Rapid Assessment of Medicines Quality Assurance Activities in a Pharmaceutical Supply System: a Checklist for Ensuring Product Quality

U. S. Pharmacopeia
Drug Quality and Information Program

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**Acronyms and Abbreviations**

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>ACT</td>
<td>Artemisinin-based Combination Therapy</td>
</tr>
<tr>
<td>AIDS</td>
<td>Acquired Immunodeficiency Syndrome</td>
</tr>
<tr>
<td>API</td>
<td>Active pharmaceutical ingredient</td>
</tr>
<tr>
<td>FDC</td>
<td>Fixed-Dose Combinations</td>
</tr>
<tr>
<td>GMP</td>
<td>Good Manufacturing Practices</td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
</tr>
<tr>
<td>MOH</td>
<td>Ministry of Health</td>
</tr>
<tr>
<td>MSH</td>
<td>Management Sciences for Health</td>
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<tr>
<td>MQA</td>
<td>Medicines Quality Assurance</td>
</tr>
<tr>
<td>MQC</td>
<td>Medicines Quality Control</td>
</tr>
<tr>
<td>RPM Plus</td>
<td>Rational Pharmaceutical Management Plus</td>
</tr>
<tr>
<td>SOP</td>
<td>Standard Operating Procedure</td>
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<tr>
<td>USAID</td>
<td>United States Agency for International Development</td>
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<tr>
<td>USP DQI</td>
<td>United States Pharmacopeia Drug Quality and Information</td>
</tr>
<tr>
<td>USP–NF</td>
<td>United States Pharmacopeia–National Formulary</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
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</tbody>
</table>
1. Introduction

Issues related to the quality of medicines are becoming an increasing global concern, especially in developing countries. The safety, efficacy, and good quality of medicines are sustained by the efforts of multiple institutions and their concerted activities. Achieving a high level of quality requires effective medicines legislation and regulation, a competent medicines regulatory authority (MRA), good clinical and manufacturing practices with adequate medicines quality assurance (MQA) programs and medicines quality control systems (MQC), and appropriate medicines information.

Good practices in a medicines supply system form an important part of ensuring that the quality of pharmaceutical products is maintained throughout the numerous steps in the distribution process. In a country with a well-established medicines regulatory agency, the pharmaceutical industry usually operates at a high level of MQA by complying with current Good Manufacturing Practices (GMP). Manufacturers achieve their pharmaceutical quality objectives during the production of their products and testing to assure quality prior to their release for distribution. This attention to quality must continue throughout the supply and distribution network. This authorized pharmaceutical product should be distributed and handled by retail pharmacists and others licensed to sell medicinal products to the general public without any alteration.

The shelf-life of a medicine is a function of the temperature and humidity under which it is packaged, stored, and transported as much as a function of the chemical and physical properties of the pharmaceutical formulation. Appropriate containers and packaging materials are essential to preventing or minimizing the quality problem caused by handling during product distribution. Since resources are often limited at all supply levels, priorities for MQA activities should be targeted. This document serves strictly as a rapid assessment tool to determine whether a particular pharmaceutical supply and

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a In this document the terms “medicines” and “pharmaceuticals” are used interchangeably.

b “Pharmaceutical supply” covers planning and programming of needs, procurement, storage and distribution, and monitoring and evaluation. “Distribution system” encompasses administrative procedures, transport facilities, storage facilities, and user facilities through which supplies move from a central point to user facilities.

c “Medicines quality” in this document refers to the conformity of a pharmaceutical product to its specifications regarding identity, strength, and other characteristics, including disintegration, dissolution, purity, packaging, and labeling, according to a label claim.

d “Medicines quality assurance” (MQA) program in this document defines a broad framework of goals to be achieved through planned activities, whether individually or collectively, to ensure that the quality of a pharmaceutical product meets the established standards and regulatory requirements.

e “Medicines quality control system” in this document means a functionally related set of elements, including standards setting and measurements, sampling, and quality testing to ensure that raw materials, intermediates, packaging materials, and finished pharmaceutical products conform to established specifications for identity, strength, purity, and other characteristics.
distribution system has a satisfactory MQA program in place to ensure product quality is maintained throughout the distribution system. This document is about product quality; it does not attempt to assess the organizational structure nor quality management of a pharmaceutical supply system. For this information, readers may refer to the Management Sciences for Health Rational Pharmaceutical Management Plus resource, *Rapid Pharmaceutical Management Assessment: an Indicator-Based Approach*.

In summary, the MQA components of a pharmaceutical supply system should consider product selection, procurement, regular access, disposal system, storage, and distribution. The latter entails receipt of procured medicines at ports of entry, clearance from customs, and transportation from a central warehouse (or the warehouse of a manufacturer) to each delivery point, including regional depots, health facilities, and retail outlets where medicines are stored and dispensed to consumers and patients.

This assessment tool can be used for supply and distribution systems in both the public and the private sectors.

2. Objectives of the assessment

This rapid assessment will help improve the understanding of concerned parties, including MRAs, suppliers, distributors, and wholesalers, regarding how their existing MQA program and MQC system operate. It will also provide guidance for developing an appropriate strategy to improve problem areas. The assessment specifically seeks to:

1. Determine whether a MQA program exists in a particular pharmaceutical supply and distribution system;
2. Examine if the supply system and MQA activities are adequate to ensure the continued quality of pharmaceuticals being supplied and distributed;
3. Examine the attitudes of the respondents about the adequacy of their MQA activities;
4. Suggest improvements, where applicable, to suppliers, distributors, and relevant authorities who develop and implement MQA/MQC procedures and activities.

3. Methodology

3.1. Methodological framework

The methodology of this review and assessment is based on the following information framework:

- Background information – review the general pharmaceutical supply and distribution systems in the country and check legal status, roles, and functions of the supplier and distributor selected for assessment.

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1 Suppliers, in this document, refer to pharmaceutical manufacturers, supply agents, and procurement agencies (including NGOs that procure medicines). Although a checklist for GMP audit is annexed to this document, it does not address QA/QC of a manufacturer.

2 Distributors refers to pharmaceutical distributors and wholesalers, not retail pharmacies or outlets.
- Process information – evaluate management’s commitment, efforts, and investment in resources and technology to achieve mandates specifically regarding:
  - organizational structure and key personnel responsibilities;
  - scope and activities of medicines MQA/MQC and responsible personnel;
  - technical elements of quality norms, standards, specifications, procedures, and good practices;
  - monitoring and evaluation mechanism.

- Outcome information – examine how the supplier’s and distributor’s MQA/MQC activities are carried out and if their objectives are being met.

3.2. Assessment process

The process to assess a pharmaceutical MQA/MQC of a supplier or distributor is illustrated in the figure below.

3.2.1. Assessment planning

Step 1: a. Set up an Assessment Team
The team should have pre-defined roles and scope of work, e.g., assessment planning, execution, documentation, and reporting. The Team should consist of at least three experienced professionals (e.g., qualified pharmacist, pharmaceutical management expert, laboratory analyst, or medicines inspector), one in pharmaceutical supply management, one in medicines MQA/MQC, and one in regulatory affairs. To reduce the potential bias in the process, ensure transparency, and avoid potential conflicts of interest, the assessment should be carried out by a non-governmental organization (e.g., an academic institution or a private organization). It can also be done by an international organization. A governmental agency, like an MRA, can perform the assessment of a private supplier/distributor.

b. Obtain necessary approvals for the assessment
The assessment, including the appointment of the Team and its role and scope of work, must be approved by the relevant authority for the validity, integrity,
and impartiality of the assessment outcomes. In many instances, the MOH or MRA would need to approve it. Approval should be secured before the actual assessment begins.

