POST-MARKETING SURVEILLANCE GUIDE
FOR
SMALL ISLAND DEVELOPING STATES

Medicines Quality Control and Surveillance Department
The Caribbean Public Health Agency is the Caribbean region’s collective response to strengthening health systems and addressing public health challenges which threaten development.

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- Dr. Rian Marie Extavour, Consultant.

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### Abbreviations

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<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>API</td>
<td>Active pharmaceutical ingredient</td>
</tr>
<tr>
<td>BP</td>
<td>British Pharmacopoeia</td>
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<tr>
<td>CARICOM</td>
<td>Caribbean Community and Common Market</td>
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<tr>
<td>CARPHA</td>
<td>Caribbean Public Health Agency</td>
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<tr>
<td>CRS</td>
<td>Caribbean Regulatory System</td>
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<tr>
<td>COA</td>
<td>Certificate of Analysis</td>
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<tr>
<td>GMP</td>
<td>Good Manufacturing Practice</td>
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<td>GSMS</td>
<td>Global Surveillance and Monitoring System</td>
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<tr>
<td>HPLC</td>
<td>High-Performance Liquid Chromatography</td>
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<tr>
<td>INN</td>
<td>International Non-proprietary Name</td>
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<tr>
<td>IR</td>
<td>Infrared</td>
</tr>
<tr>
<td>JANAAC</td>
<td>Jamaica National Agency for Accreditation</td>
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<tr>
<td>MQCSD</td>
<td>Medicines Quality Control and Surveillance Department</td>
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<tr>
<td>NMRA</td>
<td>National medicines regulatory authority</td>
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<tr>
<td>PAHO</td>
<td>Pan American Health Organization</td>
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<tr>
<td>PMS</td>
<td>Post-market surveillance</td>
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<td>PQM</td>
<td>Promoting the Quality of Medicines</td>
</tr>
<tr>
<td>SIDS</td>
<td>Small Island Developing States</td>
</tr>
<tr>
<td>SF</td>
<td>Substandard and/or Falsified</td>
</tr>
<tr>
<td>SMS</td>
<td>Short-messaging service</td>
</tr>
<tr>
<td>TBD</td>
<td>To be determined</td>
</tr>
<tr>
<td>TECHPHARM</td>
<td>CARICOM Expanded Technical Advisory Committee on Pharmaceutical Policy</td>
</tr>
<tr>
<td>TLC</td>
<td>Thin-layer chromatography</td>
</tr>
<tr>
<td>USP</td>
<td>United States Pharmacopeia</td>
</tr>
<tr>
<td>UV-VIS</td>
<td>Ultraviolet-Visible</td>
</tr>
<tr>
<td>VIGICARIB</td>
<td>Caribbean Network for Pharmacovigilance and Post-market Surveillance</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
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<tr>
<td>WHPA</td>
<td>World Health Professions Alliance</td>
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## Glossary

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Accredited laboratory</td>
<td>A laboratory that has received formal recognition that it meets or exceeds a list of standards, including the ISO/IEC 17025, and is competent to perform specific tests, or calibrations.</td>
</tr>
<tr>
<td>Batch</td>
<td>A quantity of medicine produced during a given cycle of manufacture.</td>
</tr>
<tr>
<td>Certificate of Analysis</td>
<td>A document issued upon approval of test results listing the test procedures applied to a sample, results obtained, the specification applied and compliance.</td>
</tr>
<tr>
<td>Compendial</td>
<td>Related to a compendium that serves as a standard, such as the British Pharmacopoeia, or the US Pharmacopeia.</td>
</tr>
<tr>
<td>Consignment</td>
<td>The quantity of bulk starting material, or of a pharmaceutical product, made by one manufacturer or supplied by an agent, and supplied at one time in response to a particular request or order. A consignment may comprise one or more lot-identified packages or containers and may include material belonging to more than one lot-identified batch.</td>
</tr>
<tr>
<td>Convenience sample</td>
<td>A study sample made up of participants or units who meet the entry criteria and are easily accessible to the investigator.</td>
</tr>
<tr>
<td>Cluster sample</td>
<td>A random sample of natural groupings (clusters) of individuals or units of the population.</td>
</tr>
<tr>
<td>Falsified</td>
<td>Medical products that deliberately/fraudulently misrepresent their identity, composition, or source.</td>
</tr>
<tr>
<td>Medical product</td>
<td>Products used in the care of patients to diagnose, prevent or treat medical or surgical conditions.</td>
</tr>
<tr>
<td>Original sample</td>
<td>Sample collected directly from the material.</td>
</tr>
<tr>
<td>Packaging material</td>
<td>Any material including printed material employed in the packaging of a pharmaceutical, but excluding any outer packaging used for transportation or shipment. Packaging materials are referred to as primary or secondary according to whether or not they are intended to be in direct contact with the product.</td>
</tr>
<tr>
<td>Term</td>
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<tr>
<td>Pharmaceutical product</td>
<td>Any material or product intended for human or veterinary use presented in its finished dosage form or as a starting material for use in such a dosage form that is subject to control by pharmaceutical legislation in the exporting state and/or the importing state.</td>
</tr>
<tr>
<td>Pharmacovigilance</td>
<td>The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem.</td>
</tr>
<tr>
<td>Post-market surveillance, or Post-marketing surveillance</td>
<td>Surveillance activities that occur following market approval of a medicine, including maintenance of product authorization and/or registration of variations or renewals; regular inspections of manufacturers, wholesalers, distributors, and retailers; quality control testing; pharmacovigilance; promotion control; public reporting of poor-quality products; handling of market complaints; and removal and disposal of non-compliant products.</td>
</tr>
<tr>
<td>Production</td>
<td>All operations involved in the preparation of a pharmaceutical product, from receipt of materials, through processing, packaging and repackaging, labelling and relabelling, to completion of the finished product.</td>
</tr>
<tr>
<td>Reference material</td>
<td>Material sufficiently homogeneous and stable with reference to specified properties, which has been established to be fit for its intended use in measurement or in examination of nominal properties.</td>
</tr>
<tr>
<td>Sample</td>
<td>A portion of a material collected according to a defined sampling procedure. The size of any sample should be sufficient to allow all anticipated test procedures to be carried out, including all repetitions and retention samples.</td>
</tr>
<tr>
<td>Sample collection form</td>
<td>A form used to record the details of the sample collected and observations made during sampling. A copy may be included in the sampling record.</td>
</tr>
<tr>
<td>Sample Collector</td>
<td>Person responsible for performing the sampling operation. Also, called Sampler.</td>
</tr>
<tr>
<td><strong>Sampling method</strong></td>
<td>The part of the sampling procedure dealing with the method prescribed for withdrawing samples.</td>
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<td>------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Sampling plan</strong></td>
<td>Description of the location, number of units and/or quantity of material that should be collected, and associated acceptance criteria.</td>
</tr>
<tr>
<td><strong>Sampling procedure</strong></td>
<td>The complete sampling operations carried out on a particular material for a defined purpose. A detailed written description of the sampling procedure is provided in the sampling protocol.</td>
</tr>
<tr>
<td><strong>Sampling record</strong></td>
<td>A written record of the sampling operations carried out on a particular material or product for a defined purpose. The sampling record should contain the batch number, date and place of sampling, reference to the sampling protocol used, a description of the containers and of the materials sampled, notes on possible abnormalities, together with any other relevant observations, and the name and signature of the inspector.</td>
</tr>
<tr>
<td><strong>Sampling unit</strong></td>
<td>Discrete part of a consignment such as an individual package, drum or container.</td>
</tr>
<tr>
<td><strong>Screening Technologies</strong></td>
<td>The qualitative and/or quantitative technologies that could rapidly acquire preliminary analytical information or data on the quality of medical products in the field.</td>
</tr>
<tr>
<td><strong>Selected sample</strong></td>
<td>Sample obtained according to a sampling procedure designed to select a fraction of the material that is likely to have special properties. A selected sample that is likely to contain deteriorated, contaminated, adulterated or otherwise unacceptable material is known as an extreme sample.</td>
</tr>
<tr>
<td><strong>Simple random sample</strong></td>
<td>A sample drawn from the population where each member of the population or unit has an equal chance of being selected.</td>
</tr>
<tr>
<td><strong>Small Island Developing States (SIDS)</strong></td>
<td>A distinct group of developing countries facing specific social, economic and environmental vulnerabilities. SIDS are a recognized group of 58 low-lying island nations across 3 geographical divisions – Caribbean, Pacific, and Atlantic, Indian Ocean, Mediterranean, and South China Sea (WHO/CCU/17.08)</td>
</tr>
<tr>
<td><strong>Substandard</strong></td>
<td>Also called “out of specification”, these are authorized medical products that fail to meet either their quality standards or specifications, or both.</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
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<tr>
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</tr>
<tr>
<td>Uniformity</td>
<td>A starting material may be considered uniform when samples drawn from different layers do not show significant differences in the quality control tests which would result in non-conformity with specifications.</td>
</tr>
<tr>
<td>Unregistered</td>
<td>Medical products that deliberately and/or fraudulently misrepresent their identity, composition or source.</td>
</tr>
<tr>
<td>Verification</td>
<td>The process by which a pharmacopoeial method or validated analytical procedure is demonstrated to be suitable for the analysis to be performed.</td>
</tr>
</tbody>
</table>

*Source: Definitions have been adapted from References¹–⁴.*
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INTRODUCTION

Background

Access to medicines and other medical products of good quality is essential to successful treatment and management of diseases and disability. Quality assurance in pharmaceutical supply systems aims to help ensure that each medicine that reaches patients is safe, effective and of appropriate quality. The national medicines regulatory authority (NMRA) is primarily responsible for implementing quality assurance measures prior to market authorization and while medicines are on the market, to ensure their quality and safety.5

The Pan American Health Organization/World Health Organization (PAHO/WHO), with endorsement by the Pan American Network of Drug Regulatory Harmonization (PANDRH) recommends that NMRAs of small island developing states with limited resources, like the Caribbean, perform the following essential functions:6

- Product registration, or marketing authorization: to review and evaluate products for legal sale in the market based on safety, quality, and efficacy
- Licensing of establishments: to license warehouses and distributors on the bases of compliance with good practices, such as good distribution practices
- Market surveillance and control: to conduct import and export control, and monitor medical products in the market, including substandard and falsified medicines
- Vigilance: to carry out the collection and evaluation of information related to safety of medicines and adverse events, and to make regulatory decisions from the information obtained
- Regulatory inspections: to perform inspection activities of establishments in order to verify compliance with regulations and standards.

Therefore, NMRAs, which are primarily based within Ministries of Health in the Caribbean, are responsible for monitoring the quality of pharmaceutical products while on the market. This role is an essential component of market surveillance and control and vigilance, also known as “post-market surveillance”. The WHO Global Benchmarking Tool (GBT) for evaluation of national regulatory system of medical products provides various indicators that may be used by NMRAs to identify areas for system strengthening, including indicators for medicines registration and market authorization, market surveillance and control, vigilance, and laboratory testing.7

As in other small island developing states (SIDS) around the world,4 several Caribbean countries lack the capacity to undertake all aspects of post-market surveillance, including a lack of trained personnel, testing laboratories and information technology for regulatory activities. The Caribbean Community (CARICOM), the Caribbean Public Health Agency (CARPHA), and other stakeholders including PAHO/WHO are implementing strategies to strengthen regulatory systems and post-market surveillance capacity in the small states of CARICOM. This is in accordance with regional mandates such as the PAHO Directing Council’s resolution CD50.R98 and World Health Assembly resolution 67.20.9 With endorsement by
CARICOM’s Technical Advisory Committee on Pharmaceutical Policy and the Council of Human and Social Development, and consistent with the Caribbean Pharmaceutical Policy adopted in 2011, a regional regulatory mechanism called the Caribbean Regulatory System (CRS) has been launched. This system is managed by CARPHA in close technical cooperation with PAHO/WHO.

CARPHA Medicines Quality Control and Surveillance Department, in collaboration with its partners and stakeholders, has expanded its medicines quality testing and developed a post-market surveillance programme to address medicines quality issues in the region. This technical support, along with shared guidance, training and information exchange, will support medicines regulatory systems of CARPHA Member States.
Purpose of the Guide

This guide provides information to CARPHA Member States on the conduct of post-market surveillance and the procedures for medicines quality testing at the Medicines Quality Control and Surveillance Department (MQCSD). The aims of the guide are:

i. To assist national medicines regulatory authorities of CARPHA Member States and associates in the design and conduct of programs for national post-market surveillance of medicines and

ii. To describe the procedures for sample collection, and the submission of samples of medicines for compendial testing to the MQCSD.

Section I of the guide will assist administrators of NMRAs with limited regulatory capacity by serving as a resource for policy development and planning of operations. It describes a risk-based approach to post-market surveillance in limited resource settings like the small states of CARICOM. This includes the systems required for post-market surveillance, such as a voluntary reporting system, quality testing equipment or facilities, data management, incident management protocols, policies for regulatory action, communication, financing, and human resources. Essentially, this guide will provide key insights into how to establish systems that can collect and analyse patient adverse events, and respond to substandard, falsified, and unregistered medicines.

Section II will provide guidance to supervisors and sample collectors on the procedures involved in the sample collection, and submission of samples of medicines for compendial testing at the CARPHA MQCSD.

Intended Users

The guide is written for:

- Administrators and staff of national regulatory agencies for medicines involved in planning and supervision of quality surveys
- Regional focal points for pharmacovigilance and post-market surveillance responsible for assisting with policy development and implementation
- Quality officers or officers of regional health authorities involved in monitoring the quality of medical products, planning and implementation of quality surveys
- Health professionals and technical personnel who work in or with agencies responsible for medicines distribution and/or the monitoring the quality of medicines in Caribbean markets with responsibility for monitoring the quality of medicines
• Supervisors of regulatory units responsible for implementation of medicines quality surveys
• Sample collectors (Section II).

Other stakeholders, such as regional focal points for pharmacovigilance and post-market surveillance, quality administrators or officers within NMRAs and educators may use this document as a reference to develop policies, procedures and training material.

Additional Context

Post-market surveillance of the quality of medicines is a dynamic but essential function of national medicines regulatory authorities. Although post-market surveillance generally extends to all medical products (e.g. medicines, vaccines, in vitro diagnostics), the focus of the guide will be the surveillance of medicines or finished pharmaceutical products. This guide serves as one of many tools that may be used by NMRAs, as it may be supplemented by training workshops, and updated as new approaches are developed to improve pharmaceutical systems and to meet the evolving needs of the Caribbean people.

