAC/02
- Overseas Inspection FAC/03
- GSDP Inspection Procedure STO/01
- GSDP Reporting & Certification Procedure STO/02

After confirmation that any necessary corrective actions have been taken, which may involve a follow up inspection, the findings and recommendations made in the inspection report are subject to an internal review process prior to certificate being granted.

Once the manufacturer has achieved the requirements for manufacturer licensing and GMP certification, the manufacturer will be issued with a License or Certificate.

When a medicines manufacturer has achieved licensing or certification, JFDA will provide a License to Manufacture or GMP Certificate respectively. The document includes important data such as the license or certificate number, the site address and a description of the types of products and manufacturing steps authorized (for licenses) or certified (for GMP certificates). A Schedule of

Conditions may be included outlining the restrictions imposed on the Certificate. Copies of certificates can be provided upon request and on payment of the applicable fee.

11.2. On-going inspection activities

Following certification, JFDA will Conduct inspections of the certified manufacturer's manufacturing facility at approximately 1 to 3 year intervals (depending on the risk of the products manufactured and the compliance level determined) JFDA may take one the following actions: Warning letter, alert letter, suspension of production line, revoke of "ML" or accreditation of foreign site, oblige manufacturer to conduct recall.

12.0 Refusal of a license or certificate

In the event that the manufacturer is unable to comply with the requirements of the relevant standard, the JFDA may refuse to grant a license or certificate. The decision to refuse licensing or certification by accreditation manufacturing committee will be communicated to the manufacturer in writing.

13.0 GSDP Certification

The drug and pharmacy law oblige warehouses to obtain a license from ministry of health, prior to obtain GSDP certificates. After obtaining License, warehouse submits an application to get GSDP certificate. JFDA may issue GSDP certificate after on-site inspection, if the warehouse found to be comply with Instruction on Transport and Storage of Drugs, and the Technical Specifications of Transportation Vehicles of 2019.

14.0 Handling Suspected Quality Defect

The Rational Drug Use & Pharmacovigilance Department (RDU) is responsible for monitoring the safety of pharmaceuticals product. Its main aim is to minimize the risk related to drugs used and to maximize their benefits. According to the regulations RDU receive adverse drug reaction reports and any complaint related to product quality.

RDU department categorize all recalls into one of three classes, according to the level of hazard involved:

- **Class I:** Dangerous or defective products that predictably could cause serious health problems or death.
- **Class II:** Products that might cause a temporary health problem, or pose only a slight threat of a serious nature.
- **Class III:** Products that are unlikely to cause any adverse health reaction, but that violate JFDA manufacturing guidelines.

RDU department may trigger for cause inspections –carried out by The Department - to investigate specific aspects/ complaints related to pharmaceutical product. Drug control & Inspection Department will identify (when possible) the root cause for the recall and assure the organization has implemented procedures to prevent it from recurring.

For all recall inspections, in addition to verifying the identification of the root cause: Discuss the suspected problem with management and review the firm's complaint file;

- Investigate all areas, control points and/or circumstances which may have a bearing on the product's deficiency;
- Fully develop individual responsibility for the problem;
- Review batch records, processing logs and/or other types of records for violated lots and associated lots;
- Review and obtain copies of the firm's quality control/analytical data;
- Determine any actions the firm has taken, is taking, or has planned to take to prevent similar occurrences. If corrective action is not underway, determine the firm's timetable for achieving correction
- Determine what action the firm has taken or plans to take, and the time frames involved, regarding questionable product(s) remaining in the market

When required JFDA will notify any local entity that could be affected by the recall, notification process is illustrated in standard operating procedure STO/05

15.0 Liaison With The Official Medicine Control Laboratory (OMCL)

The Official Medicines Control Laboratories (OMCL) is a separated independent directorate in JFDA, still, it support The Department in controlling the quality of medicinal products on the market by independent testing/re-testing based on legal requirements.

OMCL and all drug directorate departments may trigger for cause inspections to investigate specific aspects/ complaints related to pharmaceutical product. Such inspection my Triggered by a finding of possible non-compliance with relevant standards based on OMCL tests that are related to batch release or regular surveillance program. When required OMCL directorate may participate in such inspection. Information gained during this inspection is reported to lab committee affair to make any recommend any required action

16.0 Sub-Contracting & Assessing

Drug Inspection and Control Department don't utilize any sub-contracting services and perform all its activities by official employee.

17.0 Publications

Latest revision of this manual available on JFDA website (http://www.jfda.jo/)

18.0 Amendment Record

This Manual reviewed to ensure its continuing relevance to the systems and process that it describes. A record of contextual additions or omissions is given below:

Page No.	Context	Revision	Date
4	2nd Paragraph provides more details of the MOUs signed.	02	01/02/2021
4	3rd Paragraph, 4th add "or certification" after the word "licensing".	02	01/02/2021
5	Section 1.2, References: reference ISO 9001	02	01/02/2021
5	Section 1.3, Scope: – "Sterile and Non-sterile Medicinal Products" added to the list of products regulated by the Department? – Last line: change "is" to "are".	02	01/02/2021
6	Section 3, Documentation System: add "& Change Control" to the title to be consistent with the PIC/S requirements and the contents.	02	01/02/2021
7	List of Procedure Titles: Should the titles for the 2nd and 4th mentioned procedures also include the word "licensing" in order to be consistent with the title of section 10 (The Licensing/Certification Process)?	02	01/02/2021
9	Last Paragraph mention how the RDU Department informs the Drug Control and Inspection Department of the need for a for cause inspection.	02	01/02/2021
19	Removing the following sections – Receiving of Application – Application Review	02	01/02/2021
22	Adding new section: – Liaison With The Official Medicine Control Laboratory (OMCL)	02	01/02/2021
19	Adding new section: – Manufacturer Licensing & GMP certification	02	01/02/2021
18	Editing – Licensing of Authorization Process	02	01/02/2021
22 &23	Adding new section: – Sub-Contracting & Assessing – Publications – Amendment Record	02	01/02/2021