**Step 2:** Establish a time table and financial budget  
The budget should be based on the scope of work and timetable described in the assessment.

**Step 3:** Communicate appropriate information  
Information about the assessment should be provided to all targeted suppliers and distributors, responsible authorities, and interested persons to enlist their support and cooperation. These will usually include various units or divisions of the MRA (e.g., licensing, inspection, laboratory testing); Ministries of commerce and trade or industry; medicines suppliers (manufacturers, supply agents, procurement agencies, and importing/exporting agencies); and distributors (distributing agencies and wholesalers of medicines).

### 3.2.2. Data collection

A questionnaire will guide the team selected to do the assessment to collect the required data and information (See Information Collection Questionnaire).

Data can be collected using a variety of methods or combined techniques:

1. Conducting formal or semi-formal discussions and consultations with key informants (KI).\(^b\) Tips for selection of KI are outlined in the Annex. They may be government officials at central and provincial levels or from Ministries of health, trade/commerce, and industry; MRAs; wholesalers; distributors; procurement agencies; non-governmental bodies, national or international, secular or faith-based; medicines quality control labs; or selected key pharmaceutical establishments.\(^i\)

2. Reviewing relevant and accessible (published and unpublished) technical documents and records from primary and secondary sources. These include drug legislation and regulations, executive orders, inspection records, and annual or mid-term reports of the MRA and national medicines quality control laboratory.

3. Using other convenient techniques, such as structured interviews or questionnaires by e-mail, fax, or telephone.

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\(^b\) Key informants are those people that have a direct stake in the production, procurement, supply, distribution, or storage of pharmaceuticals, such as a managing director or persons in charge of QA/QC in a manufacturer, procurement agency, wholesaler, distributor, or retailer; officials who issue licenses for pharmaceutical establishments or medicines vendors and conduct inspections; medicines control laboratory staff; or consumer groups.

\(^i\) Pharmaceutical establishments include manufacturers, wholesalers, procurement agencies, importers/exporters, and retailers (pharmacies and retail medicines outlets).
3.2.3. Data Analysis and Clarification

Quantitative data collected from the questionnaire or obtained through other techniques should be examined, computed (meaning some form of data entry, e.g., spreadsheet), and analyzed by the assessment team with some assistance, if necessary, from external experts in the field.

To minimize subjective interpretations of responses like “yes,” “no,” “don’t know” or “not applicable,” and in order to validate those responses, the assessment team must ask a series of subordinate questions or request supporting materials from the key informants.

Example for responses with “yes,” “no,” “don’t know” or “not applicable,”

Is [name of the establishment being assessed] an officially licensed establishment? □ yes □ no □ don’t know □ not applicable
If yes, provide additional supporting information by checking boxes that apply:

| 1.  | The official license was shown | □ |
| 2.  | The issue date/month/year of the license | □ |
| 3.  | The license is valid until (date/month/year) | □ |
| 4.  | Name of authorized authority/agency who issued the license | □ |

Likert Scale Technique
Additional questions presenting a set of attitude statements for the respondents to comment on are referred to as the Likert Scale Technique. Subjects are asked to express agreement or disagreement on a five-point scale. Following a statement, the assessment team asks the KIs whether they “strongly agree,” “agree,” are “undecided,” “disagree” or “strongly disagree.” For example, a question might ask the KI to what extent he/she agrees with the statement that “Adequate storage facility room(s) and shelves for storing and/or displaying medicines is a criterion to be met for consideration of licensing decision-making.” The assessment team or the respondent will then check the appropriate box for his/her answer.

<table>
<thead>
<tr>
<th>Strongly agree</th>
<th>Agree</th>
<th>Undecided or don’t know</th>
<th>Disagree</th>
<th>Strongly disagree</th>
</tr>
</thead>
</table>

Likert Scale answers could help investigators determine – based on the attitudes and perceptions of the KIs – whether or not a particular element or component of the system (e.g., licensing) is in fact operational.

3.3. Reporting and Recommendations

The report of the assessment should be based on the data analysis findings as described in the previous section and should be presented in an appropriate format for easy
comprehension and quick action. Main findings and appropriate actions recommended should be included in the report, as should key issues and problematic areas of the medicines MQA/MQC systems to be addressed. In the recommendations, prioritization is critical for the issues and problems to be tackled or targeted to specific areas, e.g., those areas in need of strengthening due to the lack of resources or budgetary constraints. Where appropriate, a proposed step-by-step process should be described.

4. Information Collection Questionnaire

**General Consideration:** the questionnaire below serves as a guide to obtain general information and specific data for the assessment of MQA/MQC in a particular pharmaceutical establishment (wholesaler/distributor, procurement agency, importer/exporter, or main pharmacy that operates as wholesaler).

Every effort has to be made to obtain the most up-to-date information. If multi-year data is involved, indicate the year next to the data.

**Confidentiality:** all data collected and the final report of the assessment should be kept confidential and should not be disclosed to a third party, including individuals, institutions, and/or organizations that are not involved in the assessment unless agreed by the concerned parties, i.e., the assessment team, the assessed company or agency, and the MRA.

**Anonymity:** the names of interviewees or key informants should be anonymous.

4.1. Pharmaceutical regulation, policy, and essential medicines

Medicines legislation, regulations, and policies are needed to ensure that manufacturing, importing, exporting, distributing (wholesale and retail), and dispensing practices are performed according to safety, efficacy, and quality norms and standards. An MRA can perform its key functions effectively if it has a strong backing of adequate legislation, regulations, and policy. A national medicines policy provides a foundation for managing pharmaceutical supply and quality.

Q1: Does the country have drug laws and regulations that cover pharmaceutical management and quality?

☐ yes ☐ no ☐ don’t know ☐ not applicable
If yes, provide additional information below to support the answer by checking boxes that apply:

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>1.</td>
<td>Drug law book and regulations (in written form) shown □</td>
</tr>
<tr>
<td>2.</td>
<td>Direct the assessment team where to find the document □</td>
</tr>
<tr>
<td>3.</td>
<td>The law was promulgated in _________ (year) □</td>
</tr>
<tr>
<td>4.</td>
<td>The law was last updated in _________ (year), if applicable □</td>
</tr>
</tbody>
</table>
To what extent do you agree with the statement “the existing laws on pharmaceutical drugs adequately cover all aspects of medicines quality”?

<table>
<thead>
<tr>
<th>Strongly agree</th>
<th>Agree</th>
<th>Undecided or don’t know</th>
<th>Disagree</th>
<th>Strongly disagree</th>
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</table>

Q2: Are there any measures for enforcement and compliance of pharmaceutical laws and regulations?

☐ yes   ☐ no   ☐ don’t know  ☐ not applicable

If yes, check all appropriate boxes that apply.