Note: This document is written to provide guidance and should be used in the context of the national or regional reality. It is not meant to subvert the established policies and procedures of national regulatory authorities.
SECTION I: GUIDANCE FOR NATIONAL POST-MARKET SURVEILLANCE SYSTEMS
1.0 National Post-Market Surveillance Systems

1.1 Role of NMRAs and Stakeholders

Post-market surveillance (PMS) of medicines is essential to ensure that the products used to treat conditions remain of sound quality while on the market. Several activities may encompass safety assessments and quality monitoring, including clinical trials in populations that were omitted during pre-marketing trials and periodic national surveys of the quality of medicines. National PMS for quality assurance of medicines used by populations should include the development of passive surveillance (spontaneous reports by users), which would provide information to guide the development of risk minimization activities.\textsuperscript{5,7} It may also include risk-based approaches to conducting quality surveys of products in the field.\textsuperscript{12}

In addition to monitoring the quality of medicines on the market, national medicines regulatory authorities are also responsible for taking reasonable and appropriate regulatory actions to prevent and minimize harm arising from the use of unregistered products, substandard medical products and falsified medical products. This responsibility is also shared among various stakeholders including licensed distributors, manufacturers, and retailers (e.g. pharmacists, shopkeepers), who may be inspected to ensure good distribution and storage practices. The NMRA may strengthen its PMS activities through strategic collaborations with other agencies, such as the Customs divisions of National Security agencies to identify and prevent the entry and distribution of substandard, falsified or unregistered medical products.

1.2 System Objectives and Operational Elements

In order to achieve the mission of sustained national post-market surveillance, NMRAs will need to establish a system with clearly defined objectives. Broadly, these objectives should include:

- The facilitation of spontaneous reporting of suspected substandard and falsified medical products by health professionals, marketing authorization holders and the public
- Handling of market complaints
- Detection of substandard or falsified medical products
- Removal and disposal of defective and non-compliant products from the market, and
• Implementation of corrective and preventative actions to minimize future non-compliance.

The World Health Organization’s Member State Mechanism also provides guidance to NMRAs to develop national plans for preventing, detecting and responding to actions, activities and behaviours that result in substandard and/or falsified (SF) medical products.\(^\text{13}\)

1.2.1 Prevention

Operational approaches to prevent the distribution and use of substandard, falsified or unregistered medicines on the market should include:\(^\text{13}\)

(i) The verification of good manufacturing and distribution practices in the supply chain
(ii) The verification of the medical products distribution chain, by checking the source and destination or transfer of possession
(iii) The identification of SF products in the chain, through post-market surveillance, and in coordination with security agencies and market authorization holders
(iv) The identification and investigation of actions, activities and behaviors that contribute to SF products on the market
(v) The collection of samples for verification and/or analysis, and
(vi) Recall and/or prohibition of the distribution and use of SF products detected.

1.2.2 Vigilance and Detection

Pharmacovigilance (PV) falls under the broader topic of vigilance and is an important part of post market surveillance. It is defined as “the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem”.\(^\text{3}\) Pharmacovigilance often relates to the intrinsic safety of a medicine for human use, but it can also relate to the external quality elements that factor into the product’s manufacture and distribution. For example, substandard and/or falsified medicines may be part of pharmacovigilance because they may result in adverse events such as therapeutic failure and/or other adverse effects.

It is not unusual for PMS activities to be included in the operations of a national pharmacovigilance centre or vice versa, as there are several operational similarities. In addition, the integration of the two functions under one unit will enable the NMRA to optimize available resources.
1.2.3 Operational Elements

For a national post-market surveillance system to undertake the function of monitoring the quality and safety of medicines in public health, NMRAs may follow WHO’s recommendations for setting up a pharmacovigilance centre, which includes:

- A voluntary reporting system including a method of reporting
  - E.g. a printable form, or an online form, or telephone service or a short-messaging service (SMS)
- Information Technology:
  - A database for storage, analysis and retrieval of reports
  - Subscriptions to electronic databases, newsletters, and/or alert systems of other NMRAs (e.g. US Food and Drug Administration)
- Human resources: Trained personnel for:
  - Follow-up of reports, database searches
  - Data handling (entry, analysis)
  - Sample collection and
  - Use of field screening equipment (detection technologies)
- Policies and procedures for:
  - The management of reports
  - A risk-based approach to quality testing
  - Incident management, including risk assessment
  - Risk minimisation activities, including regulatory actions and/or responses
- An advisory committee of experts, with clearly defined terms of reference
- Appropriate legislation and regulations to enable law enforcement and legal action
- Adequate financing to sustain the system and ensure independence, and
- A communication system to engage health professionals and the public.

1.2.4 Voluntary Reporting system

Reporting System:

The post-market surveillance system should facilitate reporting of adverse medicine reactions, and substandard or falsified or unregistered medical products by health professionals and patients to the NMRA. To create awareness and to minimize invalid reports, educational approaches will be needed to teach the public and health professionals what to report and how to report. In general, when medicines are suspected to cause adverse reactions, or are suspected of being substandard or falsified, they should be reported.
Examples include adverse reactions that occur after taking a medicine such as rash or difficulty breathing, and product discolouration or malodorous products which may be substandard or falsified. In addition, substandard or falsified products may present with labelling or packaging that appear sub-optimal (incorrect colours, distorted text).

The WHO and the World Health Professionals Alliance (WHPA) have developed tools to approach suspected substandard or falsified products in the field (Appendices II-III). Government inspectors may also identify unregistered medicines by comparing the products distributed in local pharmacies or hospital dispensaries to the list of products with market authorization. Therefore, it is important for countries to make lists of authorized products available to the public, and to keep the lists current.

Reporting Form:

Each country should develop a reporting form and a database system to receive and manage reports, where possible.

The reporting form (or alternative medium) should be easily accessible, and easy to complete and submit to the NMRA. Instructions on how to complete the form should be provided, along with a contact for any questions the reporter may have. The case report form should capture information on:

- The International Non-proprietary Name (INN or generic name) of the medicine
- The trade or brand name
- Name of manufacturer or marketing authorization holder
- Address of manufacturer
- Lot or Batch number ¥
- Expiry Date
- Description of quality issue, including photographs if possible
- Location and/or source
- Reporter name and contact information
- Dates

¥ Note: Two of the most commonly omitted fields are manufacturer and lot or batch number. However, these are essential to enable NMRAs to investigate possible substandard or falsified products, and to enable any regulatory action against specific manufacturers of non-compliant product batches.

In developing or improving national reporting forms, NMRAs may refer to forms used by other agencies, such as the regional network for pharmacovigilance and post-market
surveillance (VIGICARIB), or by the World Health Professions Alliance under the Be Aware – Take Action campaign.

**Sample Collection**

Reporters should be instructed to retain samples of the medicine for collection by authorized sample collectors.

Standard procedures for follow-up, report validation and sample collection should be implemented by the responsible division of the NMRA (or Ministry of Health). Sample collectors should follow the procedures recommended to avoid the contamination of samples. Guidance for sample collection, handling, storage and transportation is provided in Section II-5.3.

**1.2.5 Database Management**

As far as possible, staff at the NMRA should follow-up with reporters to confirm the source and assess the credibility of the information. Questions that may be used to confirm validity are provided by the WHO Incident Management Guide (Appendix I). Errors in the case report should be corrected as far as possible to allow for accurate assessment of risk.

Case reports should be entered and stored in a secure information system. Electronic information systems are recommended as these may be backed-up periodically to a server to prevent accidental loss. This may be done using an electronic spreadsheet (e.g. Microsoft Excel®) with key information fields and reporting functions, which may be updated regularly. On a periodic basis (e.g. monthly, quarterly), summative reports should be generated and used for system improvement.

**1.3 Setting Priorities for Risk-Based Post-Market Surveillance**

**1.3.1 Determining Priority Medicines for Testing**

There is much that can be done to monitor medicines for safety and quality in the market before resorting to laboratory testing. Laboratory testing is often expensive and frequently unavailable to small states in the Caribbean, due to the lack of national medicines quality control laboratories and resources to outsource services. Unfortunately, post-market surveillance cannot be complete without medicine testing services. Thus, national post-
market surveillance programmes must include clear protocols and thresholds for the conduct of different levels of testing of medicines, including laboratory testing, and to determine which are technically reliable and financially sustainable.

PMS programmes should have the capacity for routine and emergency testing (even if sourced to international laboratories), which should be based on the risk to public health. For example, if there is a cluster of reports related to patients who are receiving an antimalarial medicine that is not having the intended therapeutic effect, it may be necessary to send the product for testing of the active ingredient.

The following criteria are recommended to determine priority medicines for testing:

- Medicines frequently used by large populations or public health programmes
- Newly marketed medicines, including innovator products with less characterized safety profiles
- Medicines with quality issues reported to regulatory authorities
- Medicines with a high prevalence of reports of substandard issues or falsification within the WHO Global Surveillance and Monitoring System (GSMS), with relevance to the Caribbean region
- Medicines imported from unregulated and/or poorly regulated markets
- Medicines with dangerous risk profiles, such as narrow therapeutic indices or complex manufacturing processes.

Medicines recommended for market authorization or registration through partner organizations (e.g. the Caribbean Regulatory System) that do not meet the above criteria may be included for monitoring.

Geographic locations (e.g. borders, coastal regions, ports of entry) and clinics that are vulnerable should also be considered in a post-market surveillance strategy.³

Risk-based sampling also means that certain testing practices may need to be reconsidered for their usefulness and sustainability. For example, a common practice in the region is to test all medicines before market authorization (called pre-registration testing). However, this is quite an expensive process and there are examples of situations where the laboratory is not able to test and so the country is not able to approve medicines for market authorization. This compromises regulatory efficiency and more importantly timely access to medicines for patients. The WHO and other authorities strongly recommend against pre-registration testing. If manufacturers are in compliance with Good Manufacturing Practices (GMPs), then quality is built into the process. Testing one sample at one point in time would not be helpful. NMRAs should focus on how to assure oversight of Good Manufacturing Practices.
1.3.2 Collection sites and sampling methods

The various routes for the distribution of medicines through public, private, or informal supply chains each pose different risks of entry of substandard, falsified and unregistered medicines. In developing site selection criteria, NMRAs should consider: local knowledge of supply chain for target medicines, the availability and accessibility of target medicines, and information on where patients obtain medicines.16

All medicines outlets (dispensaries) in the sampling area should be mapped out by name and location.

Sampling may be done using various sampling methods, such as convenience sampling, random sampling, cluster sampling or lot quality assurance sampling. NMRAs may decide to also use mystery shoppers (covert) or sample openly (overt) depending on the objectives and limitations of the study.

For example, where a product that is suspected to be substandard is identified at the central medical stores, sampling at higher points along the supply chain is not needed. Inspectors may sample from the central stores, supplier’s warehouse, and any ports and points of entry. The storage conditions at each location should be clearly documented. For a product that is suspected to be falsified, which is identified at a health facility, the sample frame should include the stores of the dispensary, the distributor’s warehouse and any other source of the product including patient’s own supply. Where applicable, the patient or his/her family should be interviewed to determine the source of the medicine.

In cases where an illegitimate source is involved, a mystery shopper may be used to approach the pharmacy or distributor to purchase the sample. Otherwise, overt sampling may be used where the manager is apprised of the purpose of the visit.

For routine surveillance, where a product is to be sampled from various regions or levels of distribution in the supply chain to gain a representative view of the quality throughout the country or district, a cluster sample may be applied. In this case, a random sample of the product is drawn from each region or level.

In urgent cases, where a medicine is considered high priority or the risk of harm is high (e.g. use among large numbers of persons, vulnerable populations), and the medicine is widely distributed e.g. through public health programme, a non-probability sample or convenience sample may be taken.

Figure 1 outlines the steps recommended for planning national risk-based surveillance programmes.
Figure 1: Steps for Planning Risk-based Surveillance of Medicine Quality

<table>
<thead>
<tr>
<th>Select Medicines for PMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Based on criteria, e.g. novelty, complexity, limited safety data, stability issues, resistance, high demand, quality, GMP compliance, population exposure</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Select Geographical areas for sampling</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Based on criteria, e.g. poor storage, poor access, high disease burden, population, porous border zone, illicit market, complex supply chain, medicines quality</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Select Collection sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Consider local knowledge of supply chain (points of entry, virtual outlets), availability and accessibility, and patient access information</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Select Collection methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Determine if convenience, random, cluster or lot QA sampling</td>
</tr>
<tr>
<td>• Overt sampling or mystery-shoppers</td>
</tr>
</tbody>
</table>
2.0 Incident Management, Risk Assessment and Decision-Making

In addition to planning PMS activities, national medicines regulatory authorities (NMRAs) will need to:

- Manage incidents with confirmed safety and quality issues
- Assess the potential risk involved, and
- Decide on the approaches need to minimize the risk of harm.

2.1 Handling Reports

The steps for incident management recommended by the WHO provides guidance for the management for substandard or falsified (SF) medical products reported to NMRAs via its Aide Memoire (Appendix I). Although the guidance is developed for suspected SF products, the approach may be used in the management of reports of suspected adverse medicine reactions. The recommended steps for incident management are:

i. Receipt of the report
ii. Establishing the facts
iii. Assessment of risk to public health
iv. Immediate actions to protect public health
v. Field screening and laboratory analysis (if applicable), and
vi. Managing the incident.

Establishing the Facts: For each report of a suspected substandard or falsified medical product, the NMRA staff should:

1. Contact the reporter
2. Assess the reliability of the source
3. Establish the facts of the case
4. Assess the credibility of the information received
5. Obtain samples of the product and photographs showing batch number and expiry dates, and
6. Determine if there have been similar reports by regulatory authorities in the region, and the WHO Global Surveillance and Monitoring System (GSMS) database. Information on regional reports may be checked through networks established by the PAHO/WHO.
During the process of establishing the facts, staff of the NMRA should submit questions to the manufacturer to determine:

- If the company manufactured the product
- If the dates on the product are authentic
- If there have been falsified or substandard versions reported previously
- If there have been any complaints about the batch, and
- If there is any other information that the NMRA should be aware of.

The WHO Incident Management Aide Memoire provides questions that NMRA staff may use to check reliability and validity of reports (Appendix I).

