UNITED REPUBLIC OF TANZANIA
MINISTRY OF HEALTH

TANZANIA FOOD AND DRUGS AUTHORITY

INSPECTOR'S HANDBOOK

Second Edition

April 2005

The official signed copy of this handbook is retained at the Office of the Tanzania Food and Drugs Authority.

Contents

FOREWORD

Drugs are decisive tools of any health care delivery system. Consequently, one objective of the national drug policy is assurance of the quality, safety, and efficacy of the drugs circulating on the Tanzanian market. An essential part of any medicine control system is the provision of an inspection body with the responsibility and authority to inspect some or all of the activities involved in research, development, manufacture, control, distribution, and supply of medicines. Qualified and experienced drug inspectors constitute an indispensable component of the inspection system.

Drug inspectors serve as the eyes and ears of the drug control authority and are on the front lines in maintaining the identity, quality, purity, and strength of drugs manufactured and marketed in any country. In this respect, drug inspectors have an important role in protecting consumers. Succinctly, the inspector's job is law enforcement. A drug inspector is empowered by the law, at all reasonable times, to enter any premises that is on the register or any premises in which he/she has reasonable cause to suspect that the law has been or is about to be contravened. The powers of drug inspectors are well stipulated in the 2003 Tanzania Food, Drugs and Cosmetics Act.

Inspectors should perform their duties according to the guidelines. This handbook is part of the attempt to harmonise the inspection techniques and to draw attention to the details that the Tanzania Food and Drugs Authority feels are important. This handbook is intended to serve as quick reference material for drug inspectors to use in the course of their inspection work.

Director-General
TANZANIA FOOD AND DRUGS AUTHORITY

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The TFDA also appreciates the individual efforts of those who have worked tirelessly toward achieving the present format of this handbook. Our profound thanks go to the MSH/SEAM Quality Assurance Program team: Dr. T. Layloff, Dr. P. Risha, and Mr. W. Mfuko. We would also like to extend our appreciation to TFDA officers for the time they have spent preparing this handbook. Special thanks go to Ms. O. Kowero, Acting Director of Inspections and Surveillance; Mr. E. Mosha, Chief Drug Inspector; and Ms. Z. Msuya, TFDA Quality Assurance Program Coordinator. We greatly appreciate the efforts made by TFDA inspectors Ms. L. Mshana, Ms. M. Hajji, Ms. D. Simon, Mr. E. Nyeura, and Mr. E. Aaron during the preparatory phase of this work.

We also appreciate the dedication of the inspectors who participated in the first training using the first edition of this handbook and who field-tested the standard operating procedures and recommended improvements to make this handbook more user-friendly. Mr. E. Mauga of the School of Allied Health Sciences, Muhimbili University College of Health Sciences (MUCHS), and Dr. O. Ngassapa and Dr. M. Chambuso, both members of the School of Pharmacy, MUCHS, are acknowledged for the time they spent during the training of the inspectors on inspection techniques and the German Pharma Health Fund Minilab testing.

ACRONYMS

AWB	airway bill
CC	column chromatography
CCC	counter current chromatography
COA	Certificate of Analysis
CRF	Clean Report of Findings
DQCL	Drug Quality Control Laboratory
FCVR	Final Classification and Valuation Report
FEFO	first expiring, first out
FOB	free on board
GLC	gas-liquid chromatography
HPLC	high-performance liquid chromatography
IC	Import Certificate
IDF	Import Declaration Form (TRA document issued for clearing consignments with a value of US$5,000 or less)
OTC	over the counter
PC	paper chromatography
PI	Pro Forma Invoice
POE	port of entry
SOP	standard operating procedure
SP	sulfadoxine-pyrimethamine
SPD	Surveillance Programme Document
SRF	Sample Receipt Form
TFDA	Tanzania Food and Drugs Authority
TLC	thin-layer chromatography
TRA	Tanzania Revenue Authority
TRA/C&E	Tanzania Revenue Authority/Customs and Excise Department

DEFINITIONS

A break in a capsule	is a fracture in the surface of the capsule.
A break in a tablet	is the separation or dislodging of more than 10 percent of the tablet.
Caking in suspensions	is the settling of the solid material in a suspension to the bottom; the cake does not easily redisperse on shaking.
Capping or cavitations of tablets	is the separation (or tendency toward separation) of a portion of the upper or lower surface of the tablet.
Capsule shapes	bulletlike conventional elliptical (oval) oblong round tapered ends various special shapes
Capsule types	• hard gelatin shell that consists of two pieces: a base containing the medicine and a cap covering the base • soft gelatin shell consisting of two flexible pieces formed into a body that is permanently sealed and that may contain a liquid, powder, or semisolid.
Chain of custody	is the record of individuals who have accessed sample material from the time of collection by an inspector until its ultimate destruction. Both the record and the sample, from its time of collection to the time of its destruction, must be kept safely (under key and lock) and under systematic control.
Certificate of Analysis	is a document supplied by the manufacturer summarising the physical and analytical data for a particular lot or batch of drug product; is the basis for the product batch or lot being released for sale.
Chipping	is removal of parts of the tablet, usually at the edges; caused by low friability.