1. Enforcement through empowered MRA
2. Regulatory measures such as ministerial orders and decrees
3. Administrative measures such as ministerial and/or MRA’s notices and warnings
4. Violators are handled through court actions
5. Other measures, specify ……………………………………………

Q3. Within these laws and regulations, which of the following aspects of quality assurance of medicines are covered? Check all boxes that apply.

5. Pharmaceutical product registration
6. Pharmaceutical establishment licensing
7. Pharmaceutical product production
8. Pharmaceutical product sale and distribution
9. Pharmaceutical product quality defect reporting and recall

Q4. Within the pharmaceutical establishment licensing regulation, does it specify the responsible authority or person for issuing the license?

☐ yes   ☐ no   ☐ don’t know  ☐ not applicable

If yes, who is responsible for issuing the official license for the pharmaceutical establishments categorized below? Check all appropriate boxes that apply.

<table>
<thead>
<tr>
<th>Type of establishment</th>
<th>License issuing agency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>National MRA</td>
</tr>
<tr>
<td>Manufacturer</td>
<td>☐</td>
</tr>
<tr>
<td>Wholesaler/distributor</td>
<td>☐</td>
</tr>
<tr>
<td>Importer/exporter</td>
<td>☐</td>
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<tr>
<td>Retail pharmacy</td>
<td>☐</td>
</tr>
</tbody>
</table>
Q5. Does the country have a national medicines policy?
   ☐ yes   ☐ no   ☐ don’t know   ☐ not applicable
   If yes, provide additional information below to support the answer by checking boxes that apply:

   1. Policy document shown ☐
   2. Direct the assessment team where to find the document ☐
   3. The policy was developed in __________________ (year) ☐
   4. The policy was last updated in __________________ (year) ☐
   5. The policy covers quality of medicines as one of its components ☐
   6. The policy covers licensing of pharmaceutical establishments as one of its components ☐

   To what extent do you agree with the statement “the national medicines policy provides appropriate guidance to key players in the proper management of pharmaceuticals and their quality”?

<table>
<thead>
<tr>
<th>Strongly agree</th>
<th>Agree</th>
<th>Undecided or don’t know</th>
<th>Disagree</th>
<th>Strongly disagree</th>
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Q6: Does the country have a national essential medicines list (EML)?
   ☐ yes   ☐ no   ☐ don’t know   ☐ not applicable
   If yes, provide additional information below to support the answer by checking boxes that apply:

   1. EML shown ☐
   2. EML was first developed in _________________ (year) ☐
   3. EML was last updated/revised in _________________ (year) ☐
   4. The number of preparations enlisted on the last version _________________ ☐
   5. EML was developed based on the WHO Model List of Essential Medicines ☐
   6. There is a committee in charge of selecting essential medicines ☐

   To what extent do you agree with the statement “quality is considered one of the key determinants in the selection of essential medicines by the committee”?

<table>
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<tr>
<th>Strongly agree</th>
<th>Agree</th>
<th>Undecided or don’t know</th>
<th>Disagree</th>
<th>Strongly disagree</th>
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</table>
Q7: Is the EML applied to and used by both the public and private sectors?
☐ yes ☐ no ☐ don’t know ☐ not applicable

If yes, provide additional information on the levels of health care operations the list is applied by checking the appropriate boxes:

1. Ministry of health procurement ☐
2. Private company procurement ☐
3. Hospitals (central and peripheral) ☐
4. Clinics and pharmacies ☐

To what extent do you agree with the statement “the local pharmaceutical manufacturers give the list of essential medicines high priority in their production”?

<table>
<thead>
<tr>
<th>Strongly agree</th>
<th>Agree</th>
<th>Undecided or don’t know</th>
<th>Disagree</th>
<th>Strongly disagree</th>
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To what extent do you agree with the statement “priority is given to those products in the EML for the supply in the public sector?”

<table>
<thead>
<tr>
<th>Strongly agree</th>
<th>Agree</th>
<th>Undecided or don’t know</th>
<th>Disagree</th>
<th>Strongly disagree</th>
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4.2. Pharmaceutical supply systems

Different pharmaceutical supply systems exist and vary considerably with respect to the role of the government, the private sector, and incentives for efficiency. In terms of technical requirements – except for cold chain versus a non-cold chain system – the MQA activities should not vary much from one supply system to another, regardless of their methods of operation, e.g., central medical store, autonomous supply agency, direct delivery system, prime vendor, or fully private system. However, one system might require a stricter monitoring mechanism than others. For example, a fully private supply system usually requires more monitoring than any other system, particularly in countries where the pharmaceutical markets are not well-regulated.

Q8: Which pharmaceutical supply and distribution systems exist in the public sector in [the name of the country being assessed]? Please check all boxes that apply. (Note that while this question helps identify the type of supply/distribution system in the country, it does not indicate whether that system is functional and effective or not.)

1. Central medical store (CMS) – a conventional supply system in which a centralized government unit/department procures and distributes medicines ☐
2. Autonomous supply agency – an alternative to the CMS system, ☐
managed by an autonomous or semi-autonomous agency with flexibility in personnel and management

3. Direct delivery system – a non-CMS and decentralized system whereby the medicines are directly delivered by the producers/suppliers to the health care facilities and retail outlets. □

4. Prime vendor system – the government contracts with a single prime vendor who may or may not receive medicines from suppliers but distributes them to health care facilities. □

5. Fully private supply – medicines are provided by private distributors and pharmacies in or near government health facilities □

6. Missions, charities, and non-governmental organizations – procure, store and distribute medicines through their own system or through one of the above mechanisms □

Q9: Is [name of the establishment being assessed] an officially licensed establishment or an establishment granted permission by a relevant authority, e.g., Ministry of Health?
☐ yes ☐ no ☐ don’t know ☐ not applicable
If yes, provide additional information below to support the answer by checking boxes that apply:

1. The official license (or permission) was shown □
2. The license is issued (or permission is granted) for the first time □
3. The issue/grant date/month/year of the license ________________ □
4. The license (or permission) is renewed □
5. The date/month/year of renewal ___________________________ □
6. The license (permission) is valid until (date/month/year)__________ □
7. Name of authorized authority/agency who issued/granted the license/permission ____________________________________ □

Q10: What type of supply mechanism best describes the [name of the establishment being assessed]?

1. Central medical store □
2. Autonomous supply agency □
3. Direct delivery system □
4. Prime vendor system □
5. Fully private supply □
6. Missions, charities, and non-governmental organizations □

The following questions are specific for manufacturers, wholesalers/distributors, procurement agencies, and importers/exporters. In the assessment of MQA/MQC in a manufacturing site, the Assessment Team should use the GMP audit checklist which is available in Annex 1 in this document.
Q11: Does [name of establishment being assessed] have an organigram (diagram/flowchart of its organizational structure)?
   ☐ yes ☐ no ☐ don’t know ☐ not applicable
If yes, provide additional information below to support the answer by checking boxes that apply:

1. The organigram was shown
2. In the organigram, there is a unit/division shown that is responsible for MQA/MQC activities

To what extent do you agree with the statement “the existing organizational structure of the company is adequate for successful operation”?