2.2 Risk Assessment and Prioritization

The aim of risk analysis and management should be to evaluate the potential impact of reports received by NMRAs with respect to substandard or falsified medical products detected by health professionals, the public, and/or quality control laboratories. NMRAs should apply a structured risk assessment to determine prioritization of risks and actions to be taken.18

2.2.1 Risk assessment categories
The following table presents broad categories of risk levels of falsified, unregistered and substandard products.18

Table 1: Categorization of Risks of Falsified, Unregistered and Substandard Medical Products

<table>
<thead>
<tr>
<th>Product Type</th>
<th>Risk Level</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Falsified product</td>
<td>High</td>
<td>Any case of falsification or suspicion of falsification should be investigated immediately. Assess risk to determine priority levels</td>
</tr>
<tr>
<td>Unregistered/Unlicensed product</td>
<td>High</td>
<td>Product has not been evaluated by NMRA and is of unknown origin. Check other NMRAs to determine if licensed / in good standing elsewhere.</td>
</tr>
<tr>
<td>Substandard products</td>
<td>Variable</td>
<td>Consider, at minimum: Severity of defect / non-compliance Potential clinical consequences Potency of medical product or therapeutic index</td>
</tr>
<tr>
<td>Product Type</td>
<td>Risk Level</td>
<td>Notes</td>
</tr>
<tr>
<td>--------------</td>
<td>------------</td>
<td>-------</td>
</tr>
<tr>
<td>All SF products</td>
<td>Patient population&lt;br&gt;Route of administration and place of action</td>
<td>Other factors:&lt;br&gt;Probable place of deviation occurrence&lt;br&gt;Exposed population&lt;br&gt;Frequency of occurrence&lt;br&gt;Market turnover and expiration date&lt;br&gt;Single product on market or widely used in public health&lt;br&gt;Detectability of defect / non-compliance</td>
</tr>
</tbody>
</table>

Adapted from Reference 17

Each NMRA should identify and select the factors to be considered in the evaluation, based on experience and available information. The selected factors, criteria and steps used in the assessment of risk for each case should be clearly documented.

### 2.2.2 Risk classification and prioritization matrix

National medicines regulatory authorities are advised to develop and implement a procedure or tool to undertake risk assessment for SF products, in order to obtain standardized and reliable results during evaluation of reports. This will avoid multiple interpretations of the same event by different personnel. The NMRA may select an established prioritization matrix, but this should be done after reviewing various types since the each utilize unique criteria to define priorities.

One possible approach is the development of a matrix to assist in the evaluation. The WHO guidance provides a suggested method for illustrative purposes only. NMRAs may opt to develop their own tools to aid in risk classification and prioritization.

**Principle 1:**

Risk factors that compound the evaluation will have different importance for the final result. That is, some factors are more relevant than others. Relevance levels and rates must be established by NMRAs individually, taking into account the national and/or regional circumstances.

**Principle 2:**
The evaluation can be performed individually for each risk factor. The combination of values will provide a final result, which indicates the severity and the prioritization level for the case. The findings should be used as a guide, rather than a strict reference.

In developing the matrix, the following four steps are recommended:

✓ Step 1: Identify the main elements involved in the risk assessment, namely ‘risk factors’.
✓ Step 2: Establish the importance level or weight (numerical value) for each risk factor.
✓ Step 3: Define the different prioritization categories of risk within each risk factor. For example: low risk (rated as 1); medium risk (rated as 2); and high risk (rated as 3).
✓ Step 4: Establish groups of prioritization, based on sums generated by the matrix. Suggested groupings are: low prioritization, medium prioritization and high prioritization.

Interpreting Results

The results should be reviewed in consideration of risk factors that were not included in the matrix. The final result should clearly fall into one of the three groups of prioritization. The higher the index, the higher the severity and importance of the case for public health. After developing a matrix, the NMRA should proceed to validate it within a specified period of time or number of reports (or notifications), to confirm its utility before full implementation.

Practical Example:

The example provided is for demonstrative purposes only to show the application of the matrix to a fictional scenario in a fictional country. Relevance levels and ratings may vary in different jurisdictions.

Step 1: The NMRA in Country Y has chosen risk assessment factors to be considered in the evaluation, namely:

- Potential clinical consequences
- Severity of defect or non-compliance
- Recommended patient population, and
- Route of administration / site of action.
Step 2: Importance Level – The NMRA has decided that the potential clinical outcomes are more relevant than the severity of the defect or non-compliance and the recommended patient population. Route of administration and site of action are the least relevant.

Step 3: Prioritization of Risks – the NMRA has defined the prioritization categories as:

- Sum of 8 – 13: Low priority
- Sum of 14 – 18: Medium priority
- Sum of 19 – 24: High priority

Situation A: Medicine (tablet) used to prevent spina bifida in infants, given to women prior to conception and during pregnancy was found to have physical contaminant (hair) embedded in tablet. The contaminant was found in a bottle in the dispensary of a public health facility.

<table>
<thead>
<tr>
<th>Risk assessment factor</th>
<th>Importance level</th>
<th>Categories</th>
<th>Rate</th>
<th>Rate per factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severity of defect / non-compliance</td>
<td>2</td>
<td>Low risk Medium risk High risk: product contamination</td>
<td>1 2 3</td>
<td>2 x 3 = 6</td>
</tr>
<tr>
<td>Potential clinical consequences</td>
<td>3</td>
<td>Low risk Medium risk: bacteria or fungi may be destroyed by stomach acid High risk:</td>
<td>1 2 3</td>
<td>3 x 2 = 6</td>
</tr>
<tr>
<td>Recommended patient population</td>
<td>2</td>
<td>Low risk Medium risk High risk: pregnant women</td>
<td>1 2 3</td>
<td>2 x 3 = 6</td>
</tr>
<tr>
<td>Route of administration, site of action</td>
<td>1</td>
<td>Low risk Medium risk: internal use, oral High risk</td>
<td>1 2 3</td>
<td>1 x 2 = 2</td>
</tr>
</tbody>
</table>

Assessment: High Priority

The information from the risk matrix used to develop recommendations for regulatory action to minimize risk to the public.
2.3 Regulatory Decision-Making and Action

2.3.1 Review of Incidents for Regulatory Actions

All alerts, reports and/or results from post-market surveillance activities regarding substandard, falsified, and unregistered medicines should be assessed by the NMRAs as soon as possible, with the goal of identifying the cases with the greatest potential to cause serious damage to public health, which require immediate action.

In order to manage the incident to minimize the risk to public health, staff at the NMRA should ensure the following are implemented:

i. **An Advisory Group or Committee**: A team of relevant regulatory specialists with a lead person, and any additional relevant external stakeholders should be convened

ii. **Documentation**: Strict records of meetings and decisions should be maintained

iii. **Strategic Plans**: The team should focus on developing actions to protect the public health by mitigating the risk posed and investigating the origin of the product

iv. **Verification** of the availability of genuine stocks and genuine replacement products

v. **Regulatory Actions**: Decisions regarding regulatory actions may include: product recall, communications to health professionals, and the media

vi. A **public notice** may be necessary

vii. **Reporting** the incident to regional and global networks, such as the WHO Global Surveillance and Monitoring System.

Figure 2 outlines a simplified sequence of the stages.

§ **Note**: For the composition and functions of an advisory committee that oversees the use of medicines, regulatory authorities may refer to the World Health Organization’s guide for Drugs and Therapeutics Committees available at: [http://apps.who.int/medicinedocs/en/d/Js4882e/](http://apps.who.int/medicinedocs/en/d/Js4882e/).
Based on the public health importance of the survey findings, the NMRA may take various actions to minimize the risk to public health. This may include requests for additional testing of samples, contacting manufacturers for further information, clarification or confirmation of the product, or other appropriate regulatory action including recall.

Focal points in the respective NMRAs in the region are asked to report medicines with suspected quality issues to the regional network for pharmacovigilance and post-market surveillance (VIGICARIB) irrespective of status (confirmed or pending). This will serve to alert other NMRAs in the region about potential threats that are under investigation, and to improve regional vigilance and regulation of confirmed threats. The guidelines for reporting incidents of suspected adverse medicines reactions, and substandard/falsified medical products to VIGICARIB are available via: [http://carpha.org/What-We-Do/Caribbean-Regulatory-System/VigiCarib](http://carpha.org/What-We-Do/Caribbean-Regulatory-System/VigiCarib).

2.3.2 Taking Regulatory Action

National medicines regulatory authorities should be adequately empowered through legislation to undertake actions to protect the public from the threat posed by substandard,
unregistered and falsified medical products. For the implementation of regulatory action plans to minimize the distribution of SF products, NMRAs also require sufficient finances through budgetary allocation for human resources, information technology, communications and record-keeping. In agencies where staff undertake multiple aspects of medicines regulation, the NMRA may identify specific personnel (full-time or part-time) to manage reports on a scheduled basis.

The action plan developed by the NMRA in response to the presence of substandard or falsified medical products should be flexible and updated based on results obtained. The actions will vary according to the needs of each case.\(^\text{13}\)

Examples of categories of actions include:

- **Immediate actions:**
  - Characterizing the activity or behaviour through tracing of supply, retention of samples
  - Containing the situation to prevent and reduce risk to public health: prohibition regulations, market recall, support for patients and relatives, reporting at international level
  - Field actions or inspections

- **Short-term actions:**
  - Communicating and disseminating case information to appropriate parties, including publication, and reporting to WHO database
  - Identifying persons or entities to be held accountable

- **Long-term actions:**
  - Continuity and improvement of monitoring programme
  - Continuity with plan for health care community support
  - Continuity of collaboration with authorities in charge of the investigation.

For **Situation A**’s example (contaminated folic acid tablet – High priority), the advisory committee may decide on the following:

**Immediate action:**

- Suspension of products with the given batch number
  - Notifications sent to public sector dispensaries and private pharmacies to remove products from shelves
- Contact the manufacturer or market authorization holder
- Send the sample for laboratory testing, if possible to determine nature of contaminant
- Issue public notice to recall products with given batch number
• Search global database for similar quality issues

Short-term action:

• Notify manufacturer of findings and request investigation into packaging processes
• Discuss remedial actions for affected patients and sanctions / regulatory actions
• Communicate issue to procurement agencies
• Communicate actions to be taken to the public to prevent harm and recurrence

Long-term action:

• Public education campaign on simple visual inspection of medicines, and the need to report issues including therapeutic failure or contamination
• Implementation of protocols for pharmacy staff to conduct visual inspection of medicines when receiving inventory
• Education of health professionals to undertake visual inspection of medicines when receiving inventory and at point of dispensing
• Establish a registry of authorized suppliers and/or donor agencies in the country
• Implementation of policies for procurement of medicines from authorized distributors, and inspection
• Discontinuation of tender contract for public health supply of folic acid from supplier/manufacturer
• Revision of laws to include sanctions and penalties for the supply of substandard medicines in public health.

Note: Each jurisdiction will need to determine the key risk factors, the relevance of each risk factor, actions related to the various risk levels or priorities, and the appropriate regulatory actions to be taken to protect the public.

2.4 Strengthening Regional Decision-making and Global Surveillance

2.4.1 Leveraging Key Regional and International Regulatory Programmes

This guide presents key principles and guidance for the development of post-market surveillance systems in limited resource settings. National medicines regulatory authorities may undertake these activities on their own, but given resource limits in the Caribbean, it is highly recommended to consider leveraging available resources where possible. There are a
number of regional and global programs that governments may use to augment their post-market surveillance programmes. These are outlined below.

The Caribbean Regulatory System (CRS) is an initiative of the Caribbean Community and Common Market (CARICOM) established to assist Caribbean states to perform key regulatory functions related to pharmaceutical regulation. Similar to the MQCSD, the CRS is administered by the Caribbean Public Health Agency (CARPHA) and is engaged in two primary functions:¹⁹

- The review of products to make recommendations to Member states for market authorization (registration), and
- Pharmacovigilance and post-market surveillance of medicines and vaccines in the region.

The CRS supports the regulatory work of NMRAs through procedural guidance, information exchange and the formulation of recommendations for product registration and risk minimization.¹⁹ Support for regional pharmacovigilance and post-market surveillance is provided through the Caribbean network for pharmacovigilance and post-market surveillance (VIGICARIB). This network was launched in late 2017 to serve as a mechanism for the receipt and assessment of reports of suspected adverse medicine reactions and reports of substandard, falsified or unregistered medical products in the region.¹⁴ It facilitates the submission of reports to the global programmes of the World Health Organization, including the WHO Program for International Drug Monitoring (PIDM), and the WHO Global Surveillance and Monitoring System (GSMS), on behalf of NMRAs with membership in the respective systems. As a result, VIGICARIB helps to improve regional and international monitoring of the quality and safety of medicines, thereby providing countries with information for regulatory decision-making.

2.4.2 Improving Local, Regional and International Post-Market Surveillance

For CARPHA Member States to benefit from the work of the network, NMRAs will need to share reports and findings of post-market surveillance and the respective regulatory decisions. The results may be captured and collated through online databases such as the WHO’s Global Surveillance and Monitoring System (GSMS), which are accessed by authorized staff or focal points for individual countries. Data shared in such platforms will encourage other countries and stakeholders to report and share information on substandard and falsified medicines to stem the global problem. In addition, this exchange of information will assist to improve regional and global surveillance of the quality of medicines.

To further strengthen regional vigilance, NMRAs are encouraged to collaborate with other national and international agencies including:
• Health care providers, such as pharmacists, physicians
• National security agencies (e.g. local police, customs and excise, coast guard)
• Scientists and members of academia
• The Pan American Health Organization (PAHO)/The World Health Organization (WHO)
• Interpol
• The wider pharmaceutical industry
• Other national governments and regulatory authorities and
• The general public.

Such transparency and information exchange may have a direct impact on the health and wellbeing of patients and populations, as well as strengthen public confidence in the health system. In addition, the information from PMS programmes may be used to strengthen the programmes directly, update national priorities and to improve the PMS activities through expansion and financing.

2.5 Case Study

The example provided is for demonstrative purposes only to show the application of the reporting procedures, risk assessment matrix and regulatory decisions to a fictional scenario in a fictional country (as above). Relevance levels and ratings may vary in different jurisdictions. It is adapted from the WHO’s recommendations for criteria for risk assessment of cases involving substandard or falsified or unregistered medical products.18

Step 1: The NMRA in Country Y has chosen risk assessment factors to be considered in the evaluation, namely: Potential clinical consequences, Severity of defect or non-compliance, Recommended patient population, and Route of administration / site of action.

Step 2: Importance Level – The NMRA has decided that the potential clinical outcomes are more relevant than the severity of the defect or non-compliance and the recommended patient population. Route of administration and site of action are the least relevant.

Step 3: Prioritization of Risks – the NMRA has defined the prioritization categories as:

- Sum of 8 – 13: Low priority
- Sum of 14 – 18: Medium priority
- Sum of 19 – 24: High priority

**Situation B:** Medicine (tablet) used as the main treatment for breast cancer.

**Steps involved:**
i. Staff at the NMRA received a case report of therapeutic failure from a private hospital. A patient had brought her own supply of medicines for breast cancer treatment, but over the past three months, her condition worsened.

ii. The NMRA staff contacted the reporter and arranged to collect the sample of the medicine from the hospital pharmacy.

iii. Visual and physical inspection of the sample did not reveal any anomalies. The product is authorized for sale on the local market.

iv. The sample collected was sent to the quality control laboratory for testing to determine the quantity of active ingredient within.

v. While waiting for test results, the staff at the NMRA contacted the manufacturer to confirm the source. The marketing authorization holder indicated that this was not from their inventory.

vi. The NMRA staff searched the WHO GSMS database and found there had been 5 similar incidents reported of low active pharmaceutical ingredient (API) in the products, which had not been produced by the manufacturer (falsified). Case reports submitted to regional network and international system, with note regarding pending test results and regulatory decision-making.

vii. A preliminary report was submitted to the advisory committee, which included the following risk assessment matrix and information found during searches of external databases.