Confiscate	is to officially take away from a vendor or importer and to assume custody of a drug consignment stocked on the premises or at the port of entry. The intention is to stop the drugs' distribution to the public. Usually done for drugs shown to be counterfeit or of substandard quality or associated with unexpected illness or death.
Consignment or "R" number	is a consignment tracking reference number assigned by the Tanzania Revenue Authority. "R" stands for "reference." This number, together with the date, distinctively identifies an imported consignment.
Detain	is to perform the following actions: 1. Write "DETAIN" in the space provided in the Port of Entry Consignment Inspection Form. 2. Stop the inspection, complete the Rejection/Detention Form, and inform the Tanzania Revenue Authority/Customs and Excise Department of the rejection or detention. 3. Give a copy of the form to the Tanzania Revenue Authority and the customer. 4. Refer the importer/consignee to the TFDA. 5. Upon resolution of detention issues by written instructions from the TFDA, continue the inspection from where it stopped.
Detention	is the retention of a consignment pending resolution of outstanding issues by the TFDA. However, if the issues are not resolved to the satisfaction of the TFDA, detention status, upon written instructions from the TFDA, is converted to rejection.
Final Classification and Valuation Report	is prepared at the exporting country port by COTECNA, which is the third-party contractor to the Tanzania Revenue Authority/Customs and Excise Department. The Final Classification and Valuation Report, a Customs and Excise Department document, confirms that the imported goods have the correct quality, quantity, and value.
First expiring, first out	is a practice intended to keep the product inventory in good rotation to prevent pharmaceuticals and supplies from expiring on the shelf.
GPHF Minilab	stands for German Pharma Health Fund Minilab, a pharmaceutical product testing kit that has materials for colour reaction, thin-layer chromatography, and disintegration testing of essential drugs.

Immediate container	is a type of packaging such as a tin or a bottle that is in direct contact with the medicine; also referred to as the "primary container."
Import Certificate	is a document issued by the TFDA authorising the importation of approved drugs into the country.
Liquid or semisolid dosage forms	can be a clear liquid, a suspension, or a dry powder for a suspension that must be reconstituted as directed on the manufacturer's label before use.
Percent (%) of remaining shelf life	This value is equal to: $\frac{\text{(Expiry date – Date on receipt at port of entry)}}{\text{(Expiry date – Manufacturing date)}} \times 100$ Or: $\frac{\text{(Remaining shelf life on arrival)}}{\text{(Shelf life of the product)}} \times 100$
Port of entry name	is the name of an authorised place of entry for drug consignments; this name must be filled in on the Port of Entry Consignment Inspection Form.
Pro Forma Invoice	is presented to the TFDA for approval before a shipment can enter Tanzania. A properly endorsed Pro Forma Invoice has two signatures from TFDA officials and the TFDA stamp. The signatures and the stamp indicate that the exporter and consignee are both properly licensed and that the drug manufacturer, product, and dosage forms are in compliance with TFDA requirements.
Quarantine	is the retention of a consignment, not allowing its use until further tests are performed to ascertain its quality.
Sample Receipt Form	is a document drug inspectors must complete for every sample of a batch of drug product collected.
Secondary container	is a type of packaging that holds a number of immediate or primary containers.
Splitting of a tablet	describes the partial or complete separation of the top or bottom crowns of a tablet from the main body.
Surveillance Programme Document	defines which pharmaceutical products are to be examined, collected, and tested.

Tablet types	buccal hypodermic impregnated (including delayed-action, repeat-action, prolonged-action, and sustained-action tablets) ophthalmic oral pellet solution sublingual vaginal

PART I

Chapter 1. Introduction to Drug Inspection

This chapter covers what inspection is, what needs to be inspected, the different types of inspection, the do's and don'ts of inspectors, and what is expected of inspectors. It also includes guidelines for conduct and safety. It is important for inspectors to read this chapter, especially during the preparatory phase of inspections.

What Is Inspection?

To "inspect" is "to look closely at something, especially to check that everything is in good order." Inspection is, therefore, the act of looking closely at something to ensure that it meets certain prescribed or known standards and specifications.

What, then, is drug inspection? Based on the definition of "inspection," drug inspection is the act of examining or looking closely at all the attributes of the drugs and the condition of all the facilities that deal with drugs.

What is the overall objective of drug inspection? To ensure that drugs and related supplies, either locally manufactured or imported from outside the country, meet set standards of quality.

Why do we want to achieve this objective? We want, first and foremost, to ensure the safety of the patients and members of the public. How do we ensure the safety of patients and the public? Safety of drugs can be assured by enforcing drug laws and regulations governing compounding, distribution, importation, exportation, storage, and use of drugs.

What Needs to Be Inspected?

To ensure the quality of drugs entering or circulating in the Tanzanian market, the following establishments associated with drug supply and the distribution chain should be inspected regularly:

- Ports of entry (POEs)
- Pharmacies, Duka la Dawa Muhimu, and Duka la Dawa Baridi (both established and new ones, before they are licensed)
- Wholesalers (both established and new ones before they are licensed)
- Manufacturing facilities (both established and new ones before they are licensed)

Types of Inspections

There are five types of inspections:

- Routine
- Concise
- Follow-up
- Special
- Investigative

Routine Inspection

Routine inspections are generally intended for a new establishment or for an establishment that has applied for a permit to extend its scope of operations, made important changes in its key personnel, moved to a new premises, or has not been inspected in a long time. The inspection should be announced except when an inspection has not been conducted in a long time; in these cases, when unannounced inspections are the norm.

Concise Inspection

Concise inspections are generally for establishments that have previously been inspected. These inspections are done with a view to assessing standards of good pharmacy practice, and the outcome helps in the proper assessment of the establishment. Concise inspections can be announced or unannounced.

Follow-Up Inspection

Follow-up inspections are normally carried out to ensure that corrective measures have been undertaken following advice and notice given during a previous inspection. If a time limit was given for applying the corrective measures, the inspection should be unannounced.

Special Inspection

Special inspections are used to assess the performance of a new establishment whose scope of operations was previously unknown. The inspection should be unannounced.