<table>
<thead>
<tr>
<th>Strongly agree</th>
<th>Agree</th>
<th>Undecided or don’t know</th>
<th>Disagree</th>
<th>Strongly disagree</th>
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Q12: Does [name of establishment being assessed] have a policy document (QA policy document) on its quality assurance program?
   ☐ yes ☐ no ☐ don’t know ☐ not applicable
If yes, provide additional information below to support the answer by checking boxes that apply:

1. The QA policy document is shown
2. The QA policy document has been reviewed by qualified external experts
3. The organization or company implements the policy which is reflected in the following activities:
   - A designated person or team in charge of MQA/MQC activities
   - Written standard operating procedures exist covering various activities it performs, e.g., product selection, consignment reception, delivery, and plan for recall
4. The organization or company provides training on the QA policy and each SOP it issues

To what extent do you agree with the statement that “the policy on quality assurance of medicines in [the name of establishment being assessed] is adequately followed”?

<table>
<thead>
<tr>
<th>Strongly agree</th>
<th>Agree</th>
<th>Undecided or don’t know</th>
<th>Disagree</th>
<th>Strongly disagree</th>
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</table>
Q13: Do the normal activities of [the name of establishment being assessed] incorporate procedures from any type of guidelines for ensuring its good practices?

☐ yes  ☐ no  ☐ don’t know  ☐ not applicable

If yes, provide additional information below to support the answer by checking boxes that apply:

1. The organization or company follows [specify the name of the guideline, e.g., WHO Good Distribution Practices for Pharmaceutical Products¹; WHO Guide to Good Storage Practices for Pharmaceuticals²] ___________________________

☐ The applicable guidelines are shown

4.3. Product and supplier selection

Q14: Product selection: What measures has [name of the establishment being assessed] been taking to ensure that the medicines it selects meet the quality standards acceptable in compliance with the national regulatory requirements?

Check all boxes that apply:

1. There is an officially appointed committee responsible for the product selection

☐

2. Product quality specification, based on reliable information, e.g., pharmacopeial monograph standards, where applicable, are required

☐

3. Product certification, e.g., WHO Model Certificate of a Pharmaceutical Product, or something similar, is required

☐

4. Select only products that are on the national EML

☐

5. Purchase only products that are registered in the country

☐

6. The product is registered in other countries: (name) __________

___________________________________________________

7. Products that have been pre-qualified by WHO (for HIV/AIDS, malaria, and tuberculosis medicines)

☐

To what extent do you agree with the statement “the MRA provides appropriate guidance for product selection and their quality”?

<table>
<thead>
<tr>
<th>Strongly agree</th>
<th>Agree</th>
<th>Undecided or don’t know</th>
<th>Disagree</th>
<th>Strongly disagree</th>
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<td>☐</td>
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</tr>
</tbody>
</table>

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² [http://www.who.int/medicinesdocs/collect/medicinedocs/pdf/s6156e/s6156e.pdf](http://www.who.int/medicinesdocs/collect/medicinedocs/pdf/s6156e/s6156e.pdf)

1 WHO Certification Scheme is a voluntary scheme requiring participating MRAs to provide the following certificates: a) Certificate of pharmaceutical product, issued by MRA in exporting country, providing licensing status of the product and inspection status of the manufacturer; b) Statement of licensing status, issued by MRA in exporting country, stating that the product is licensed/registered; and c) batch certificate of analysis, issued by the manufacturer or MRA, confirming that individual batches conform to established specifications.
Q15: **Supplier selection:** Are there regulatory requirements that [name of the establishment being assessed] must follow to select reliable suppliers for pharmaceutical procurement or purchasing to ensure product quality?

- [ ] yes  [ ] no  [ ] don’t know  [ ] not applicable

Check all boxes that apply:

1. There is an officially appointed committee responsible for the supplier selection (of active pharmaceutical ingredient(s) (APIs), excipients, or finished dosage forms)

2. A statement of licensing status, stating that the supplier is officially licensed or registered (locally if it is a local producer/supplier; in the exporting country if it is a foreign company) issued by an MRA, is required

3. Reference checks and information exchange between other MRAs (where the products were produced or supplied or marketed) took place

4. Manufacturing/supplier site inspection was conducted

5. Targeted samples were collected for laboratory testing

6. Uses suppliers that are pre-qualified by reputable international agencies, e.g., WHO

7. Product certification, e.g., WHO Model Batch Certificate of Analysis issued by the manufacturer or MRA in exporting country, or something similar, is required

To what extent do you agree with the statement “the MRA has provided useful technical advice on the selection of suppliers based on their product quality and reliability of services”?

<table>
<thead>
<tr>
<th>Strongly agree</th>
<th>Agree</th>
<th>Undecided or don’t know</th>
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<th>Strongly disagree</th>
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</table>

4.4. **Product packaging and labeling**

**Packaging requirements:** Good manufacturing and pharmaceutical distribution practices require that product packaging should meet certain norms, e.g., pharmacopeial standards. These apply for the primary container, packaging material, and secondary container, including the shipping containers. Packaging materials and containers should not interact with the sampled material, nor should they allow contamination.

For pre-packaging and re-packaging pharmaceutical products, the following requirements should apply:

- The re-packaging materials/containers should be labeled with the same labeling information as the market label that is used by the manufacturer. Written procedures should be maintained to ensure that correct labels,
labeling, and packaging materials are used for pharmaceutical products.

- The re-packaging container should show the equivalent of, or be better in protective properties than, the manufacturer's original container. For moisture-sensitive products, a higher-barrier container should be used for re-packaging.

- The re-packager should have proper documentation in place to show the equivalency in protection of the container used.

Q16: **Primary packaging and its labeling:**

Does [name of the establishment being assessed] apply any measures to ensure proper packaging of the pharmaceutical products it orders?

- [ ] yes
- [ ] no
- [ ] don’t know
- [ ] not applicable

If yes, check all boxes that apply:

1. [Name of the establishment being assessed] specifies the pharmacopeial monograph requirements for the type of material or container, e.g., plastic, glass, light protection, and closure description

2. [Name of the establishment] requires that the primary packaging bear the following information:
   - [ ] the product name (brand and generic, if applicable)
   - [ ] list of each API (using International Non-proprietary Name, if applicable)
   - [ ] the amount of content expressed in volume or mass of each present API
   - [ ] Batch or lot number
   - [ ] Manufacturing date and/or expiry date
   - [ ] Name of manufacturer and address

To what extent do you agree with the statement “the quality requirements of the primary container or packaging materials are critical to ensure the quality of a pharmaceutical product”?

<table>
<thead>
<tr>
<th>Strongly agree</th>
<th>Agree</th>
<th>Undecided or don’t know</th>
<th>Disagree</th>
<th>Strongly disagree</th>
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</tbody>
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m Primary or immediate container is the container that comes into direct contact with the pharmaceutical substance and ingredients. For the majority of oral dosage forms, the primary container consists of a cap and a bottle or a blister or pouch package that can be made from many different materials, including glass, plastic, single or laminated flexible materials, and metal.
Q17: **Secondary packaging and its labeling:**

Does [name of the establishment being assessed] apply any measures to ensure proper (secondary) packaging and labeling of the pharmaceutical products it orders?