### Risk Assessment Matrix

<table>
<thead>
<tr>
<th>Risk assessment factor</th>
<th>Importance level</th>
<th>Categories</th>
<th>Rate</th>
<th>Rate per factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severity of defect / non-compliance</td>
<td>2</td>
<td>Low-risk</td>
<td>1</td>
<td>2 x 3 = 6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Medium-risk</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>High risk: assay below specification</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Potential clinical consequences</td>
<td>3</td>
<td>Low-risk</td>
<td>1</td>
<td>3 x 3 = 9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Medium-risk</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>High risk: medicine used in breast cancer</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Recommended patient population</td>
<td>2</td>
<td>Low-risk</td>
<td>1</td>
<td>3 x 2 = 6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Medium-risk</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>High risk: immunocompromised patients</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Route of administration, site of action</td>
<td>1</td>
<td>Low-risk</td>
<td>1</td>
<td>1 x 2 = 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Medium risk: internal use, oral</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>High risk</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

**Assessment:** High Priority
Lab Result:
Compendial testing confirmed that the samples of the product contained 30-50% (average of 40%) of the active pharmaceutical ingredient. The quality issue is classified as substandard – low API.

Regulatory Decisions / Actions to be taken:

Immediate:
- Notices to distributor(s) and pharmacies to suspend sale and distribution of product with given batch number
- Public notices were issued to advise the public to discontinue use of the product with given batch number, and to report these to the NMRA for further investigation
- Updates to case report submitted to regional and/or international network

Short-term:
- Investigation into sources of substandard medicine
- Public education activities to increase awareness about purchase of medicines from unauthorized suppliers
- Referral to law enforcement agencies for application of penalties to unauthorized distributors as per local laws

Long-term:
- Assessment of supply chain vulnerabilities to reduce stock-outs;
- Review and/or updating of national treatment protocols for breast cancer to support sustainable supply.

1.3.3 USP’s Risk-Based PMS Tool

The USP’s Promoting the Quality of Medicines (PQM) programme has developed a risk-based post-market surveillance tool, called MedRS that may be used to assist to develop a risk-based surveillance plan. It applies information related to the three dimensions of risk: medicines, geographic area and supply chain, to develop cluster sampling of facilities based on their risk profile. It may also be used for less rigorous methods, such as convenience sampling. The tool may assist NMRAs to identify the most susceptible medicines, determine the number of samples required, and prioritize sampling at the most vulnerable locations. A pilot version of the tool is available at: https://drive.google.com/file/d/0B6mAAO0Fp82fa2xwMEMyZFF1ZVE/view.
SECTION II: GUIDANCE FOR QUALITY TESTING OF MEDICINES
3.0 Guiding Principles for Risk-Based Testing

Post-market surveillance for the protection of public health may extend beyond identifying substandard medicinal products, to include the identification of falsified and unregistered medical products. The inclusion of the latter categories depends on the needs of the country and the purpose of the surveillance activities, which may vary based on the types of product issues reported by users. For example, Country A may experience several reports of adverse medicine reactions, while Country B may be challenged by reports of therapeutic failure or inappropriate packaging.

In general, the steps involved in planning quality surveys for risk-based post-market surveillance include:

1. Identification of objectives of the quality survey
   - These may be informed by product complaints, adverse reaction reports, and pharmaceutical assessment activities
2. Identification of medicines and/or geographical areas at high-risk
3. Determining priorities and criteria for selection of medicines to be tested and sample collection sites
4. Application of a tiered approach to risk-based sampling and testing (Levels 1-3).
5. Development of a sampling plan that is appropriate for the post-market surveillance (PMS) programme objectives and types of facilities involved
6. Recruitment and training of sample collectors
7. Undertaking sample collection and field testing, using appropriate documentation
8. Submission of samples for Level 3 testing to qualified quality control (QC) laboratory, where applicable
9. Reporting of findings to an advisory committee

Additional steps or actions may be included, and some steps may be omitted based on the objectives and testing priorities of national surveys.

3.1 Applying a Risk-Based Approach to Testing

In a tiered (three-level) approach to testing of medicines quality, the number of samples required and the types of tests are reduced without compromising the quality of the post-market surveillance. For example, where the objective of sampling and testing activities is to assess the stability of medicines at different levels of supply chain, it may not be necessary to conduct full compendial testing at each level of the system. If product identification,
disintegration and dissolution were done on samples at the central level, samples at the district level may only benefit from testing related substances. On the other hand, if the initial screening of the sample from the district level showed discoloration, it may not be necessary to conduct compendial testing of the sample.\textsuperscript{1,12}

NMRAs may refer to the Three-Level Approach used by the USP’s Promoting Quality of Medicines (PQM) programme for quality testing, which are:\textsuperscript{1}

1) In the field through visual and physical inspection
2) Field-based tests using field screening tools, and
3) At the laboratory as needed, using compendial or other methods.

This approach enables NMRAs to screen a large number of samples across geographical areas at limited cost. The use of basic analytical (screening) tests in the field could reduce the number of units required per sample, as only a subset of medicines would be tested in QC laboratories using compendial methods.

Several falsely-labelled and unregistered medicines may be detected and removed from circulation through the use of visual inspection and field-based screening in sampling and collection activities. Level 1 screening may be undertaken at staff at various points throughout the supply chain, and by patients.

A national medicines registration database inclusive of photos of labels of registered medicines is recommended to provide information to health professionals and patients and thereby improve the detection of falsified and unregistered medical products.

Table 2 presents the various tests that may be done using three-level approach. For the CARPHA Member States, the CARPHA MQCSD may provide testing at Levels 2 and 3 on behalf of NMRAs for selected medicines.
<table>
<thead>
<tr>
<th>Level</th>
<th>Type of Analysis</th>
<th>Type of Test</th>
<th>Purpose / Possible product quality issue</th>
<th>Personnel Responsible / Resources</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Visual and Physical inspection</td>
<td>- Labelling and packaging properties - Appearance, conditions and physical characteristics of medicine</td>
<td>Identify falsified medicines and/or medicines with insufficient, erroneous and/or fraudulent information; damage to packaging; damage and/or alterations to condition of medicine; Unregistered medicines</td>
<td>Staff at each stage of supply chain, and patients</td>
</tr>
<tr>
<td>2</td>
<td>Simple, Rapid and Cost-Effective Screening Tests</td>
<td>- Thin-layer chromatography (TLC) - Disintegration - Colorimetric reactions (alternate to TLC) - Spectroscopy based technologies</td>
<td>Identify medicines deficient in at least four critical quality attributes (identity, content, impurities, and disintegration for solid dosage forms)</td>
<td>Personnel trained in Screening Tests - Medicines Quality Control Lab</td>
</tr>
<tr>
<td>3</td>
<td>Pharmacopoeial or Manufacturer’s Validated Tests</td>
<td>According to registration specifications</td>
<td>Assessment of all critical quality attributes of the medicine</td>
<td>Medicines Quality Control Lab</td>
</tr>
</tbody>
</table>

*Source: Pribluda et al, 2014*
3.1.1 Guidance for Visual and Field-based Screening (Levels 1 and 2)

**Physical and Visual Inspection (Level 1)**

Simple visual and physical inspections may identify poor-quality medicines, either by identifying anomalies in important characteristics (e.g., registration status, expiry date, and packaging) or by identifying issues with physical characteristics of the dosage form (e.g., presentation, colour, texture, viscosity). Visual and physical inspections may be conducted by health professionals who suspect a medical product is substandard or falsified. Patients and/or caregivers may be instructed to routinely screen medicines and report anomalies to health professionals and/or the national regulatory authority. Figure 3 presents the flowchart of steps recommended for visual inspection (Level 1), which includes an assessment of the product label, packaging and presentation.

Checklists and guides by The World Health Professionals Alliance (Appendix II) and the World Health Organization (Appendix III) may be used during Level 1 screening to facilitate inspection of packaging and physical characteristics of the medicine. These tools highlight questions that may be asked to identify anomalies of therapeutic effect, packaging, supply source and other factors, such as smell and storage.

**After A Problem Is Identified at Level 1:**

On the identification of a quality problem during Level 1 inspection, the product should be reported to the NMRA to determine the next steps with respect to incident management and regulatory action. Reporters should be instructed to retain the sample for collection by inspectors. The NMRA may decide to seek clarification from the manufacturer and/or distributor, proceed with other levels of testing, or take other regulatory actions based on the findings. Guidance for the management of incidents involving suspected substandard or falsified products is provided in Section I-2.0.

Level 2 testing is not required if:

i. The product is not registered with the NMRA (report as unregistered)
ii. The product is expired, or
iii. There are physical issues or anomalies related to: labelling, batch number, scientific name, company’s logo, number of units per container, dosage form, strength, manufacturer’s address, package insert, or damage to packaging.

If the product passes visual inspection or if a determination cannot be made, the product should proceed to testing at Level 2.
Figure 3: Flowchart for Visual and Physical Screening (Level 1) 

Start

Level 1: Visual inspection

- Is product registered?
  - No: STOP: No additional testing needed.
  - Yes: Is product expired?
    - Yes: STOP: No additional testing needed.
    - No: Did product fail other aspects of L1?
      - Yes: STOP: No additional testing needed.
      - No/Questionable: Level 2: Field-based Screening

Footnote:

1 – Level 1: Visual inspection to include assessment of registration status, expiration date, labelling, batch number, scientific name, company logo, number of units per container, dosage form, strength, manufacturer’s address, presence of package insert, damage to packaging.

Report suspected substandard / falsified medical products to NMRA as per country regulations and protocols.
Field-based Screening (Level 2)

At Level 2, analytical testing of product quality using field-based screening technologies may identify potential product issues that may not be apparent at Level 1.1

Suspicious samples identified by visual inspection may be further screened using one or more advanced screening tests, such as:

- Thin-layer chromatography (TLC)
- Colorimetric methods
- Disintegration tests and
- Spectroscopy: Raman and/or near infrared (NIR) spectroscopy.

These tests may range from qualitative to semi-quantitative, according to the capability of the screening technology used. The tests may be used to identify the presence of the active ingredient, possible degradation and/or impurities. NMRAs should assess the various screening tests available prior to procurement and compare the features to source the product that best meets their needs.

Based on the objectives of the study, a product that passes identification and other field-based tests usually provides sufficient information to eliminate the need for further testing. However, based on the screening tools used and the tests done, the regulatory authority may decide to send a portion of the passed samples for compendial testing (Level 3) to confirm the results. Figure 4 describes the steps involved when testing medicines at Level 2.

Where a product is confirmed as substandard at Level 2, a report should be submitted to the responsible division of the NMRA as soon as possible. The WHO guidance provided for management of incidents where substandard or falsified products are identified should be followed to facilitate confirmation of source(s) and credibility of the information (Appendix I). Staff of NMRAs may use the guides to develop checklists. Based on the NMRAs protocols for incident management, the findings should be disseminated to the relevant committees or units of public health authorities for regulatory action.
Figure 4: Guidance for Field-based Screening (Level 2) ¹

Level 2:
Field-based Screening

Does product pass ID?

Yes
Conduct other screening tests as

Pass
A portion of samples may go on to L3 to confirm results

Fail
Move to Level 3 Testing

No API detected
STOP: No need to verify at Level ²

Footnotes:
1: Level 2: Field-based screening may include assessment of a product's identity (ID) and other screening tests as applicable.

2: If a product passes identification, additional tests should be prioritized in the following order: content, disintegration, and impurities.
3.1.2 Prioritizing for Compendial Testing (Level 3)

Compendial testing provides the most extensive information on the quality of medicines, but is complex, expensive and time-consuming. Compendial testing should be done on the following:

(i) Suspected samples that fail field-based screening tests, and
(ii) A portion of samples to confirm Level 2 results, according to study protocol.

Figure 5 presents steps for prioritizing compendial testing. If product fails a test at Level 2, the same test should be done at Level 3 before initiating tests for other product quality attributes.

If the result from Level 2 is confirmed as ‘Fail’ at Level 3, no further testing is needed.

If the result from Level 2 is not confirmed as ‘Fail’ at Level 3, the analysts should proceed with the recommended prioritization of compendial tests as shown in Figure 5.

The recommended steps in Figure 5 should be used together with the applicable pharmacopoeial requirements for the product.

Adjustments to the sequence of testing may be necessary based on the dosage form, formulation or other considerations. Some products may require additional tests not shown in Figure 5. The flow diagram is not intended as a list of required tests and does not apply to every testing scenario. Instead, the flow diagram illustrates the prioritization of analytical tests to guide the sequence for testing the majority of samples, as applicable.

Depending on the dosage form involved, appropriate adjustments to the sequence may be needed. For example, injectable liquid dosage forms would not undergo disintegration and dissolution tests. For products procured by the funding or donor organizations with sound quality assurance measures in place, a selection of appropriate compendial tests may be considered based on where in the supply chain samples were collected.
Figure 5: Recommended Prioritization for Compendial Testing (Level 3)

Legend:

¥ For injectable products, basic tests such as pH should be confirmed before starting Level 3 testing.

¤ No further testing required.

START

Did product fail at Level

Yes

Confirm failed result

Pass

Fail

STOP ¥

N

Disintegration

Pass

Fail

STOP ¥

Identification

Pass

Fail

STOP ¥

Assay

Pass

Fail

STOP ¥

Dissolution

Pass

Fail

STOP ¥

Uniformity of units

Pass

Fail

STOP ¥

Related substances

Pass

Fail

STOP ¥

Sterility

Pass

Fail

STOP ¥

Other tests

Pass

Fail

STOP ¥

STOP. Product passed quality testing
4.0 Medicines Quality Testing at The MQCSD

4.1 Services at the Medicines Quality Control and Surveillance Department (MQCSD)

The Caribbean Regional Drug Testing Laboratory (CRDTL), was established in 1975 by CARICOM Governments as a regional institution to provide laboratory services to support the evaluation of the quality of pharmaceutical products. In 2011, the CRDTL was among regional health institutes and entities that were brought under the umbrella of the Caribbean Public Health Agency (CARPHA). In its strategic plan 2018-2020, under Strategic Priority 1, the agency aims to: “strengthen CARPHA Member States’ Health systems through training, policies, standards and guidelines, access to laboratory services and essential medicines through the Caribbean Regulatory System.” Towards this objective, the CRDTL was restructured and renamed CARPHA Medicines Quality Control and Surveillance Department (MQCSD).