Investigative Inspection

Investigative inspections are undertaken to deal with specific complaints received about lapses or noncompliance with standards of professional practice. The inspection should be unannounced.

Do's & Don'ts for Inspectors

- Exercise confidentiality: do not reveal to a third party findings/observations regarding your work.
- Make accurate reports of the facts observed.
- Be courteous and demonstrate poise and competence in your work.
- Refrain from expressing personal views; such remarks or opinions may be interpreted as official.
- Do not lose your temper when abused or accused. Always stay calm.
- Be careful not to overlook any correspondence, record, accounts book, chit, rough book, or other relevant papers that may prove to be material evidence in determining the conduct, transactions, circumstances, and so on of the establishment being inspected.
- Do not fail to record all items seized. Full details and descriptions of the incriminating articles or circumstances for which a charge will be opened (in case of intention to institute legal charges) should be recorded with witnesses present, and signatures of responsible persons should be obtained on the seizure document.

What Is Expected of a Drug Inspector?

- Contact the person in charge of the establishment by approaching him or her in a dignified, authoritative, and cordial manner. Avoid being arrogant.
- Present credentials (e.g., your identity card) and explain the purpose of your visit.
- Use diplomacy, tact, and persuasiveness to acquire the necessary information and all necessary inspection details. To achieve this, use the appropriate standard operating procedures (SOPs) for the particular type of inspection and fill in the respective inspection form.
- In case of refusal to undergo inspection, explain that refusing is a criminal offence and courteously discuss the matter with the owner or responsible person on the premises.
- Make suggestions for minor corrections to be made as you perform the inspection. Upon completion of inspection, discuss the findings with the owner or person in charge. Adopt a courteous attitude in calling attention to the practices or conditions observed at the time of inspection.
- If any samples have been taken for testing, furnish a receipt for these samples to the person from whom samples are taken.

At the port of entry and during postmarketing surveillance, follow the appropriate SOPs for:

- Inspection of Pharmaceutical Consignments at POEs (SOP No. TFDAINS 001)
- Physical Examination Procedures for Pharmaceutical Products (SOP No. TFDAINS 002)
- Suspicious Sample Surveillance Programme (SOP No. Surveillance Program Document [SPD] 02-00)
- Drug Quality Surveillance Programme: Antimalarials (SOP No. SPD 02-01), Antibiotics (SOP No. SPD 03-01), and Antiretrovirals (SOP No. SPD 05-01)
- Postmarketing Surveillance Programme: Dispensing Outlets Inspection (SOP No. TFDAINS 003)
- Chain of Custody, Packing, and Shipping Procedures (SOP No. TFDAINS 004)

At all times when conducting inspection activities, adhere to the code of conduct for inspectors as outlined below.

Code of Ethics and Conduct for Inspectors

Core Values

1. The TFDA inspector shall strive to achieve the highest ethical standards for conduct that he/she is capable of.

2. The TFDA inspector shall uphold the honour and dignity of his/her profession and avoid association with any enterprise of questionable character or apparent conflict of interest.

3. The TFDA inspector shall protect and promote the interests of the client to the best of his/her ability and knowledge, recognising that the client has placed its trust and confidence in the TFDA.

4. The TFDA inspector shall always endeavour to maintain and increase his/her level of knowledge regarding new developments in the field.

5. The TFDA inspector shall conduct his/her business in a manner that will ensure that he/she is independent from outside influence and interest, which would compromise his/her ability to render a fair and impartial opinion regarding any activity conducted.

6. The TFDA inspector shall promptly disclose to the client any interest in any other business that may affect the client or the quality or result of his/her work or remediation.

7. The TFDA inspector shall not knowingly use his/her position or the remediation process to obtain work in another field.

8. The TFDA inspector shall make every effort to uphold, maintain, and improve the professional practice, integrity, and reputation of TFDA technical experts and the institution as a whole.

General Obligations

1. The TFDA inspector shall put forth an honest effort to follow established procedures in discharging his/her duties and in making decisions.

2. The TFDA inspector shall not solicit or accept gifts or any other item of monetary value from any individual/organisation/company/entity doing business with or carrying out activities regulated by the TFDA or whose interest may be substantially affected by the performance or nonperformance of the inspector's duties.

3. The TFDA inspector shall not participate in any matter with an outside individual/organisation/company/entity that will substantially affect his/her financial interest, performance, or efficiency.

4. The TFDA inspector shall not use the nonpublic information gained in the course of discharging their duties or from their day-to-day duties for their personal gain, nor allow the improper use of such information to further their private interests.

5. The TFDA inspector shall not, without prior approval by the TFDA, engage in outside employment or activities and shall not seek or negotiate for employment that will directly conflict with the duties/interests of the TFDA.

6. The TFDA inspector shall act impartially and not give preferential treatment to any individual/organisation/company/entity.

7. The TFDA inspector shall conserve TFDA property and shall not use it for private gain or any activity that is not authorised.

8. The TFDA inspector shall disclose fraud, abuse of power, or corruption, including the appearance of such, to the TFDA.

9. The TFDA inspector shall endeavour to avoid any actions that create the appearance that they are violating the law or ethical standards or not acting impartially, as determined by the perspective of a reasonable person with knowledge of the relevant facts.

10. The TFDA inspector shall be required to adhere to the established rules, regulations, and standard operating procedures in executing his/her functions.

11. It should be noted that failure to comply with the established rules, regulations, and standard operating procedures is an offence that shall warrant disciplinary action.