- [ ] yes
- [ ] no
- [ ] don’t know
- [ ] not applicable

If yes, check all boxes that apply:

<table>
<thead>
<tr>
<th>[Name of the establishment] requires that the secondary packaging bear the following information:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- the product name (brand and generic)</td>
</tr>
<tr>
<td>- list of each API (using International Non-proprietary Name, if applicable)</td>
</tr>
<tr>
<td>- the amount of content expressed in volume or mass of each present API</td>
</tr>
<tr>
<td>- batch or lot number</td>
</tr>
<tr>
<td>- manufacturing and expiry date</td>
</tr>
<tr>
<td>- pack size (in number, weight or volume) of the product units</td>
</tr>
<tr>
<td>- producer’s, wholesaler’s or agent’s name and address</td>
</tr>
</tbody>
</table>

Q18: **Additional packaging and its labeling:**

Does [name of the establishment being assessed] apply any measures to ensure proper packaging and labeling of the pharmaceutical products it orders?

- [ ] yes
- [ ] no
- [ ] don’t know
- [ ] not applicable

If yes, check all boxes that apply:

<table>
<thead>
<tr>
<th>[Name of the establishment] requires that the additional packaging bear the following information for shipping or transportation:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- the product name (brand and generic)</td>
</tr>
<tr>
<td>- list of each API (using International Non-proprietary Name, if applicable)</td>
</tr>
<tr>
<td>- the amount of content expressed in volumetric or mass of each present API</td>
</tr>
<tr>
<td>- batch or lot number</td>
</tr>
<tr>
<td>- manufacturing date and expiry date</td>
</tr>
<tr>
<td>- producer’s name and detailed contact address</td>
</tr>
<tr>
<td>- consigner’s name and detailed contact address</td>
</tr>
<tr>
<td>- container record/serial number</td>
</tr>
<tr>
<td>- consignee’s name and detailed contact address</td>
</tr>
<tr>
<td>- other information, e.g., program or project code/name, where applicable</td>
</tr>
</tbody>
</table>

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n Secondary packaging does not come in direct contact with the pharmaceutical substance or article but provides essential protection for product stability and is usually designed for the final market presentation. It is often used simply to carry required labeling or to keep individual primary containers together with delivery systems or other add-on features. Secondary containers can also provide protection against damage in the handling and distribution system.

o Additional and final packaging: a wide variety of additional packaging, such as trays, display cartons, corrugated fiberboard boxes (cases), or a wrapper. The shipping case label is affixed to this outermost layer and incorporates all of the bar codes as required by national regulation. This final package is normally shipped on pallets to distribution centers, wholesalers, and other large-volume customers.
4.5. Product delivery and transportation

The quality of medicines should be ensured during dispatching for distribution and transportation by following written standard operating procedures (SOPs) and having adequate means of transportation.

Q19: Are there written SOPs concerning product delivery or dispatching?

☐ yes ☐ no ☐ don’t know ☐ not applicable

If yes, check all boxes that apply:

1. SOP documents are shown (either printed or electronic format)
2. SOPs cover verification for completeness, correctness of invoice (e.g., product same as ordered), accuracy of quantity, and addressee’s details
3. Product quality is checked before dispatching (right product, dosage, strength, lot/batch number, complete and valid accompanied documents, and proper packaging)
4. Dispatching document is double signed by the responsible person
5. A copy of the dispatching document is kept for future reference

To what extent do you agree with the statement “[name of the establishment being assessed] follows strictly the delivery protocol or SOPs for every delivery”?

Strongly agree ☐ Agree ☐ Undecided or don’t know ☐ Disagree ☐ Strongly disagree ☐

Q20: Are there written SOPs concerning transportation to maintain products’ quality?

☐ yes ☐ no ☐ don’t know ☐ not applicable

If yes, check all boxes that apply:

1. SOP documents are shown (either printed or electronic format)
2. [Name of the establishment being assessed] has appropriate vehicles for transportation of its products to clients
3. Temperature control device is in good working order in the vehicles
4. Humidity control device is in good working order in the vehicles
5. Cooling system is in good working condition for transporting heat-sensitive agents such as vaccines or artemisinin-derivative preparations, e.g., artesunate injection
To what extent do you agree with the statement “[name of the establishment being assessed] has always used vehicles with appropriately controlled temperature and humidity and protection from rain and direct sunlight to transport its medicines to its clients”?

<table>
<thead>
<tr>
<th>Strongly agree</th>
<th>Agree</th>
<th>Undecided or don’t know</th>
<th>Disagree</th>
<th>Strongly disagree</th>
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Q21: An effective port clearance procedure at ports of entry should be in place to reduce storage charges and prevent physical damages and losses. Inadequate storage conditions at the port may adversely influence the quality of medicines.

Does [name of the establishment being assessed], follow appropriate measures to clear customs effectively?

☐ yes  ☐ no  ☐ don’t know  ☐ not applicable
If yes, check all boxes that apply:

<table>
<thead>
<tr>
<th>1. A written protocol concerning customs clearance that [name of the establishment being assessed] follows was shown</th>
<th>☐</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Every incoming shipment/consignment is checked by a designated person for accuracy and completeness of the documents and certifications.</td>
<td>☐</td>
</tr>
<tr>
<td>3. [Name of the establishment being assessed] performs the visual/physical inspection of the consignment for physical damages of suspected containers or products.</td>
<td>☐</td>
</tr>
<tr>
<td>4. Suspected or random samples are taken and sent to the laboratory for medicines quality control before accepting the consignment(^p)</td>
<td>☐</td>
</tr>
<tr>
<td>5. Usually customs clearance takes less than one (1) week. If it takes longer, specify __________________________________</td>
<td>☐</td>
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</table>

To what extent do you agree with the statement “the ports of entry have storage areas suitable for medical products”?

<table>
<thead>
<tr>
<th>Strongly agree</th>
<th>Agree</th>
<th>Undecided or don’t know</th>
<th>Disagree</th>
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Q22: **Receipt of ordered pharmaceutical products at warehouse**: Written SOPs should be in place and followed by the person(s) responsible e.g., every incoming consignment is quarantined until the receiving report is cleared by authorized personnel for release into the allocated storage positions.

Does [name of the establishment being assessed], follow appropriate measures to ensure that the products received are of good quality?

- [ ] yes
- [ ] no
- [ ] don’t know
- [ ] not applicable

If yes, check all boxes that apply:

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<tbody>
<tr>
<td>1. A written protocol or SOPs concerning the receipt of a consignment that [name of the establishment being assessed] follows was shown</td>
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<tr>
<td>2. Every incoming consignment is checked by a designated person for accuracy and completeness of the documents and certifications</td>
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<tr>
<td>3. Quarantine area is available and shown</td>
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<tr>
<td>4. [Name of the establishment being assessed] performs the visual/physical inspection of the consignment for physical damages of suspected containers or products</td>
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<tr>
<td>5. Suspected or random samples are taken and sent to the MQC unit in the warehouse or a MQC laboratory and, based on the results, the goods are accepted and placed in their appropriate stock locations</td>
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</table>

To what extent do you agree with the statement “[name of the establishment being assessed] follows strictly the receiving protocol or SOPs and therefore it can detect any quality problems with its products”?