The primary goal of the MQCSD is to support CARPHA Member States in the assurance of the quality of medicines towards the preservation of public health, by verifying that medicines used in the region are reliable and of good quality. The core functions of the department are:

1. Performance of analyses of pharmaceutical products and evaluate the technical data for CARPHA Member States on request.
2. Provision of information and advisory services to CARPHA Member States on issues pertinent to medicinal quality.
3. Facilitation of training in analytical techniques for pharmaceutical quality control laboratories.

In addition, the MQCSD will offer educational materials and training to regulatory personnel in the region to develop capacity within the national medicines regulatory authorities (NMRAs) post-market surveillance activities.

For products that require compendial testing for market authorization of products, or for routine or spontaneous post-market surveillance of the quality of medicines, NMRAs may request the services of the CARPHA Medicines Quality Control and Surveillance Department.

The application for testing may include requests for:

- Verification of pharmaceutical identity, and
- Complete or partial pharmacopoeial testing.
4.1.1 Testing Services and Accreditation

The MQCSD offers the following testing services for finished pharmaceutical products:

**CHEMICAL AND PHYSICO-CHEMICAL ANALYSIS**

- Disintegration
- Loss on Drying
- Water content
- Qualitative Identifications (colour reactions, precipitation and other tests)
- Titration
- Potentiometry
- Dissolution
- pH
- Thin Layer Chromatography
- Uniformity of Dosage Units (mass, content)
- Specific Gravity/Weight per mL

**INSTRUMENTAL ANALYSIS**

- High Performance Liquid Chromatography (Ultraviolet-Visible (UV-VIS))
- Spectrophotometry: Ultraviolet-Visible (UV-VIS) and Infrared (IR)

In September 2017, the CARPHA Medicines Quality Control and Surveillance Department was awarded accreditation through the Jamaica National Agency for Accreditation (JANAAC) to the international ISO standard 17025 “General requirements for the competence of testing and calibration laboratories”.

The Department has been accredited to the ISO/IEC 17025 for the following tests:

- High Performance Liquid Chromatography:
  - Assay, dissolution, identification, content uniformity
- Ultraviolet-Visible Spectrophotometry
  - Assay, dissolution, identification, content uniformity
- Disintegration
- pH
- Uniformity of weight

To verify the maintenance of the scope of accreditation, the Jamaica National Agency for Accreditation (JANAAC) will conduct annual surveillance visits during a four-year accreditation cycle, with a full reassessment in the fourth year.

Sterility tests are not performed at the MQCSD at this time and will not be part of the MQCSD’s post-market surveillance programme. The staff of the MQCSD will advise focal points regarding the recommended tests for the product based on the dosage form and the quality issue.
4.1.2 Medicines Tested by the MQCSD

The current list of medicines with accredited tests that can be tested by the MQCSD is available in Appendix IV. This list may be updated periodically based on the department’s capacity. This list may be used as a reference for NMRAs or other partners seeking to submit requests for testing of medicines as part of medicine quality surveys.

Regulators with requests for testing outside of the Department’s schedule, or for testing of unlisted medicines should submit information about the product to the Head of the MQCSD for technical review and to determine feasibility based on the Department's capacity to test.

4.2 The MQCSD Post-Market Surveillance Programme

In June 2018, MQCSD established a post-market surveillance programme with an introductory phase to be conducted in the first two years. Through this programme, MQCSD undertakes the monitoring the quality of selected medicines circulating in the pharmaceutical markets of participating CARPHA Member States.

The objectives of the programme are to:

1. Develop risk-based criteria for the selection of medicines to be tested, in order to prioritize those that pose risks to public health.
2. Proactively monitor selected medicines on the Caribbean market for quality, safety and efficacy.
3. Develop competencies to enable sampling and testing of medicines on the market, as routine surveillance of the quality of medicines.
4. Collaborate with the CARPHA CRS, TECHPHARM, and national focal points to select medicines for annual post-market surveillance, including drawing on the CARPHA CRS regional network for pharmacovigilance and post-market surveillance.

All CARPHA Member States are eligible to participate. The activities of the programme will involve:

- Identification of priority medicines by focal points for compendial testing, based on risk-based criteria
- Sampling of medicines by assigned personnel of the NMRA
- Shipping of samples to the MQCSD with appropriate permits and documentation;
- Testing of samples
- Communication of results to NMRAs, and
- Annual reporting of programme activities to CARPHA Member States.
A pre-determined list of medicines will be selected and revised annually, in collaboration with regional NMRAs, CRS and TECHPHARM. The procedures of the programme are subject to review during the annual evaluation of the programme. An overview of the sequence of activities involved in the MQCSD post-market surveillance programme is shown in Figure 6.

**Figure 6: MQCSD Post-Market Surveillance Programme Sequence**

**Key:** MQCSD – Medicines Quality Control and Surveillance Department; NMRA – national medicines regulatory authority
4.2.1 Risk-based Criteria used in Selection of Medicines

The following criteria will be used to select the medicines for the post-market surveillance programme:

1. Medicines/manufacturers reported by NMRA/Ministry of Health, procurement agencies, MQCSD for quality/substandard/falsification issues
2. Medicines produced by countries with limited regulated systems
3. Medicines with limited time on market (less than 5 years on the market of a stringent regulatory authority)
4. Medicines listed on recognized standard guidelines and used in high volume/wide regional distribution such as the WHO Essential Medicine List, National Institute for Health and Care Excellence, Joint National Committee 8 Guidelines, National Guidelines, CRS recommended medicines.
5. Medicines with narrow therapeutic index/drug therapeutic monitoring
6. Medicines with formulation challenges/complex production processes

The criteria were finalized at a meeting on post-market surveillance and the Caribbean Pharmaceutical Policy held by the Department in March 2019, with the assistance of TECHPHARM and the national focal points of the Caribbean Regulatory System.
5.0 SAMPLING PLANS AND PROCEDURES

5.1 Developing Sampling Plans

National medicines regulatory authorities are responsible for developing quality surveys for post-market surveillance, including the identification of medicines to be surveyed, geographic areas, collection sites and methods. The specific objectives of the survey, sampling priorities and methods should be used to guide the development of subsequent sampling plans. The NMRA should clearly identify roles of collaborators or affiliates (e.g. importers) that would be involved in facilitating sample collection.

Plans should be prepared for each area, region or country involved in the survey and should comply with requirements identified in the survey protocol.

The following should be specified in the sampling plans:

1. The individual sites where collectors should collect samples (by facility type and address)
2. Medicines to be sampled (by active pharmaceutical ingredients, dosage form, strength, and if needed, by package size)
3. The sampling method: cluster, simple random or convenience sampling
4. The minimum number of dosage units to be collected per sample
5. The number of samples to be collected per medicine
6. Total number of samples to be collected in the relevant area, region or country.

In addition, plans should include clear instructions for sample collectors.

The MQCSD does not undertake sampling directly but will work with NMRAs to confirm the requirements for submission of samples that are eligible for compendial (Level 3) testing.

5.2 Sampling Preparation

5.2.1 Training of Sample Collectors

Sample collectors should be trained in:

- Procedures for sample collection and handling
- Documentation of samples
- The use of field-based screening devices, where applicable.

The completion of training should be documented in the individual's training records.
5.2.2 Preparing for Sample Collection

Prior to sampling activities, field inspectors or sample collectors should be familiar with:

1. The objectives of the quality survey
2. The individual sites for sample collection (by facility type and address)
3. The medicines to be sampled (active pharmaceutical ingredients, dosage form, strength, and if needed, package size)
4. The minimum number of dosage units to be collected per sample
5. The number of samples to be collected per medicine
6. Total number of samples to be collected in the relevant area, region or country
7. The tools and equipment required, including personal protective equipment
8. The procedures for sample collection, handling, storage and transportation.

*Screening Devices:* Where field-based screening devices are available, sample collectors should review instructions for their use according to the survey protocol.

*Documentation:* Ensure that sufficient copies of the Sample Collection Form are available for the site (Appendix V for example of a Sample Collection Form).

If photos of the product package labels are available, use these to verify the product being sampled.

*Tools:* Before and after using collection tools (e.g. scoops), collectors should ensure they are thoroughly washed and rinsed with water or suitable solvent, and dried. Tools should be stored under clean conditions.

*Vigilance:* Sample collectors should be meticulous, paying close attention to details and cleanliness. He or she should remain alert to any signs of contamination, deterioration or tampering. Where the finished product is to be sampled from a storage container, collectors should check to ensure that the exterior and opening of the container is clean before sampling. If necessary, sample collectors may need to clean the exterior of the storage container or its opening to remove dust or dirt.

Distributors, pharmacists and/or inventory managers at health facilities should be familiar with the conditions required to facilitate clean collection of samples.

5.2.3 Sampling Facilities

Sampling facilities should be designed or maintained to:

- Prevent contamination of opened containers, the products and the handler
- Prevent cross-contamination by other materials, products and the environment and
- Protect the individual who samples (sample collector) during the sampling procedure.

The site from where the sample is taken, and its conditions should be recorded in the sampling record. A log should be kept of all products sampled from a site.
5.2.4 Health and Safety

In preparing for sampling from a site, the following should be ensured:

- Safe access to and egress from the site by sample collectors
- Pathways should be unobstructed to avoid spills
- Storage areas should be adequately lit and ventilated, to enable reading of labels and to ensure safety.

Sample collectors should:

- Read the relevant health and safety information before sampling the product;
- Wear appropriate protective clothing, such as a laboratory coat and gloves during sample collection;
- Be trained in the use, and use equipment required for special precautions, where applicable.

5.2.5 Minimum Number of Sample Units

The number of units to collect per sample depends on:

- the objectives of the sampling and testing activity
- the type of medicine
- the planned tests, and
- the approved medicine specification.

The number of dosage units per sample should allow:

- The planned tests to be conducted
- Investigation and confirmatory testing of samples found to be out-of-specification, and
- Sufficient retention samples to be used in case of dispute.

Tests of unit dosage forms for uniformity of weight, volume or content may require a considerable number of units.
For samples of products to be submitted to the MQCSD, the following minimum quantities are required for testing:21

I. For Complete Pharmacopoeial Analysis:

<table>
<thead>
<tr>
<th>Dosage Form</th>
<th>Number of Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablets and Capsules (&gt; 5mg)</td>
<td>100</td>
</tr>
<tr>
<td>Oral solutions (bottles &gt;200mL each)</td>
<td>5 bottles</td>
</tr>
<tr>
<td>Ointments and Creams (tubes &gt;5g or &gt;5mL)</td>
<td></td>
</tr>
<tr>
<td>- For tubes &lt;5g or &lt;5mL contact the lab</td>
<td>5 tubes</td>
</tr>
</tbody>
</table>

Note: For products (tablets, capsules or oral solutions) containing 5mg or less of the active pharmaceutical ingredient, and for tubes containing less than 5g or less than 5 ml of medicine, contact the department for guidance.

II. For Individual Tests:

<table>
<thead>
<tr>
<th>Test</th>
<th>Notes</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight Variation</td>
<td>Performed on tablets, capsules, solids in single unit containers and solids for parenteral use, where average weight is &gt;25mg or &gt;25% of active ingredients by mass</td>
<td>30</td>
</tr>
<tr>
<td>Assays</td>
<td>Tablets, capsules or Other dosage forms, e.g. creams, parenterals – depends on type of assay</td>
<td>TBD</td>
</tr>
<tr>
<td>Identification/Related substances/Breakdown products</td>
<td>Tablets, capsules or Other forms – depends on method of analysis</td>
<td>TBD</td>
</tr>
<tr>
<td>Dissolution/Disintegration</td>
<td>Performed on tablets or capsules</td>
<td>24</td>
</tr>
<tr>
<td>Uniformity of Content</td>
<td>Performed on tablets or capsules</td>
<td>30</td>
</tr>
</tbody>
</table>

Key: TBD – to be determined

5.3 Sample Collection Procedures

The principles should be stated in instructions for collectors regarding target medicines, drawing samples, handling samples, storage and transportation.
5.3.1 Target Medicines

For the sampling of target medicines:

- The target medicines, their dosage forms, strengths and package sizes should be defined.
- The minimum number of dosage units per sample and number of batches to be collected from each collection site for each medicine in the sampling plan should be adhered to.
- All units of one sample should have the same batch number.
- Samples should have at least six months remaining before expiry.
- Each sample should be recorded separately using the sample collection form. Note any abnormalities including missing information, missing leaflets or product abnormalities.
- Each sample should be identified by a unique sample code, defined on the sample collection form and specified on all original packages belonging to the respective sample.
- Sampling records should clearly indicate the date of sampling, the sampled container and the identity of the person who sampled the batch. A copy of the Sample Collection Form may be included in the sampling record (Appendix V Sample Collection Form).
- The sample collection form should always be kept with the collected sample.
- The manufacturer’s batch certificates of analysis should be collected with the samples, if available, and kept with the sample collection form.

Where Level 2 or 3 testing is required, sampling units should consist of whole packs. Individual packs should not be broken open for sampling.

5.3.2 Drawing Samples

If the consignment consists of one very large batch, or if there has been little experience with the product, two independent analyses may be done. The two independent samples should be taken from different sampling units.

If a consignment is composed of two or three batches from the same manufacturer, a single sample taken from each batch may be adequate, provided that there is evidence from the expiry date, or other information that the batches were produced at approximately the same time.
During or prior to sampling the following steps may be applied:

1. Check condition of containers for integrity of packaging material.
2. Check for cleanliness of containers.
3. Check condition of containers for shape and colour.
4. Check the labelling of containers for damage.
5. Check the labels for spelling mistakes.
6. Check the labels for manufacturing and expiry dates.
7. Check the product registration to confirm market authorization
8. Count, categorize and record the number of defects.
9. Check the supplier certificate against the specifications, if applicable.

Note: When sampling finished products, packaging materials may be retained for testing.

5.3.3 Packaging Materials (primary and secondary)

To avoid mixing up printed packaging materials during the sampling operations, only one material should be handled at a time.

Samples of packaging materials should never be returned to the consignment. Primary packaging materials should be adequately protected during the sampling operation to avoid environmental contamination.

5.3.4 Labelling

Closures and labels should be such that unauthorized opening can be detected.

Labelling of samples should provide appropriate details (below). Identification should be provided for the sample (labelling) to avoid mixing or damage.

Labels should be applied at the time of sampling, and the container used to store the sample should be properly labelled with appropriate details, such as:

1. Product description: name, dosage form, strength
2. Identification code, batch/lot number
3. Quantity
4. Date sampled
5. Storage conditions, handling precautions and
6. Assigned container number.

When a container is sampled from, the following precautions should be taken:

- If a tamper-proof seal is broken, the consignee should be informed and the container resealed with an appropriate seal.
- If a bag has been punctured, the hole should be appropriately closed and identified as a sampling hole made by an authorized sample collector.
• Sampled containers should be identified, as they no longer contain the quantity stated on the label. Exceptions may include products under investigation for falsification or adulteration.