Guidelines for the Security and Safety of Inspectors

Law enforcement is the mainstay of the work of a TFDA drug inspector. The inspector has the duty to protect public health by ensuring that all regulated products, including medicinal products, in the market comply with the required standards. This compliance is achieved by ensuring that all products circulating in the market have market authorisation and that the premises where these medicines are dispensed are operated according to the prescribed rules and regulations. An inspector, in addition to being a guardian of public health in issues related to medicines, is expected to discharge his/her duties diligently and professionally. The role of the inspector is to help ensure the integrity of the market and create a fair business environment where conscientious players can compete. It should be noted that the marketplace generally falls to the lowest level of competition; unless law enforcement keeps the market fair and competitive, anarchy will rule the market and consumers will suffer.

The work of drug inspectors as law enforcers is certainly associated with risks to their safety.[1] This risk is understandable because in the process of discharging their duties, inspectors frequently interfere with illegal and unscrupulous commercial interests. In many instances, the inspection activities cause financial losses to proprietors. In some cases, the inspector may encounter unscrupulous individuals whose business may have thrived in the unregulated environment and who may resort to any means to maintain their illegal business dealings. Problems of security for inspectors cannot be entirely eliminated, but the risks to the inspector can be reduced if inspectors adhere to the following guidelines:

1. Upon a new appointment or transfer to a new station, make sure that you are introduced and that you have an introductory letter from the TFDA. Introduce yourself and present your credentials and letter to the regional authorities, including the Regional Administrative Secretary, Regional Medical Officer, Regional/District Police Commander, Regional Tanzania Revenue Authority (TRA) Manager, and so on. Explain to them what your duties and responsibilities as a drug inspector are. By doing so, you create a politically and technically conducive work environment for executing your duties with support from other state entities and stakeholders.

2. Whenever you have inspection work to do, it is good practice and safer not to do it alone. (It is easier to threaten an individual than a group of officials.) To meet this requirement, involve the relevant district or regional officers (e.g., pharmacists, health officers, veterinary officers, militia or police officers) whenever necessary.

3. Always perform inspections in a courteous but firm manner. Follow the SOPs. Inform the other members of the inspection team and the owner of what is expected and of any deficiencies identified during the inspection.

4. Whenever there is a threat to your life (communicated verbally, in writing, or through a third person), inform the police and the Regional Medical Officer immediately. The Chief Drug Inspector should be apprised of this situation by telephone and in writing immediately.

[1] Some of the risks faced by inspectors in the course of executing their duties include but are not limited to physical assault leading to bodily injuries, permanent disability, or death; restrictions in their freedom to perform their duties; and threats.

5. If a threat has been issued, be careful with whatever you do, especially after office hours. Avoid situations that would put your life in jeopardy. Don’t let people know about your travel plans. If possible, do not drive your car alone and be careful where you take your meals. The risk of intentional food or drink poisoning cannot be overlooked when threats have been made against you.

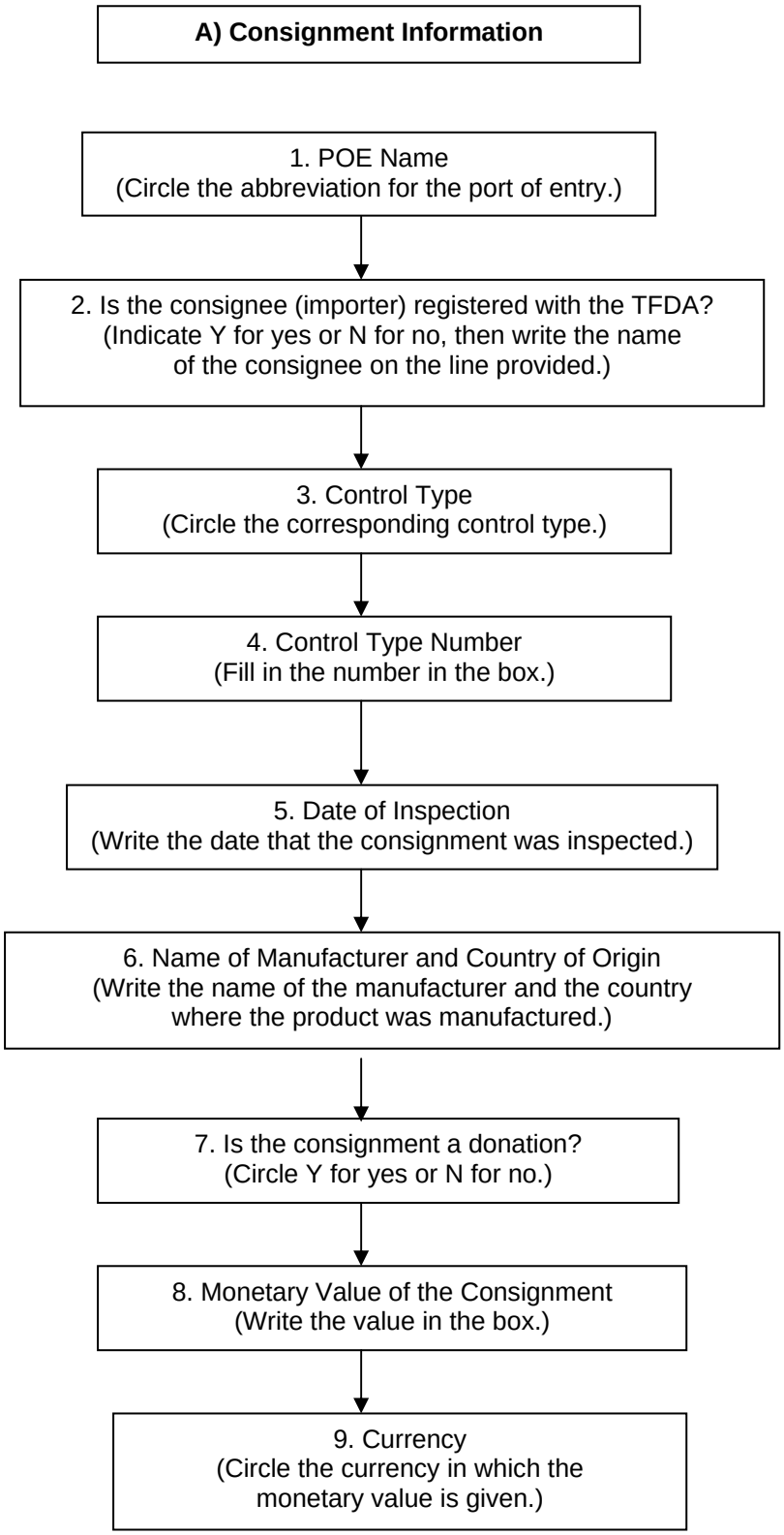
If you uncover any criminal violations in the course of your work, immediately involve the police in the matter, as they are trained and equipped to deal with criminal investigations.