- [ ] Strongly agree
- [ ] Agree
- [ ] Undecided or don’t know
- [ ] Disagree
- [ ] Strongly disagree

Q23: **A laboratory testing facility** is a requirement for many well-established international and national procurement agencies, as is a large warehouse equipped with appropriate facilities and equipment to carry out product quality testing. To determine if laboratory testing and warehousing meet requirements, the investigator should visit the facility in question and meet with management and ask the following questions. For more specific questions, the assessment team is advised to consult Part B Questionnaire in the *Rapid Assessment of a Drug Quality Assurance Program and Drug Quality Control Systems*.q

---

Does a MQC lab exist in the facility?
- yes
- no
- don’t know
- not applicable

If yes, check all boxes that apply:

1. A written SOP or protocol on sample collection is shown
2. Product samples are sent to the lab for quality testing together with a testing request form
3. There is a person responsible for coordinating the sample testing with the MQC laboratory
4. Results of the test are used to determine whether or not the product in question conforms with the quality standard specifications
5. Results of the test are used for accepting or rejecting the product in question

To what extent do you agree with the statement “[name of the establishment being assessed] has never procured any substandard or counterfeit products”?

<table>
<thead>
<tr>
<th>Strongly agree</th>
<th>Agree</th>
<th>Undecided or don’t know</th>
<th>Disagree</th>
<th>Strongly disagree</th>
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Q24: Minimum types of analytical tests the lab is able to perform:

1. Identification test
2. Disintegration test
3. Dissolution test
4. Assay for content of API(s)
5. Other tests, specify: _____________________________________

Q25: **Storage and Stock Management** from a Quality Perspective: The quality of medicines depends, in part, on proper storage and stock management practices. This is very significant in tropical climate countries with high temperature and humidity.

Does [name of the establishment being assessed] apply any measures to ensure proper storage and stock management to maintain the quality of the pharmaceutical products it possesses?
- yes
- no
- don’t know
- not applicable

If yes, check all boxes that apply:

1. It ensures proper storage conditions by equipping the necessary devices to monitor:
   - temperature
   - humidity
   - lighting
   - ventilation
2. Receiving area of incoming products is well segregated with a clearly defined quarantine area

3. The storage areas are well organized (e.g., with specified block/bay, shelves) and clearly labeled

4. Expiry date is clearly labeled on all containers

5. Products are arranged by “first-expired-first-out” then “first-in-first-out” principles

6. Written SOPs on each main storage activity are available

7. Written SOPs on each main storage activity are followed (the assessment team should ask for records/documentation on SOP implementation)

8. Regular inventories are performed with documentation or records (check if an inventory was performed in the last 12 months)

9. Updated stock records for all products in the storage are maintained (check the record book or cards or computer, if a computerized inventory system is used)

10. Quantity and value of expired items are recorded

11. Product quality problem reports are documented and maintained

12. Information is fed back to QA office

To what extent do you agree with the statement “the MRA or institution has established appropriate regulations and guidelines concerning the good storage practices for relevant parties to follow”?

<table>
<thead>
<tr>
<th>Strongly agree</th>
<th>Agree</th>
<th>Undecided or don’t know</th>
<th>Disagree</th>
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4.6. Post-delivery performance and monitoring for product quality

Post-delivery performance (quality of service) and monitoring for medicines quality should be required by the MRA as an integral part of any contract with suppliers or distributors/wholesalers. Problems related to poor performance on the part of a supplier or distributor/wholesaler in addressing a product quality defect should be documented and produced upon request to the MRA. Reports of a quality defect in a pharmaceutical product from a consumer or client should be addressed to the MRA. Reports of quality defects of any type can be used to evaluate the supplier in the future.
Q26: Average delivery time\(^1\) that the [name of the establishment being assessed] could be able to complete an order delivery. A shorter delivery time is better from a stock management and quality point of view.

Check all boxes that apply:

1. Less than two months for those products that are in stock. If it takes longer, specify: □
2. Less than six months for those products that are not in stock. If it takes longer, specify: □
3. Less than eight months for those products that need to be procured from foreign countries. If it takes longer, specify: □

Q27: Does [name of the establishment being assessed] have a monitoring mechanism for their products' quality once they are out in the market or have been distributed?

- [ ] yes
- [ ] no
- [ ] don’t know
- [ ] not applicable

If yes, check all boxes that apply:

1. A written policy or protocol on quality monitoring is available □
2. There is an assigned staff person responsible for this activity □
3. In the policy or protocol, there are sections that cover when, how, and who is in charge of sampling, testing, documentation, and reporting □
4. There are records or documentation of cases reported on product quality problems □

To what extent do you agree with the statement “the medicines quality monitoring of [name of the establishment being assessed] is functioning properly and if a quality defect is identified, the system will pick it up and document it”?

<table>
<thead>
<tr>
<th>Strongly agree</th>
<th>Agree</th>
<th>Undecided or don’t know</th>
<th>Disagree</th>
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4.7. Defective product recall and handling of rejected or returned products

The manufacturers and distributors/wholesalers are traditionally responsible for the recall of their products from the market if they are or if they become defective in their quality, safety, or efficacy or are potentially harmful. The recall could be voluntary or requested by the national or local MRA depending on the level of hazard involved. Within the product recall program, a formal reporting system should be established in all supply systems which encourages personnel to report potential problems with poor product

\(^1\) Delivery time in this context is the time interval needed to complete an order, i.e., from the day of receiving a request to the day of delivering the products to the client.
quality, ideally using pre-printed, simple reporting forms. It should be made clear at every level, i.e., retailer, distributor/wholesaler, manufacturer/supplier, who should report the perceived quality problem and to whom the report should be delivered at the next level. All reports should be carefully assessed to establish the need for further laboratory testing and to determine what appropriate follow-up action must be taken, including product recall if warranted. Product defect reports and results should be recorded as part of the supplier monitoring system in both the supplier and distributor product files.

Q28: Does [name of the establishment being assessed] have a defective product reporting system in place?

☐ yes  ☐ no  ☐ don’t know  ☐ not applicable

If yes, check all boxes that apply:

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<tbody>
<tr>
<td>1.</td>
<td>Availability of a written policy or protocol on defective product reporting on the premise</td>
</tr>
<tr>
<td>2.</td>
<td>Availability of a defective product reporting form (printed or electronic)</td>
</tr>
<tr>
<td>3.</td>
<td>A responsible person(s) is assigned to coordinate the assessment/evaluation of defective product reports</td>
</tr>
<tr>
<td>4.</td>
<td>Availability of record book or documentation of cases of defective product reports, if there were any cases reported</td>
</tr>
</tbody>
</table>

Q29: Does [name of the establishment being assessed] have an emergency or contingency plan for product recalls that can be put into effect if and when needed?