5.3.5 Handling

The medicine samples should not be removed from the original primary and secondary packaging, as far as possible.

• For loose tablets or capsules packaged in large volume containers (e.g. >1000), the sample may be collected in plastic bottles with snap-caps or screw-tops.
• Containers such as bottles and vials should not be opened. Seals should remain intact.
• Do not remove or allow damage to medicine labels or package leaflets. Where medicines are supplied without package leaflets, or in unlabelled plastic bags from larger containers (repackaged), or as individual dosage forms, this should be recorded.
• Keep a sample collection form and all packages belonging to one sample together.
• Do not return samples to bulk.

5.3.6 Visual and Physical Inspection

During sampling, attention should be paid to any signs of nonconformity of the product, such as:

• Differences in physical characteristics of tablets/capsules:
  o Uniformity of shape, size, texture and colour; markings; breaks, crack or splits; embedded surface spots or contamination; presence of empty capsules and smell
• Moist crusts on hygroscopic substances; Deposits of solid product in liquid or semi-liquid products
• Stratification of liquid products and
• Tampering, damage or anomalies of the packaging: container, label, leaflet or package insert.

Sample collectors may refer to the checklists by the World Health Professionals Alliance’s Tool for Visual Inspection of Medicines to guide the inspection process (Appendix II), or the World Health Organization’s guide for identifying suspect substandard and falsified medical products (Appendix III).
Sample collectors should have access to a medicines registry, and photos or samples of the product packages to allow identification of any falsified products during Level 1 testing.

The following should also be reviewed by sample collectors:

- Batch number
- Scientific name
- Company logo
- Manufacturer address
- Number of units per container

Any suspicious signs of contamination, deterioration or tampering should be recorded.

Sample collectors should avoid pooling of samples from different portions (non-homogenous), as this can mask contamination, low potency or other quality problems.

Where available, sample collectors should utilize field-based (mobile) screening equipment to identify the presence of active pharmaceutical ingredients (APIs). The tests should be applied as per on guidance for Level 2 testing shown in Figure 5, Section 2.

In the event that substandard or falsified products are identified during sampling, with confirmation via visual or physical inspection or Level 2 testing, a report should be immediately sent to the NMRA.

### 5.3.7 Site Storage Conditions

Storage conditions at the site (temperature, humidity, access of light and other observations) should be described in the sample collection form. When overt sampling is used, collectors can measure the temperature if it is not controlled at the site.

- Samples should be collected and kept under controlled conditions in line with product requirements. The cold chain must be maintained where needed.
- Samples should be protected from light, excessive moisture or dryness.
- Ensure safety measures are in place to secure samples. Packages should be kept in a locked area.
- The period within which samples should be collected and the deadline for sending the last sample to the testing laboratory should be clearly indicated and adhered to.

### 5.3.8 Storage Containers and Transportation of Samples

Storage and transportation of samples to the testing laboratory should be done according to the requirement set out in the WHO Guidelines for sampling of pharmaceutical products and related materials:6
- Containers used to store samples should not interact with the sampled material or allow contamination. They should protect samples from light, air and moisture. Containers should be sealed and preferably tamper-evident.
- Samples of loose products (solid or liquid) should be placed in clean containers. Liquids should be transported in suitable bottles closed by screw tops with inert liners that provide a vapour-proof seal for the contents.
- Light sensitive materials should be protected by using amber glass containers or by wrapping colourless glass containers in foil or dark-coloured paper. Head-space should be kept to a minimum to minimize any possible degradation.
- Solid dosage forms should be protected during transit, either by totally filling the container with the product or by filling any residual space with a suitable material, such as sterile cotton.
- For all containers that come apart (e.g. screw-capped jars) precautions should be taken to avoid any mix-up when they are opened for examination, e.g. all components should be labelled (jars and covers).
- Transportation should be prompt and as direct as possible to avoid jeopardizing the quality of the collected samples.
- The samples should be kept in their original packaging and stored under the conditions specified on the label. Avoid freezing, and maintain the cold chain where required.
- For transport, all samples should be packaged adequately and transported in such a way as to avoid breakage and contamination. Any residual space in the container should be filled with a suitable material.
- For temperature-sensitive medicines, temperature monitors may be included with shipments to document maintenance of an appropriate temperature during prolonged transit.
- A covering letter, sample collection forms and if available, the manufacturer's certificate of analysis should accompany the samples.
6.0 SUBMITTING PRODUCTS FOR TESTING TO THE MQCSD

6.1 The Medicines Quality Testing Process at the MQCSD

6.1.1 Process for MQCSD’s Post-Market Surveillance Programme

For the MQCSD’s post-market surveillance programme, the list of products will be issued with an invitation to NMRAs to participate in the surveillance activity. Once regulators confirm interest, the number of products to be submitted and feasibility, the MQCSD begins preparations to acquire import permits.

Ad hoc testing of products is discouraged as tests and reagents are limited. Instead, NMRAs are encouraged to apply risk-based approaches to post-market surveillance to reduce costs and to improve efficiency of monitoring the quality of medicines.

The steps involved in the MQCSD PMS quality testing process are as follows:

<table>
<thead>
<tr>
<th>Step</th>
<th>Mode/Documents</th>
</tr>
</thead>
</table>
| 1. Regulator or NMRA is informed of proposed quality survey and list of products | Email  
List of medicines |
| 2. NMRA confirms acceptance of proposed tests and the estimated costs (where applicable). NMRA staff returns form to lab via email. | Email  
Request Form  
Product documentation |
| 3. Reagents and reference standards are procured by lab, if needed. Import permits submitted | Procurement process |
| 4. MQCSD staff will notify NMRA regarding when to ship medicine sample | Email |
| 5. NMRA staff acquires required number of units for testing from local site(s) | Physical sampling  
Sample Collection Form |
| 6. NMRA staff completes Product Submission Form (MQCSD-Guide-01 Form 2) and prepares supporting documents | Product Submission Form  
Sample Collection Form  
Manufacturer’s COA |
| 7. NMRA staff packages sample with supporting documents and sends to shipper or courier | Packaging  
Documents  
Letter from NMRA  
Invoice of minimum amount  
Courier |
### 6.1.2 Process for Requests for Standard Product Testing

For NMRA with requests for quality testing of medicines based on national surveys, the steps involved in the standard quality testing process are as follows:

<table>
<thead>
<tr>
<th>Step a</th>
<th>Mode/Documents</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Requestor completes and submits the Request for Analysis Form (MQCSD-Guide-01 Form 1) to the lab.</td>
<td>Email Request Form</td>
</tr>
<tr>
<td>2. MQCSD staff conducts technical review of request to determine ability to test.</td>
<td>MQCSD staff Product documentation</td>
</tr>
<tr>
<td>3. Requestor is informed of MQCSD’s ability to test, proposed tests, proposed schedule, and estimated costs, where applicable (budget).</td>
<td>Email Request Form</td>
</tr>
<tr>
<td>4. Requestor confirms acceptance of proposed tests, including proposed deviations from test methods, and estimated costs. Requestor returns form to MQCSD via email.</td>
<td>Email Request Form Product documentation</td>
</tr>
<tr>
<td>5. Reagents and reference standards are procured by MQCSD, if needed. Import permits submitted.</td>
<td>Procurement process</td>
</tr>
<tr>
<td>Step</td>
<td>Mode/Documents</td>
</tr>
<tr>
<td>------</td>
<td>----------------</td>
</tr>
<tr>
<td>6. MQCSD submits applications for import permits to Ministry of Health, Jamaica.</td>
<td>Import permit application</td>
</tr>
<tr>
<td>7. MQCSD staff notify requestor regarding when to ship medicine sample.</td>
<td>Email</td>
</tr>
<tr>
<td>8. Requestor acquires required number of units for testing from local site(s).</td>
<td>Physical sampling Sample Collection Form</td>
</tr>
<tr>
<td>9. Requestor completes Product Submission Form (MQCSD-Guide-01 Form 2) and prepares supporting documents.</td>
<td>Product Submission Form Sample Collection Form Manufacturer’s method and COA</td>
</tr>
<tr>
<td>10. Requestor packages sample with supporting documents and sends to shipper/courier.</td>
<td>Packaging Documents Letter from NMRA Invoice of minimum amount Courier</td>
</tr>
<tr>
<td>11. Reagents and reference standards received by MQCSD.</td>
<td>Suppliers</td>
</tr>
<tr>
<td>12. Sample received by lab and verified against product submission form. Any discrepancies with the sample or documentation must be resolved before registration of the sample for testing.</td>
<td>Courier MQCSD staff</td>
</tr>
<tr>
<td>13. Sample is tested and results are reviewed by Chemist.</td>
<td>MQCSD staff Report</td>
</tr>
<tr>
<td>14. Results are sent to Senior Chemist for secondary review and confirmation of validity of results. Anomalies are addressed, if needed.</td>
<td>Final Report</td>
</tr>
<tr>
<td>14. Results are sent to Head of MQCSD for preparation and submission of COA.</td>
<td>Final Report MQCSD COA</td>
</tr>
<tr>
<td>15. COA is sent to requestor via email and post.</td>
<td>Email and via post Final report</td>
</tr>
</tbody>
</table>

Key: a. Steps 1-4, 7-9, 11-14 are part of routine testing sequence. COA – certificate of analysis, NMRA – national medicines regulatory authority
Procedural delays may occur in the event that there is a need to procure reagents and/or reference standards or where the lab has to acquire import permits. Delays in sample analysis may occur where method verification or system suitability requirements are not met. The MQCSD staff will inform customers in writing of all events that may delay sample submission and analysis.

6.2 Submitting a Request for Testing of Samples

To submit a request for testing of the quality of medicinal products, the Request for Analysis form (MQCSD-Guide-01 Form 1) must be completed and submitted to the MQCSD. The forms may be downloaded from the website at http://carpha.org/What-We-Do/Medicines-Quality-Control-and-Surveillance/Testing-and-Customer-Service for completion by direct entry and submission via email to carphajam@carpha.org.

Note: Testing for manufacturers will only be conducted with the approval of the relevant national medicines regulatory authority.

Staff at NMRAs should complete the Request for Analysis form provided by indicating:

- **Administrative Information:**
  - Name of Submitting Agency
  - Name of person making request, Designation, Telephone number, Email address
  - Date of request

- **Product Information:**
  - Generic name of product (International Non-proprietary Name or INN)
  - Dosage Form
  - Specification: British Pharmacopoeia (BP), United States Pharmacopoeia (USP), manufacturer's method, Other

- **Acceptance:** When the lab returns the form identifying the tests to be done, the requestor indicates acceptance or agreement (Yes or No) in column 5. Where the Department advises the requestor of the need for deviation from a test method for a product, the requestor must give approval in writing for testing to proceed.

For products where there is no official specification or reference standard provided, the manufacturer's method, specification, reference standard and Certificate of Analysis (COA) are required.
6.3 Submitting Samples for Testing

Each sample submission must be accompanied by a completed Product Submission Form (MQCSD-Guide-01 Form 2), a copy of the Sample Collection Form, a Cover letter and the manufacturer's batch certificate of analysis, if available.

The requestor must complete the Product Submission Form by indicating:

I. Administrative Information:
   a. The submitting agency
   b. Name and address of contact

II. Reason for submission

III. Manufacturer's Information:
   a. Name, address

IV. Product Information:
   a. Brand name, generic name (INN)
   b. Labelled claim
   c. Expiry date
   d. Lot/batch number

The MQCSD staff will add the following information:

   a. Assigned sample number, number of sampled units, condition of sample
   b. Persons registering and checking the sample
   c. Dates
   d. Comments

6.3.1 Sending Samples by Courier

Where collectors do not transport samples directly to the laboratory, samples and documents should be sent by a courier service.

Confirm terms of use with couriers or shipping agents. Ensure they can maintain storage conditions and requirements for handling and packaging. Give clear instructions to shipping agent regarding storage and handling.

The documentation with each shipment should indicate the following:

- The samples are being sent for laboratory testing purposes only
- The samples will not be used on humans or animals
- The samples have no commercial value and will not be placed on the market.
Include sample details on the courier invoice and shipping label. Where possible, include a letter from the NMRA describing the purpose for shipping the sample.

Import permits are required before samples can be shipped to the MQCSD. The permit should be given to the courier service prior to shipping. The samples submitted to the department must match the import permit to avoid penalties to the department incurred by the Collector of Customs, Jamaica.

Once approval to ship the samples is acquired and the samples are shipped, the MQCSD should be informed of the shipment details, including the tracking number assigned by the courier service to enable them to follow the shipment and arrange prompt collection of samples. Scanned copies of the enclosed documents (Cover letter, Sample Collection Form, Product Submission Form, Import Permit) should also be sent to the department prior to shipping.

### 6.4 Communication with the MQCSD

The MQCSD will provide requestors with periodic updates on medicines submitted for testing by email and on request, including any unexpected delays in testing. The results of tests will be communicated to the respective requestor. In the event product testing identifies a substandard or falsified medicine, the department will submit a report to the requestor, and/or the national focal point for further action and decision-making. Where product testing is conducted on request from manufacturers, only information pertinent to their product will be made available to the requestor.

**Note:** Testing for manufacturers will be conducted only with the approval of the relevant national medicine regulatory authority.

#### 6.4.1 Estimated response times for requests for analysis

The estimated response times from the MQCSD for requests varies with the type of testing or requests as follows:

- Routine testing: within 5 working days after receiving the request
- Emergency requests: within 24 to 48 hours of receiving the request
- Post-market surveillance: response will be based on PMS schedule.
The MQCSD may be contacted by:

Mail: **CARPHA Medicines Quality Control and Surveillance Department**
    Hope Gardens
    Kingston 6
    Jamaica

Tel: +1-876: 977-3540; 702-4235
Fax: +1-876: 977-0974
Email: carphajam@carpha.org
Website: [http://carpha.org/](http://carpha.org/)

6.4.2 Communication of Results

The average turn-around time for routine testing at the MQCSD from receipt of sample to communication of result is between 30 to 45 working days.

For the PMS programme, the results will be communicated based on an agreed schedule.

Results from the laboratory testing of products will be reviewed and approved by the Head of the MQCSD. These will be presented as a certificate of analysis and will be sent to the customer via email. In addition, the original certificate of analysis will be dispatched via post to the customer.

The certificate of analysis will include:

i. The name and address of the Department
ii. The name and address of the customer who requested the analysis
iii. Unique identification of the COA chronological numbering starting with 001/YEAR, e.g. 001/2018
iv. Page number and identification on each page
v. Lab identifier (ID) of the sample
vi. The name, description, condition, expiration date, date of manufacture and lot number of the sample
vii. The date the certificate is issued
viii. The date of receipt of the test item
ix. The tests performed and the results with the units of measurement where appropriate
x. The specifications and test methods used to analyse the sample
xi. The limits of the specifications
xii. Whether the sample meets specifications
xiii. Name and address of original manufacturer, or name and address of distributor or re-packaging plant
xiv. Submitter’s code if available
xv. Name and signature of the Head of MQCSD or designate, authorizing the COA
xvi. A statement that the COA shall not be reproduced, except in full, without the written approval of the laboratory
xvii. Deviations from official test methods.