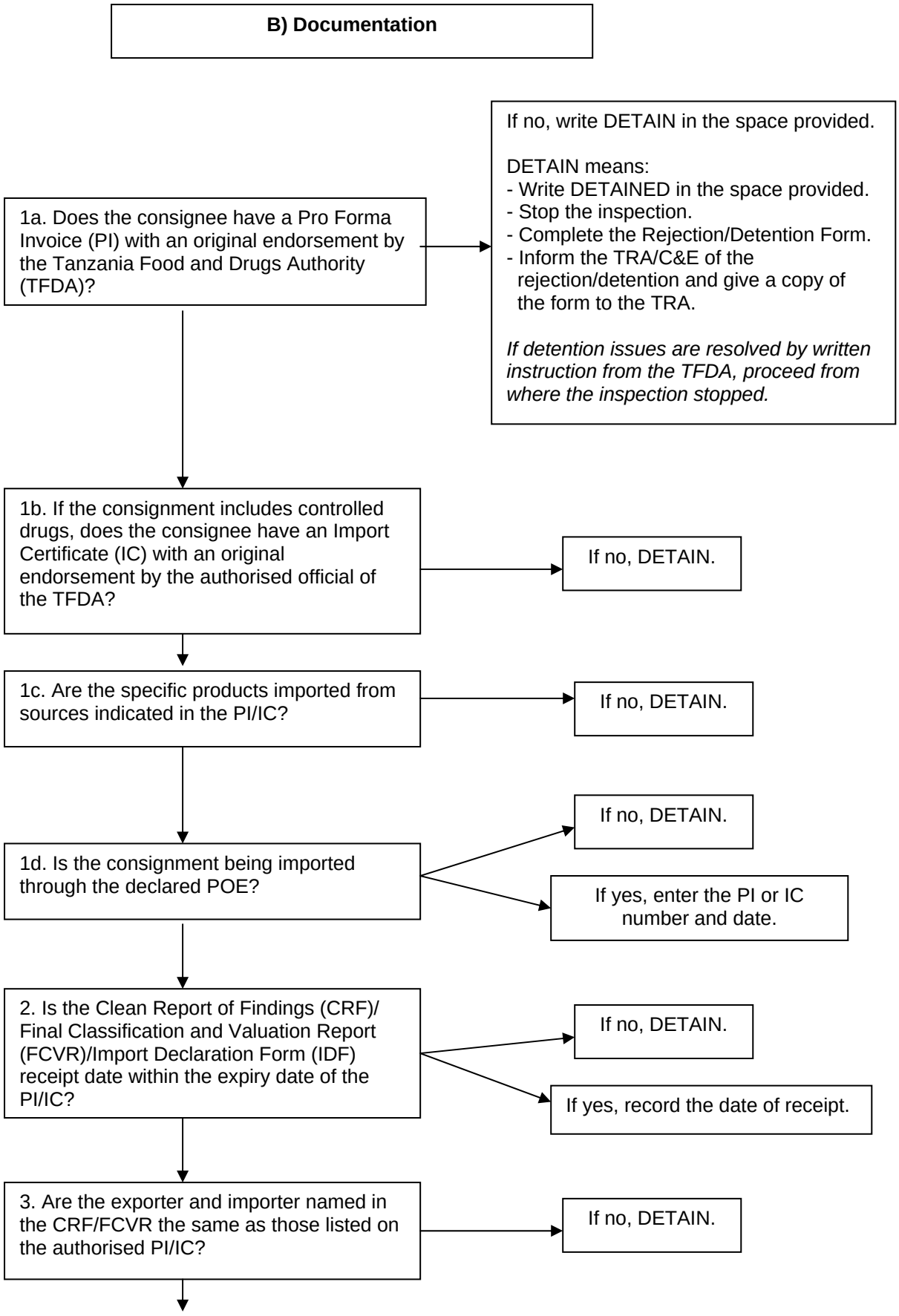
Chapter 2. Ports of Entry Consignment Inspection