☐ yes  ☐ no  ☐ don’t know  ☐ not applicable

If yes, check all boxes that apply:

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<tbody>
<tr>
<td>1.</td>
<td>Availability of a written policy or plan on defective product recall in the premise</td>
</tr>
<tr>
<td>2.</td>
<td>A responsible person(s) is designated for coordinating the recall process (recall coordinator)</td>
</tr>
<tr>
<td>3.</td>
<td>Recall coordinator is also responsible for organizing and implementing the recalls, documenting, and reporting the recall details to relevant agencies, including the MRA, and communicating the progress and success/outcomes</td>
</tr>
<tr>
<td>4.</td>
<td>Availability of record book or documentation of recall cases involving product quality defects, if there were any incidences in the past</td>
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**Immediate notification** of defective product: The recipient of the medicines consignment must notify the supplier immediately of quality problems based on the test results of the samples during various stages of the product supply chain. These quality problems are usually detectable upon visual inspection and do not require further laboratory testing (e.g., crumbling tablets, particles in injectables, oral suspensions that harden).
Q30: In what instances below does the immediate notification apply?
Check all boxes that apply:

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<tbody>
<tr>
<td>1.</td>
<td>During or after the pre-shipment inspection at the country of export, if applicable</td>
</tr>
<tr>
<td>2.</td>
<td>During or after the post-shipment inspection at the port of entry at the importing country, if applicable</td>
</tr>
<tr>
<td>3.</td>
<td>During or after the receipt of a consignment at the warehouse of the distributor/wholesaler or national program warehouse</td>
</tr>
<tr>
<td>4.</td>
<td>After distribution to pharmacies and health facilities</td>
</tr>
</tbody>
</table>

Handling rejected and returned products due to safety, efficacy, or defective quality is an important activity of any supplier, distributor, or wholesaler when addressing the suitability of the medicines they had supplied. A careful evaluation of the rejected or returned products should be made by a designated and qualified person. Where any doubt arises over the quality of a pharmaceutical product returned, it should not be considered suitable for redistribution or sale.

Q31: Does [name of the establishment being assessed] have a mechanism to handle the rejected or returned products?

- [ ] yes
- [ ] no
- [ ] don’t know
- [ ] not applicable

If yes, check all boxes that apply:

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<tbody>
<tr>
<td>1.</td>
<td>Availability of a written procedure on handling the rejected or returned products from clients deemed to be quality defective, including substandard, counterfeit, or fake products</td>
</tr>
<tr>
<td>2.</td>
<td>A responsible person(s) is designated for handling the rejected or returned products, including documenting the incidents and reporting to relevant parties, including the MRA in the case of fake or counterfeit products</td>
</tr>
<tr>
<td>3.</td>
<td>Existence of a quarantine area or room to collect and store the products in question in accordance with their specified storage conditions until a decision by the designate person in the organization or company has been made for the product disposition</td>
</tr>
</tbody>
</table>

4.8. Internal and External Audits or Inspections

Internal audits or self-inspections refer to audits conducted by an auditor who is employed by the company, whether it is a supplier, wholesaler, or distributor of medicines. Internal audits are also known as first-party audits. External inspections are performed by a second-party (e.g., by a client that makes a purchase from the supplier, wholesaler, or distributor), or a third-party (e.g., by an auditing organization or agency that is independent of the purchaser or supplier). The system of quality assurance should include self-inspections to monitor the implementation and compliance with the
principles of good distribution practices adopted or accepted and to plan for necessary corrective actions and preventive measures.

Q32: Does [name of the establishment being assessed] have an internal audit mechanism or activity in place?

☐ yes  ☐ no  ☐ don’t know  ☐ not applicable

If yes, check all boxes that apply:

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<td>1.</td>
<td>Availability of a written procedure on internal audit</td>
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<td>2.</td>
<td>A qualified person(s) is designated to conduct internal audits</td>
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<td>3.</td>
<td>The designated person responsible for auditing of [name of the establishment being assessed] is present during the assessment</td>
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<td>4.</td>
<td>The designated person responsible for auditing of [name of the establishment being assessed] is able to demonstrate the past and recent internal audit reports/records</td>
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<td>5.</td>
<td>Record the date/month/year of the last internal audit: _____________</td>
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Q33: Has [name of the establishment being assessed] ever been audited or inspected by a second or third party?

☐ yes  ☐ no  ☐ don’t know  ☐ not applicable

If yes, check all boxes that apply:

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<tr>
<td>1.</td>
<td>Availability of documentation or written record proving that [name of the establishment being assessed] has been inspected</td>
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<td>2.</td>
<td>Note the last inspection date/month/year __________________</td>
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<td>3.</td>
<td>Note the name of the auditor/inspector and his/her affiliation __________________________________________________________________________</td>
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<td>4.</td>
<td>Note key findings of the last external audit/inspection, where feasible ______________________________________________________________________</td>
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Annex 1: Guidance to prepare for assessment, interview and informant selection

Selecting key informants
- Select the key informants (KIs) based on their experience and current involvement in or knowledge of medicines policy, management and systems.
- It is necessary to have a balance of KIs and not a sample that over-represents specific actors.
- Interview as many KIs as possible to reinforce the assessment findings.

Preparing for the interviews
- Find as much information about the KIs as possible before starting the interviews or consultations.
- Request an appointment for a time and date convenient for each of the KIs, arranged at least one week in advance of the actual interview.
- If applicable, send the questionnaire – with a cover letter explaining the purpose and objectives of the exercise – to each participant. This would allow him/her to review and, in most cases, provide answers to the questions, making the assessment process quicker and easier. The face-to-face appointment will then allow more time for discussion, consultation, clarification or verification of supporting evidence.

Conducting the assessment interviews
- First, remind KIs about the purpose and objectives of the exercise.
- Emphasize that you will strive to keep their identity and responses confidential.
- Remind participants that they have the right to refuse to respond to any questions.
- Ask questions politely.
- Take as many additional notes as possible during the interviews besides marking the appropriate boxes in the questionnaire.

After interview
- Review all notes and complete them as needed.
- Keep all data strictly confidential.
- Analyze and report according to the findings of the questionnaire.
Annex 2: A GMP checklist

For a Government or MRA:
- Provide national legislation and regulations for controlling pharmaceutical production.
- Establish good manufacturing practice guidelines.
- Promote compliance with current GMP guidelines for medicine production by regulation.
- Enforce compliance with current GMP guidelines by all medicine manufacturers.

For Manufacturers:

OPERATIONS AND PRACTICES
- Establish a quality assurance unit to perform routine internal GMP audits.
- Establish key functions for quality control and assurance:
  - Check and clear all incoming raw pharmaceutical materials, including inert pharmaceutical substances, active pharmaceutical ingredients, and packaging and labeling materials.
  - Write and approve standard operating procedures, and validate testing methods, equipment, and production processes.
  - Conduct review of in-process control activities, including testing for quality of all materials to be used in manufacturing before their use, and semi-finished and finished product testing.
  - Approve batch or lot release.

PERSONNEL AND QUALIFICATIONS
- Establish adequate professional knowledge, experience, and technical skills:
  - Write a defined job description for each position.
  - Place at least one pharmacist in charge of manufacturing each dosage form production unit.
  - Assign at least two responsible pharmacists to oversee quality assurance and quality control in small-scale manufacturing plants.
  - Assign at least two responsible pharmacists or chemists in quality control laboratories.

- Require employees to participate in each current training on standard operating procedures and batch record keeping.
- Attend to current GMP regulations and guidelines.
- Assign a qualified person to specific equipment or production processes.
- Establish continuing training and a training record for each employee.
- Periodically review each employee’s performance.