The Senior Chemist or designate will record the date of issue of the certificate of analysis for the sample in the Sample Register.

Amendments and Reissue of COAs:
When amendments (e.g. corrections) to a COA are required, a new COA will be prepared. The statement “Reissue of Certificate of Analysis No. X Dated Y” will be placed on the COA. Date ‘Y’ will reflect the issue date of the original COA. An “R” is placed beside the COA number to indicate that the new COA is a reissue, e.g. 001/2018R.

Queries about the findings may be communicated via email to the department at carphajam@carpha.org or via telephone.
APPENDIX I: WHO Suspected SF Products Incident Management – Aide Memoire

1 Receipt of Report
- Report of SF medical product received by NMRA
  - Contact the source of the information
  - Assess the reliability of the source (see textbox)
  - Establish the facts
  - Assess the credibility of the information received (see textbox)
  - Obtain samples of the product and photographs showing batch number and expiry dates
  - NATIONAL FOCAL POINT SHOULD IMMEDIATELY SEARCH THE WHO GSMS DATABASE TO CHECK IF THE PRODUCT IS KNOWN

2 Establish Facts
- Is the suspected SF product available in hospitals, clinics, pharmacies, health centres?
- Is the product available in illegal markets, or through internet sites or smartphone applications?
- Have any adverse reactions been reported? Check with national PV centre.
- What quantities of suspected SF products have been discovered?
- Is there evidence that the suspected SF medical product is in recent circulation?
- Is the suspected SF product in wide circulation within your country, or neighbouring countries?
- Is this product in strong demand, or in short supply?
- Consult with stated manufacturer of the reported product (see textbox)

3 Assess Risk to public health
- Quarantine or seize any suspected medical product dependent on risk
- Ensure the product is stored securely and in compliance with storage conditions
- Ensure appropriate treatment is available to affected patients

4 Immediate Actions
- If product is suspected of causing adverse reactions, send directly to the lab
- Screen suspected SF product with handheld equipment or other field-testing equipment if available
- Secure up to 100 samples for testing, if not, as many samples from from same source as reported product as possible and store in controlled conditions
- Request sample from genuine manufacturer for comparison purposes
- Arrange for testing as a priority dependent on risk to public health

5 Field Screening / Lab analysis
- Establish a team of relevant regulatory specialists, appoint a lead person and invite relevant external stakeholders / experts
- Keep strict records of all meetings and all decisions that are made
- Focus on protecting the public health, mitigating risk posted by the product and investigating the origin
- Consider a recall of the medical product and associated communications and media messages
- Verify stocks / availability of genuine replacement product
- Consider an alert or public notice
- REPORT TO THE WHO GLOBAL SURVEILLANCE AND MONITORING SYSTEM FOR SUBSTANDARD AND FALSIFIED MEDICAL PRODUCTS
Supplementary Questions Textbox

**REMEMBER**, these incidents attract a lot of attention, unnecessary delays are difficult to explain, public health and the reputation of your organization may be at risk.

National Focal Points are strongly advised to conduct a search of the WHO database when dealing with a suspected SF medical product at the earliest opportunity. Irrespective of whether you receive a match with other products in the database you should report the suspected or confirmed medical product to WHO as soon as possible. Other Member States may be seeing the same product in circulation and your report will assist them. It should be remembered searches can yield matches with your product on a separate continent or in another region. This information can help you assess risk, manage and respond to your case more efficiently and effectively and in serious cases save lives.

**Assessing the Reliability of a Source**

- Anonymous information should be treated with caution
- Is the source a whistle blower or a current or ex-employee of a company that they are providing information about?
- What is the motivation for supplying the information?
- Is the source easily contactable?
- If contact details are supplied are they accurate (dialling codes, telephone numbers, email addresses, physical addresses)?
- Has information been received from the same source previously? If so, was the information accurate?
- Is the source willing to be contacted, met, or supply further information?

**Assessing the Credibility of the Information**

- Has any similar information been received from different sources?
- Are there any other sources that can corroborate the information provided?
- Are there any obvious inaccuracies in the information?

**Questions to Manufacturers?**

- Did you manufacture this product?
  - Does the product and packaging look genuine? – Photographs and samples will be provided if available
- Are the manufacturing / batch / expiry dates authentic?
  - If the batch number is genuine, where, and when was it distributed?
- Have you had falsified or substandard versions of this batch reported previously?
  - If so, when and where?
- Have you received any complaints about this batch?
  - If so, from whom, where, and when?
- Have you received any reports of unexpected adverse reactions relating to this product or batch?
  - Is so, when, where, numbers, and severity?
- Is there any other information we should be aware of?
APPENDIX II: Tool for Visual Inspection of Medicines
Source: World Health Professions Alliance

This tool is designed to help health professionals carry out a visual inspection of medicines for signs of falsification (counterfeiting) such as improper packaging, labelling, description of dosage, etc. All suspicious medicines with incorrect labels, missing information about the strength, dosage or expiration date should be reported to the appropriate authority. The term 'drug' has been replaced with 'medicine' and the term 'counterfeit' has been replace with 'falsified' from the original version.

1. Packaging

Any medicine should be packaged in a container, which can be anything from a glass bottle to a blister pack, to a tube of glass, plastic or metal. A folding carton bearing the label very often protects the container. Check the type of packaging and compare it to known containers for the same medicine from the same manufacturer. The packaging and labelling of pharmaceutical products is a very complex and expensive business. Thus, the process and the quality of packaging material are very difficult to falsify. This is why a thorough visual inspection could be an important screening step for medicines quality control. However, producers of falsified products are quick to copy special labelling and holograms.

<table>
<thead>
<tr>
<th>1.1 Container and closure</th>
<th>Yes</th>
<th>No</th>
<th>Other observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do the container and closure protect the medicine from the outside environment e.g. properly sealed?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do they assure that the medicine will meet the proper specifications throughout its shelf life?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Are the container and the closure appropriate for the medicine inside?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is the container safely sealed?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1.2 Label The information written on the label is very important. The information can be printed on a label adhered to the container, or printed directly onto the container itself, but all information must be legible and indelible.

<table>
<thead>
<tr>
<th>1.2.1 The trade name</th>
<th>Yes</th>
<th>No</th>
<th>Other observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is the trade name spelled correctly?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is the medicine (trade name) registered in the country by the NMRA (national regulatory authority)?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is the medicine legally sold in the country?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does the symbol ® follow the trade name?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>1.2.2 The active ingredient name (scientific name)</th>
<th>Yes</th>
<th>No</th>
<th>Other observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is the active ingredient name spelled correctly?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do the trade name and the active ingredient name correspond to the registered medicine?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>1.2.3 The manufacturer’s name and logo</th>
<th>Yes</th>
<th>No</th>
<th>Other observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are the manufacturer’s name and logo legible and correct?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does the logo or hologram (if applicable) look authentic?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does it change colour when viewed from different angles?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### 1.2.4 The manufacturer’s full address

All manufacturers are required by international law to print their complete address on the label. Many companies making substandard or falsified medicines do not have traceable address on the label.

<table>
<thead>
<tr>
<th>Is the manufacturer’s full address legible and correct?</th>
<th>Yes</th>
<th>No</th>
<th>Other observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has the company or its agent registered the medicine in the country?</td>
<td>Yes</td>
<td>No</td>
<td>Other observations</td>
</tr>
</tbody>
</table>

### 1.2.5 The medicine’s strength (mg/unit)

Is the strength – the amount of active ingredient per unit – clearly stated on the label?

### 1.2.6 The dosage form (e.g. tablet / capsule)

Is the dosage clearly indicated?

<table>
<thead>
<tr>
<th>Is the indicated medicine under this dosage form registered and authorized for sale in the country?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
</tr>
</tbody>
</table>

### 1.2.7 The number of units per container?

Does the number of tablets or capsules listed on the label match the number stated on the container?

### 1.2.8 The batch (or lot) number

Medicines under the same batch/lot number are expected to be equivalent. In a continuous process, a batch corresponds to a defined portion of the production, based on time or quantity. Medicines from the same batch number should have the same history of manufacturing, processing, packing, and coding. All medicine quality control testing should be based on batch/lot numbers.

<table>
<thead>
<tr>
<th>Does the numbering system on the package correspond to that of the producing company?</th>
<th>Yes</th>
<th>No</th>
<th>Other observations</th>
</tr>
</thead>
</table>

### 1.2.9 The date of manufacture and the expiry date

An expired medicine should not be sold under any circumstances.

<table>
<thead>
<tr>
<th>Are the manufacture and expiry dates clearly indicated on the label?</th>
<th>Yes</th>
<th>No</th>
<th>Other observations</th>
</tr>
</thead>
</table>

### 1.3 Leaflet or package insert

All product packages should contain a leaflet explaining dosage, the product content, the adverse effects, the medicine’s actions, and how the medicine should be taken. The only exceptions are where the packaging includes all the information that would otherwise be in the leaflet.

<table>
<thead>
<tr>
<th>Is the package insert printed on the same coloured or same quality paper as the original?</th>
<th>Yes</th>
<th>No</th>
<th>Other observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is the ink on the package insert or packaging smudge-proof?</td>
<td>Yes</td>
<td>No</td>
<td>Other observations</td>
</tr>
</tbody>
</table>
2. Physical characteristics of tablets/ capsules

All types of medicine can be and have been falsified from cough syrups to injections. As mentioned in Section 1, it is important to check the packaging of these products. Additionally, medicines in the form of tablets or capsules can be checked for signs of moisture, dirty marks, abrasion erosion, cracks, or any other adulteration.

<table>
<thead>
<tr>
<th>2.1 Uniformity of shape</th>
<th>Yes</th>
<th>No</th>
<th>Other observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are the tablets / capsules uniform in shape?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2.2 Uniformity of size</th>
<th>Yes</th>
<th>No</th>
<th>Other observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are the tablets / capsules uniform in size?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2.3 Uniformity of colour</th>
<th>Yes</th>
<th>No</th>
<th>Other observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are the tablets / capsules uniform in colour?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2.4 Uniformity of texture</th>
<th>Yes</th>
<th>No</th>
<th>Other observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablets can be film-coated, sugar-coated or enteric-coated</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do the tablets have a uniform coating?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is the base of the tablets fully covered?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Are the tablets uniformly polished, free of powder, and non-sticking?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2.5 Markings (scoring, letters, etc.)</th>
<th>Yes</th>
<th>No</th>
<th>Other observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are marking uniform and identical?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2.6 Breaks, Cracks and Splits</th>
<th>Yes</th>
<th>No</th>
<th>Other observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are the tablets / capsules free of breaks, cracks, splits or pinholes?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2.7 Embedded surface spots or contamination</th>
<th>Yes</th>
<th>No</th>
<th>Other observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are the tablets / capsules free of embedded surface spots and foreign particle contamination?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2.8 Presence of empty capsules in the case of a sample of capsules</th>
<th>Yes</th>
<th>No</th>
<th>Other observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is the sample examined free of empty capsules?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2.9 Smell</th>
<th>Yes</th>
<th>No</th>
<th>Other observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does the medicine smell the same as the original?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX III: WHO Tool - Identifying Substandard and Falsified Medical Products

IDENTIFYING SUSPECT SUBSTANDARD AND FALSIFIED MEDICAL PRODUCTS

Some substandard and falsified medical products are almost visually identical to the genuine product and very difficult to detect. The following signs should raise your suspicion.  
Please note that this guide is a non-exhaustive list

| THERAPEUTIC EFFECT | • Patients report that it is not working properly (unexpected lack of efficacy), or  
|                     | • Patients suffer unexpected adverse reaction(s) |
| OUTER (SECONDARY) PACKAGING | • Packaging is not in good condition, or  
|                         | • Manufacturers details are not clearly stated, or  
|                         | • Incorrect language, grammatical and spelling errors, or  
|                         | • Batch numbers and expiry dates appear altered |
| INNER (PRIMARY) PACKAGING | • Batch numbers, manufacturing and expiry dates on inner packaging (e.g. blister) are different to outer packaging, or  
|                         | • Patient information leaflet is in the wrong language |
| SUPPLY SOURCE | • Any suspicion on the source, price, or authenticity of accompanying documents, or  
|             | • Any suspicion on quantities available, for example products that are usually in short supply are suddenly available very regularly or in large quantities |
| OTHER FACTORS | • Product does not look, smell, taste and feel correct, or  
|               | • Packaging components are empty or separated  
|               | • Product was not properly stored |

IF IN DOUBT, VERIFY THE TO THE GLOBAL SURVEILLANCE AND MONITORING SYSTEM PORTAL AND REPORT PRODUCT OR CONTACT RAPIDALERT@WHO.INT

FOLLOW GUIDANCE PROVIDED IN THE AIDE-MEMOIRE ON HOW TO MANAGE AN INCIDENT OF AN SF MEDICAL PRODUCT.
Therapeutic Failure

- **Is there an unexpected lack of efficacy?** Often the product will not cause a toxic reaction, but will fail to treat the condition for which it was intended, with potentially devastating consequences. For example, a patient failing to respond to their anti-malarial will rarely consider that the cause of the problem may be their medicine.

- **Is there an unexpected adverse reaction?** Some substandard and falsified medical products do cause adverse reactions and sometimes fatalities. A patient may experience an unexpected or unusual worsening of their medical condition.

Outer (Secondary) Packaging and Inner (Primary) Packaging

- **Is the packaging in good condition?** The container should appropriately protect the medical product inside (e.g. properly sealed, airtight, etc.).

- **Are the manufacturer's details clearly stated and in correct language?** The manufacturer's details (name, logo, hologram, full address, registration number, etc.) should be correct and in the appropriate language for the market/country in which the product is distributed.

- **Are there any spelling or grammatical errors?** There should be no spelling or grammatical errors, particularly for the trade (brand) name and active ingredient(s).

- **Are the batch/lot numbers and manufacturing and expiry dates altered?** They should be clearly indicated, should not be possible to erase, be easily readable, and there should be no irregularity in the embossing, impressing or imprinting.

- **Is the dosage form or medicine strength clearly indicated on the label?** They should be the appropriate strength and dosage form for the medicine and be the same on all parts of the packaging.

- **Is the information the same on the inner and outer packaging?** This information should be the same on all parts of the packaging (with no signs of alteration and discrepancies).