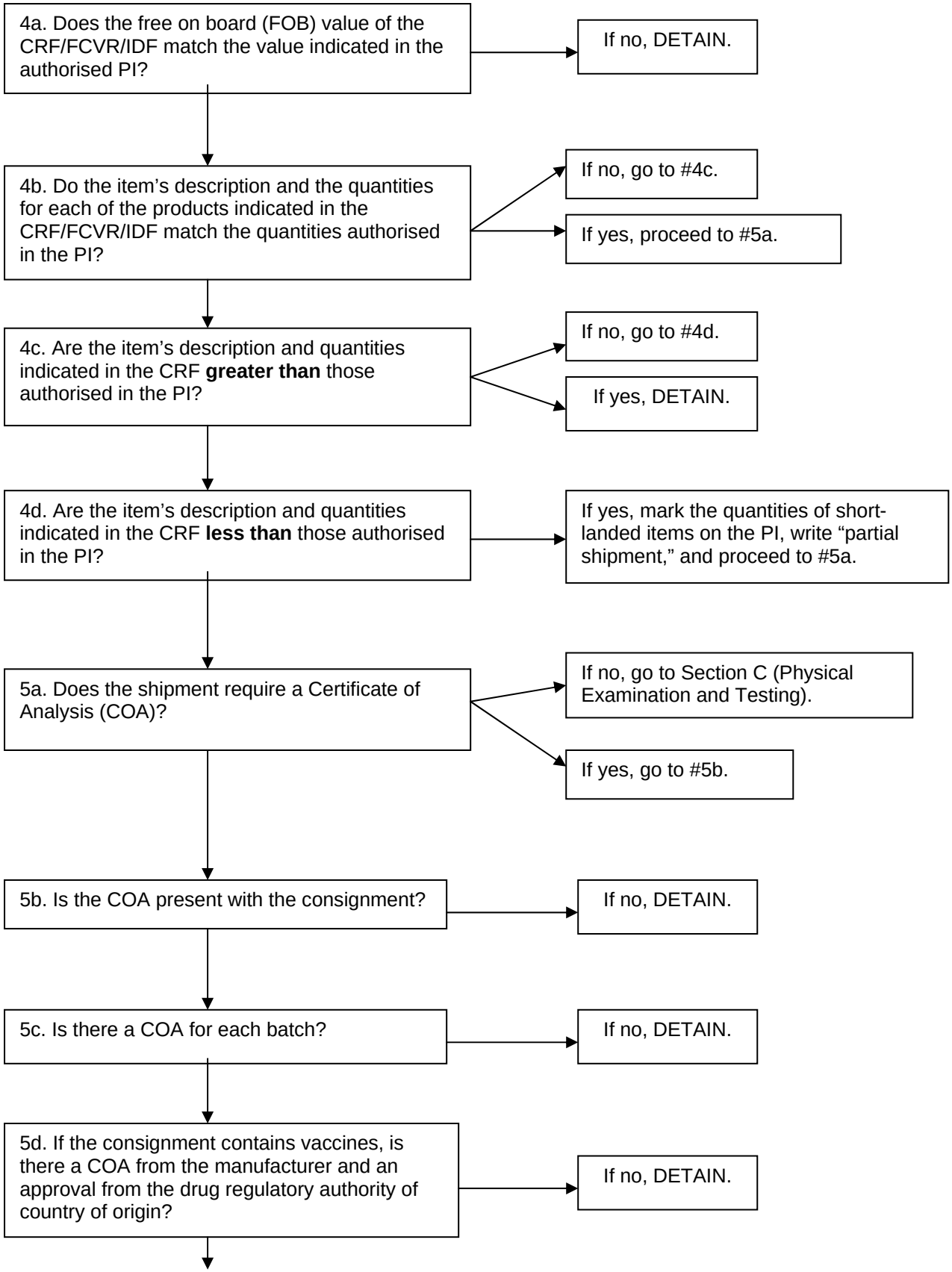
This chapter describes the procedures used by drug inspectors at ports of entry. The standard operating procedure for Inspection of Pharmaceutical Consignments at Ports of Entry and the SOP for Physical Examination Procedures for Pharmaceutical Products are included in this chapter, as well as the forms to be used for those SOPs.