TECHNOLOGY AND EQUIPMENT
- Use appropriate technology and equipment to manufacture medicines.
- Maintain manufacturing and quality control equipment according to current standards.
- Ensure validation activities.
  - Validate process:
    - Calibration, use, cleaning, and maintenance of equipment
    - Installation of unique equipment identification, establishment of a log book, fulfillment of utility requirements at the specified site
    - Performance qualification to verify that processed materials meet acceptance criteria
    - Cleaning validation to ensure —
      - Proper cleaning
      - No risk of cross-contamination
      - Cleanliness testing based on acceptance criteria
      - Use of acceptable cleaning agent

Note to multi-product facilities:
Manufacturers of multiple products must pay particular attention to validated procedures existing for product turnover:
- Equipment cleaning
- Facility cleaning

- Validate utilities
  - Purified water
    - Water source routinely sampled and tested for compliance with regulatory requirements
- Major contaminant groups (particulates, inorganics, organics, and microbes) removed
- Samples collected at least weekly at sampling points and point-of-use ports, and tested for quality based on acceptance criteria.
- Test data records for trends are maintained.

- **Air handling**
  - Rooms for production of medicinal production equipped with air handling unit in accordance with GMP requirements
  - Air monitored for controlled environments requirement of particulate measuring
  - Filters tested for leaks and efficiency
  - Pressure differentials maintained for clean rooms and controlled environments requirement
  - Air flow speed, uniformity, and pattern recorded
  - Environment monitored for particles, microorganisms, temperature, and humidity.

- **Compressed air**
  - Adequate filter (pre-final) for compressed air unit in accordance with GMP requirements
  - Pipe constructed with suitable materials.
  - System monitored for possible contamination (oil, water, particles, bio burden)
  - Air flow direction labeled at any point
  - System in place to monitor leakage, filter integrity, and pressure control.

- **Validate facility**
  - Verify facility design to ensure:
    - Logical flow of materials and personnel
    - No mix-up or cross-contamination
    - Sufficient space for operation and maintenance of equipment
    - Facility cleanliness

  - Verify construction to ensure:
- As-built facilities conform to design drawings
- Construction materials meet specifications
- Equipment installed as planned
- Utilities routed as planned

- Verify operation and performance to ensure:
  - Facility supports the manufacturing process
  - Facility meets cleanliness specifications
  - Production of three successful consecutive batches using qualified materials, equipment and utilities, and methods have been validated.

**DOCUMENTATION**

- Establish a documentation system that maintains an inventory of all required documents and records.
- Review manufacturing and control documents so that —
  - Lot/batch of raw materials can be traced
  - Equipment used in manufacture can be identified
  - Work performed by an assigned person can be identified
  - All calculations are checked
  - All labels are correct
  - Quality control record is complete.

**STORAGE**

**Organization and quality management**

- Is there a defined quality structure?
- Is there a quality policy?
- Are all personnel responsibilities clearly defined?
- Is a person assigned to every distribution point?
- Have job descriptions been established for all employees?

**Personnel**

- Is there an adequate number of qualified personnel to achieve pharmaceutical quality assurance objectives?
- Have all personnel received proper training in relation to good storage practice, regulations, procedures, and safety?
- Have all members of the staff had been trained in personal
hygiene and sanitation? Do they observe high levels of hygiene and sanitation?

☐ Do all personnel employed in storage areas wear suitable protective or working garments appropriate for the activities they perform?

Premises and facilities

Storage areas

☐ Have precautions been taken to prevent unauthorized persons from entering storage areas?

☐ Are storage areas of sufficient capacity to allow the orderly storage of the various categories of materials and products, namely: starting and packaging materials; intermediates; bulk and finished products; products in quarantine; and released, rejected, returned or recalled products?

☐ Have storage areas been designed or adapted to ensure good storage conditions? In particular, are they clean and dry and maintained within acceptable temperature limits?

☐ Are storage areas clean and free from accumulated waste and vermin?

☐ Is there a written sanitation program available indicating the frequency of cleaning and the methods to be used to clean the premises and storage areas?

☐ Is there a written program for pest control?

☐ Are the receiving and dispatch bays designed and equipped to protect materials and products from the weather?

☐ Are reception areas designed and equipped to allow containers of incoming materials and pharmaceutical products to be cleaned, if necessary, before storage?

☐ Are rejected materials and pharmaceutical products identified and controlled under a quarantine system designed to prevent their use until a final decision is made on their outcome?

☐ Are narcotic drugs stored in compliance with international conventions, and national laws and regulations on narcotics?

☐ Are broken or damaged items withdrawn from usable stock and separated?

☐ Do storage areas provide adequate lighting to enable all operations to be carried out accurately and safely?

Storage conditions

☐ Are storage conditions for pharmaceutical products and materials in compliance with the labeling, which is based on the results of stability testing?
**Monitoring of storage conditions**

- Are recorded temperature monitoring data available for review?
- Are temperature registers available?
- How long is the data kept?
- Has the equipment used for monitoring been checked at suitable predetermined intervals and the results of such checks recorded and retained?

**Documentation**

- Are written instructions and records available that document all activities in the storage areas including the handling of expired stock?
- Does permanent information, written or electronic, exist for each stored material or product indicating recommended storage conditions, any precautions to be observed, and retest dates?
- Are records kept for each delivery?

**Labeling and containers**

- Are all materials and pharmaceutical products stored in containers which do not adversely affect the quality of the materials or products concerned, and which offer adequate protection from external influences? In some circumstances, this could include bacterial contamination.
- Are all containers clearly labeled with at least the name of the material, the batch number, the expiry date or retest date, the specified storage conditions, and reference to the pharmacopoeia, where applicable? Unauthorized abbreviations, names or codes should not be used.

**Receipt of incoming materials and pharmaceutical products**

- Is each incoming delivery checked against the relevant purchase order and each container physically verified, e.g., by the label description, batch number, type of material or pharmaceutical product, and quantity?
- Is each consignment examined for uniformity of the containers? Should the delivery comprise more than one batch, should it be subdivided according to the supplier's batch number?
- Are containers carefully inspected for possible contamination, tampering and damage?
Are measures being taken to ensure that rejected materials and pharmaceutical products cannot be used?

Stock rotation and control

- Is periodic stock reconciliation performed by comparing the actual and recorded stocks?
- Are stock discrepancies investigated as a check against inadvertent mix-ups and/or incorrect issue?

Control of obsolete and outdated materials

- Are all stocks checked regularly for obsolete and outdated materials and pharmaceutical products? Are all due precautions observed to prevent the issue of outdated materials and pharmaceutical products?

Returned goods

- Are returned goods, including recalled goods, handled in accordance with approved procedures?

Dispatch and transport

- Are materials and pharmaceutical products transported in such a way that their integrity is not impaired and that storage conditions are maintained?
- Are there procedures for transport?
- Are devices used to monitor conditions, such as temperature, during transportation?
- Are devices calibrated?
- Are the dispatch and transport of materials and pharmaceutical products carried out only after receipt of a delivery order?
- Are there dispatch procedures established and documented, taking into account the nature of the materials and pharmaceutical products concerned and any special precautions taken?
- Are records for dispatch retained for at least one year after the stated expiration date?
Bibliography List


USP-NF, 2006. The Official Compendia of Standards. General Chapters <1078> Good manufacturing practices for bulk pharmaceutical excipients, <1079> Good storage and shipping practices, and <1178> Good re-packaging practices.