- **Is there a patient information leaflet and is it in the correct language?** The information on the patient information leaflet should be clearly indicated and should match the information on other parts of the packaging and product container. There should be no irregularity in how it is printed and the quality of the colour, shape, texture, and size of paper (e.g. ink should not be smudged, paper is not too rough, etc.).

Source of Supply

- **Is there any suspicion of the source, price, quantities available, regularity of products that are usually in short supply or authenticity of accompanying documents?** Those engaged in the manufacture, distribution and supply of substandard and falsified medical products have shown they respond quickly to demand, thoroughly understanding the market and are fast to exploit opportunities. Most commonly, substandard and falsified medical products enter the legal supply chain at distribution level through hospitals, clinics, pharmacies and wholesalers, who have obtained medical products from unknown sources and intermediaries without checking their credentials or conducting any due diligence. For example, products whose price appears unusually low, or which are available in unusually large quantities should raise suspicions and further checks should be conducted.

Other Factors

- **Did the patient (or did you) notice that the medical product looks, tastes, smells or feels different?** Any irregularity in the uniformity of appearance (colour, shape, texture, size, clarity), flavour, and odour should raise suspicion. For example, the product is discoloured or degraded.

- **Are there any empty or separated packaging components (bottle caps, spoons, bottles, flat packs, capsules)?** Signs of empty or separated packaging components may indicate signs of smuggling or tampering.

- **Was the product properly stored?** Storage conditions (temperature, humidity, etc.) should be stated on the label and maintained. Signs of degradation may include leakage, discoloration, etc.
### APPENDIX IV: MQCSD List of Pharmaceutical Products with Accredited Tests

<table>
<thead>
<tr>
<th>No.</th>
<th>NAME OF PRODUCTS</th>
<th>SPECIFICATIONS</th>
<th>TESTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Acetaminophen Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 2 (UV); Assay (HPLC)</td>
</tr>
<tr>
<td></td>
<td>Paracetamol Tablets</td>
<td>BP</td>
<td>Dissolution: Apparatus 2 (UV); Assay (UV)</td>
</tr>
<tr>
<td>2</td>
<td>Aciclovir Tablets</td>
<td>BP</td>
<td>Dissolution: Apparatus 2 (UV); Assay (HPLC)</td>
</tr>
<tr>
<td></td>
<td>Acyclovir Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 2 (UV); Assay (HPLC)</td>
</tr>
<tr>
<td>3</td>
<td>Amlodipine Besylate Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 2 (UV); Assay (HPLC)</td>
</tr>
<tr>
<td></td>
<td>Amoxicillin Capsules</td>
<td>BP</td>
<td>Assay (HPLC)</td>
</tr>
<tr>
<td>4</td>
<td>Amoxicillin Capsules</td>
<td>USP</td>
<td>Dissolution: Apparatus 1 &amp; 2 (UV); Assay (HPLC); Uniformity of Content (HPLC)</td>
</tr>
<tr>
<td>5</td>
<td>Amoxicillin for Oral Suspension</td>
<td>BP &amp; USP</td>
<td>pH; Assay (HPLC)</td>
</tr>
<tr>
<td></td>
<td>Atenolol Tablets</td>
<td>BP</td>
<td>Assay (UV)</td>
</tr>
<tr>
<td></td>
<td>Atenolol Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 2 (HPLC); Uniformity of Content (HPLC); Assay (HPLC)</td>
</tr>
<tr>
<td>7</td>
<td>Bendroflumethiazide Tablets</td>
<td>BP</td>
<td>Assay (UV)</td>
</tr>
<tr>
<td></td>
<td>Bendroflumethiazide Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 2 (UV); Assay (HPLC)</td>
</tr>
<tr>
<td>8</td>
<td>Captopril Tablets</td>
<td>BP</td>
<td>Assay (HPLC)</td>
</tr>
<tr>
<td></td>
<td>Captopril Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 1 (UV); Assay (HPLC)</td>
</tr>
<tr>
<td>9</td>
<td>Carbamazepine Tablets</td>
<td>BP</td>
<td>Assay (HPLC)</td>
</tr>
<tr>
<td></td>
<td>Carbamazepine Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 2 (UV); Assay (HPLC)</td>
</tr>
<tr>
<td>10</td>
<td>Chlorpromazine Tablets</td>
<td>BP</td>
<td>Assay (UV)</td>
</tr>
<tr>
<td>11</td>
<td>Chlorpromazine Hydrochloride Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 1 (UV); Assay (HPLC)</td>
</tr>
<tr>
<td></td>
<td>Chlorpropamide Tablets</td>
<td>BP</td>
<td>Dissolution: Apparatus 1 (UV); Assay (HPLC)</td>
</tr>
<tr>
<td></td>
<td>Chlorpropamide Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 2 (UV); Assay (HPLC)</td>
</tr>
<tr>
<td>12</td>
<td>Chlortalidone Tablets</td>
<td>BP</td>
<td>Disintegration; Assay (UV)</td>
</tr>
<tr>
<td></td>
<td>Chlorthalidone Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 2 (UV); Assay (HPLC)</td>
</tr>
<tr>
<td>13</td>
<td>Ciprofloxacin Tablets</td>
<td>BP &amp; USP</td>
<td>Dissolution: Apparatus 2 (UV); Assay (HPLC)</td>
</tr>
<tr>
<td>14</td>
<td>Clotrimazole Cream</td>
<td>BP &amp; USP</td>
<td>Assay (HPLC)</td>
</tr>
<tr>
<td>15</td>
<td>Diazepam Tablets</td>
<td>BP</td>
<td>Assay (UV)</td>
</tr>
<tr>
<td></td>
<td>Diazepam Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 1 (UV); Assay (HPLC)</td>
</tr>
<tr>
<td>16</td>
<td>Diclofenac Tablets (Gastro-resistant)</td>
<td>BP</td>
<td>Assay (HPLC)</td>
</tr>
<tr>
<td>17</td>
<td>Enalapril Maleate Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 2 (HPLC); Uniformity of Content (HPLC); Assay (HPLC)</td>
</tr>
<tr>
<td>No.</td>
<td>NAME OF PRODUCTS</td>
<td>SPECIFICATIONS</td>
<td>TESTS</td>
</tr>
<tr>
<td>-----</td>
<td>----------------------------------</td>
<td>----------------</td>
<td>----------------------------------------------------------------------</td>
</tr>
<tr>
<td>18</td>
<td>Furosemide Tablets</td>
<td>BP</td>
<td>Dissolution: Apparatus 2 (UV); Assay (UV)</td>
</tr>
<tr>
<td></td>
<td>Furosemide Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 2 (UV); Assay (HPLC)</td>
</tr>
<tr>
<td>19</td>
<td>Glibenclamide Tablets</td>
<td>BP</td>
<td>Dissolution: Apparatus 2 (HPLC); Assay (HPLC)</td>
</tr>
<tr>
<td></td>
<td>Glyburide Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 1 &amp; 2 (HPLC); Assay (HPLC)</td>
</tr>
<tr>
<td>20</td>
<td>Ibuprofen Tablets</td>
<td>BP</td>
<td>Disintegration; Assay (HPLC)</td>
</tr>
<tr>
<td></td>
<td>Lamivudine Tablets</td>
<td>BP</td>
<td>Dissolution: Apparatus 2 (UV); Assay (HPLC)</td>
</tr>
<tr>
<td></td>
<td>Lamivudine Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 2 (UV &amp; HPLC); Assay (HPLC)</td>
</tr>
<tr>
<td>22</td>
<td>Levofoxacin Oral Solution</td>
<td>USP</td>
<td>pH; Assay (HPLC)</td>
</tr>
<tr>
<td>23</td>
<td>Levofoxacin Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 1 &amp; 2 (UV); Assay (HPLC)</td>
</tr>
<tr>
<td>24</td>
<td>Levothyroxine Tablets</td>
<td>BP</td>
<td>Dissolution: Apparatus 2 (HPLC); Uniformity of Content (HPLC); Assay (HPLC)</td>
</tr>
<tr>
<td></td>
<td>Levothyroxine Sodium Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 2 (HPLC); Uniformity of Content (HPLC); Assay (HPLC)</td>
</tr>
<tr>
<td>25</td>
<td>Lisinopril Tablets</td>
<td>BP</td>
<td>Dissolution: Apparatus 2 (HPLC); Assay (HPLC)</td>
</tr>
<tr>
<td></td>
<td>Lisinopril Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 2 (HPLC); Uniformity of Content (HPLC); Assay (HPLC)</td>
</tr>
<tr>
<td>26</td>
<td>Loratadine Tablets</td>
<td>BP</td>
<td>Disintegration; Assay (HPLC)</td>
</tr>
<tr>
<td></td>
<td>Loratadine Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 2 (UV); Assay (HPLC)</td>
</tr>
<tr>
<td>27</td>
<td>Loratadine Oral Solution</td>
<td>USP</td>
<td>pH; Assay (HPLC)</td>
</tr>
<tr>
<td>28</td>
<td>Losartan Potassium Tablets</td>
<td>BP</td>
<td>Dissolution: Apparatus 2 (UV); Assay (HPLC)</td>
</tr>
<tr>
<td></td>
<td>Losartan Potassium Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 1 &amp; 2 (UV &amp; HPLC); Uniformity of Content (HPLC); Assay (HPLC)</td>
</tr>
<tr>
<td>29</td>
<td>Metformin Tablets</td>
<td>BP</td>
<td>Dissolution: Apparatus 1 (UV); Assay (UV)</td>
</tr>
<tr>
<td></td>
<td>Metformin Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 1 &amp; 2 (UV); Assay (UV)</td>
</tr>
<tr>
<td>30</td>
<td>Metronidazole</td>
<td>USP</td>
<td>Dissolution: Apparatus 1 (UV); Uniformity of Content (UV); Assay (HPLC)</td>
</tr>
<tr>
<td>31</td>
<td>Mycophenolate Mofetil Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 2 (UV); Assay (HPLC)</td>
</tr>
<tr>
<td>32</td>
<td>Omeprazole Delayed-Release Capsules</td>
<td>USP</td>
<td>Dissolution: Apparatus 2 (HPLC); Assay (HPLC)</td>
</tr>
<tr>
<td>33</td>
<td>Prednisolone Tablets</td>
<td>BP</td>
<td>Dissolution: Apparatus 2 (HPLC); Uniformity of Content (HPLC); Assay (HPLC)</td>
</tr>
<tr>
<td></td>
<td>Prednisolone Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 2 (UV); Uniformity of Content (HPLC); Assay (HPLC)</td>
</tr>
<tr>
<td>34</td>
<td>Prednisone Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 2 (UV); Uniformity of Content (HPLC); Assay (HPLC)</td>
</tr>
<tr>
<td>35</td>
<td>Propranolol Tablets</td>
<td>BP</td>
<td>Disintegration; Assay (UV)</td>
</tr>
<tr>
<td>No.</td>
<td>NAME OF PRODUCTS</td>
<td>SPECIFICATIONS</td>
<td>TESTS</td>
</tr>
<tr>
<td>-----</td>
<td>-----------------</td>
<td>----------------</td>
<td>-------</td>
</tr>
<tr>
<td>35</td>
<td>Propranolol Hydrochloride Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 1 (UV); Uniformity of Content (UV); Assay (HPLC)</td>
</tr>
<tr>
<td>36</td>
<td>Pyrazinamide Tablets</td>
<td>BP</td>
<td>Disintegration; Assay (UV)</td>
</tr>
<tr>
<td></td>
<td>Pyrazinamide Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 2 (UV); Assay (HPLC)</td>
</tr>
<tr>
<td>37</td>
<td>Ramipril Capsules</td>
<td>BP</td>
<td>Dissolution: Apparatus 2 (HPLC); Uniformity of Content (HPLC); Assay (HPLC)</td>
</tr>
<tr>
<td></td>
<td>Ramipril Capsules</td>
<td>USP</td>
<td>Dissolution: Apparatus 2 (HPLC); Uniformity of Content (HPLC); Assay (HPLC)</td>
</tr>
<tr>
<td>38</td>
<td>Ranitidine Tablets</td>
<td>BP</td>
<td>Disintegration; Assay (HPLC)</td>
</tr>
<tr>
<td></td>
<td>Ranitidine Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 2 (UV); Assay (HPLC)</td>
</tr>
<tr>
<td>39</td>
<td>Risperidone Tablets</td>
<td>BP &amp; USP</td>
<td>Dissolution: Apparatus 2 (HPLC); Uniformity of Content (HPLC); Assay (HPLC)</td>
</tr>
<tr>
<td>40</td>
<td>Terbinafine Tablets</td>
<td>BP &amp; USP</td>
<td>Dissolution: Apparatus 2 (UV); Assay (HPLC)</td>
</tr>
<tr>
<td>41</td>
<td>Warfarin Tablets</td>
<td>BP</td>
<td>Dissolution: Apparatus 1 (UV); Uniformity of Content (HPLC); Assay (HPLC)</td>
</tr>
<tr>
<td></td>
<td>Warfarin Sodium Tablets</td>
<td>USP</td>
<td>Dissolution: Apparatus 2 (HPLC); Uniformity of Content (HPLC); Assay (HPLC)</td>
</tr>
</tbody>
</table>
## APPENDIX V: Sample Collection Form

<table>
<thead>
<tr>
<th>Survey Title</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Area / Region / Country</td>
<td></td>
</tr>
<tr>
<td>Sampling Location / Site</td>
<td></td>
</tr>
<tr>
<td>Address</td>
<td></td>
</tr>
<tr>
<td>Sample Code</td>
<td></td>
</tr>
<tr>
<td>Date of Sampling</td>
<td></td>
</tr>
<tr>
<td>Name(s) of Samplers</td>
<td>1.</td>
</tr>
<tr>
<td></td>
<td>2.</td>
</tr>
<tr>
<td>Product Name of sample</td>
<td></td>
</tr>
<tr>
<td>Name of APIs (INN) and strength</td>
<td></td>
</tr>
<tr>
<td>Dosage form</td>
<td>Package Size:</td>
</tr>
<tr>
<td>Batch / Lot Number</td>
<td>Expiry Date:</td>
</tr>
<tr>
<td>Date of Manufacture</td>
<td></td>
</tr>
<tr>
<td>Name and Address of Manufacturer</td>
<td></td>
</tr>
<tr>
<td>Date received at location</td>
<td></td>
</tr>
<tr>
<td>Quantity collected</td>
<td></td>
</tr>
<tr>
<td>Brief physical description / Appearance of sample</td>
<td></td>
</tr>
<tr>
<td>Temperature and Humidity</td>
<td>Controlled conditions? Yes No</td>
</tr>
<tr>
<td></td>
<td>Comments on suitability of premises, abnormalities, or observations</td>
</tr>
<tr>
<td>Signatures of Samplers</td>
<td>1.</td>
</tr>
<tr>
<td></td>
<td>2.</td>
</tr>
</tbody>
</table>

**Key:** API – active pharmaceutical ingredient, INN – International Nonproprietary Name
REFERENCES