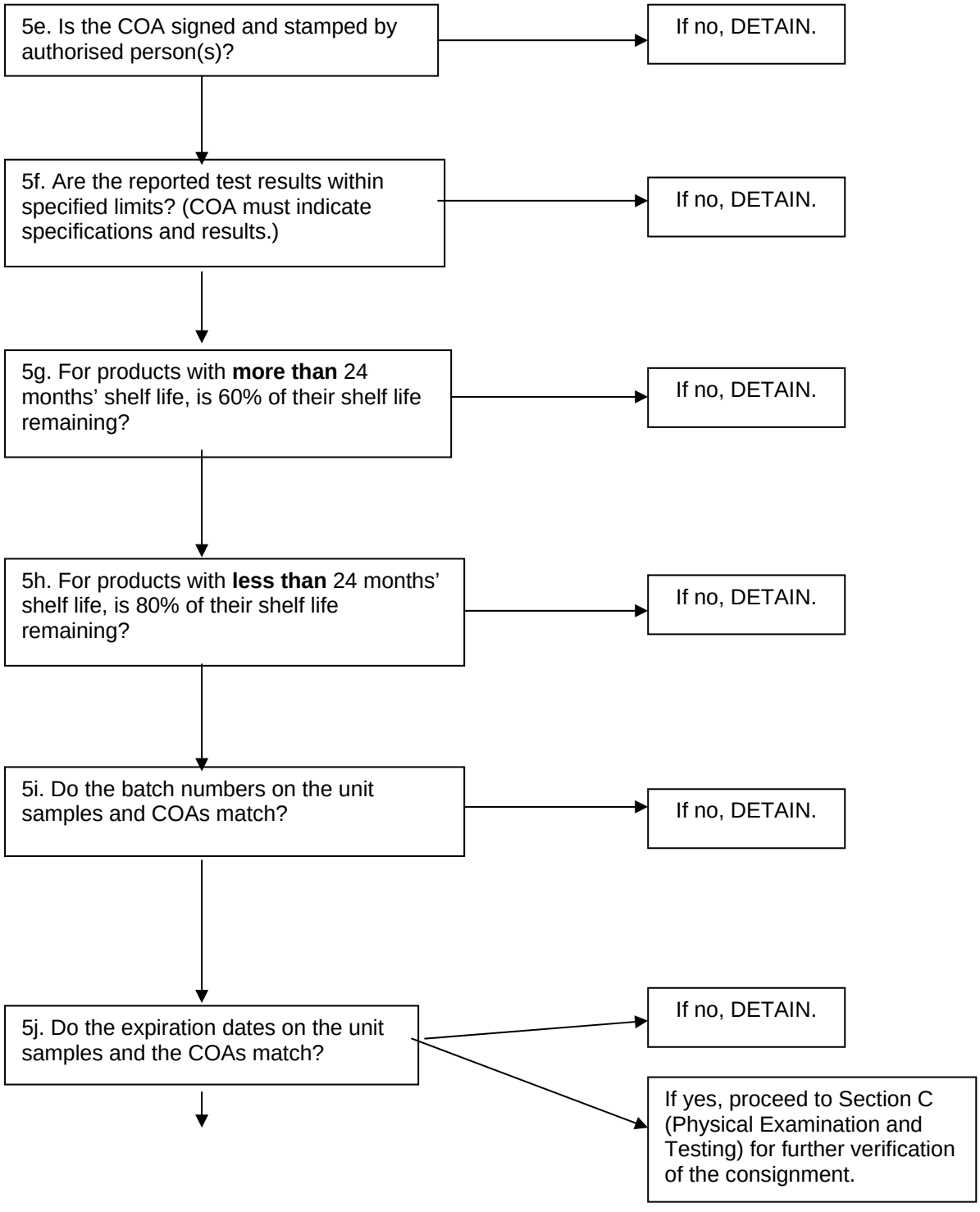
In addition, both the flowchart on the following pages and the diagram presented in the annex summarise step-by-step the actions and decisions that inspectors at the POE must adhere to when inspecting consignments containing human medicines, medical supplies and equipment, pharmaceutical raw materials, vaccines, or veterinary medicines entering the country.

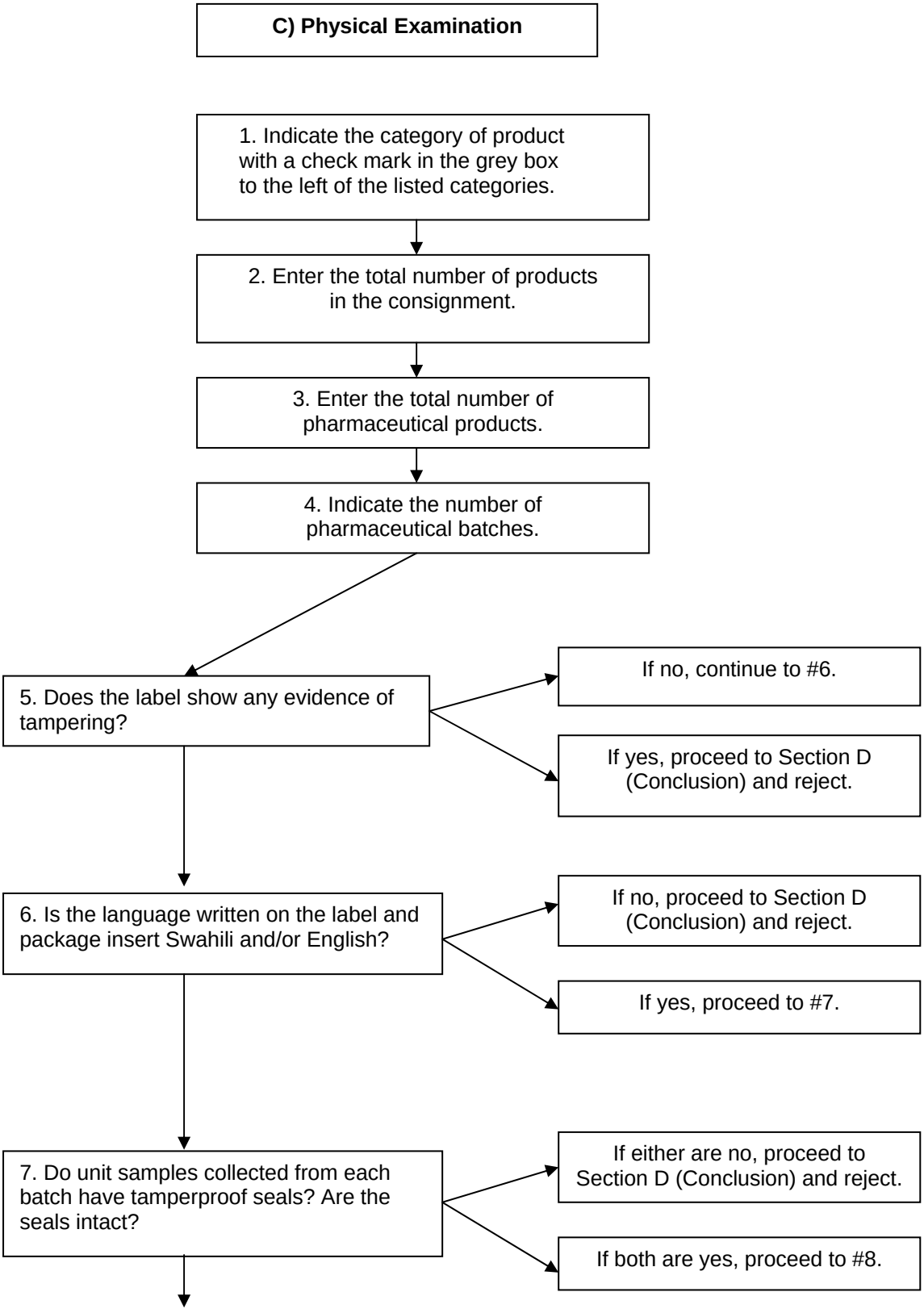
Ports of Entry Consignment Inspection Flowchart

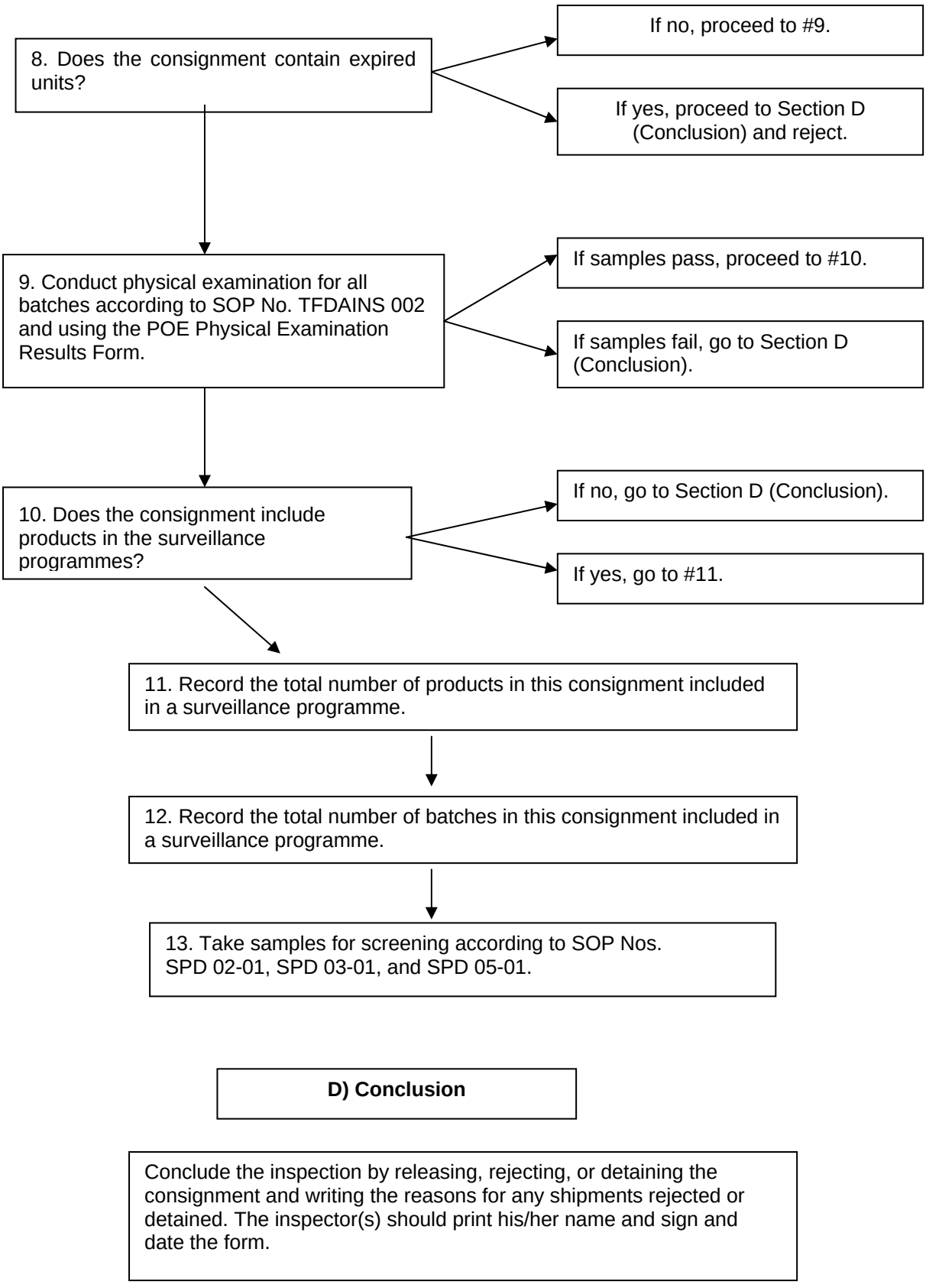



B) Documentation
1a. Does the consignee have a Pro Forma Invoice (PI) with an original endorsement by the Tanzania Food and Drugs Authority (TFDA)?
If no, write DETAIN in the space provided.
DETAIN means:
- Write DETAINED in the space provided.
- Stop the inspection.
- Complete the Rejection/Detention Form.
- Inform the TRA/C&E of the rejection/detention and give a copy of the form to the TRA.
If detention issues are resolved by written instruction from the TFDA, proceed from where the inspection stopped.
1b. If the consignment includes controlled drugs, does the consignee have an Import Certificate (IC) with an original endorsement by the authorised official of the TFDA?
If no, DETAIN.
1c. Are the specific products imported from sources indicated in the PI/IC?
If no, DETAIN.
1d. Is the consignment being imported through the declared POE?
If no, DETAIN.
If yes, enter the PI or IC number and date.
2. Is the Clean Report of Findings (CRF)/ Final Classification and Valuation Report (FCVR)/Import Declaration Form (IDF) receipt date within the expiry date of the PI/IC?
If no, DETAIN.
If yes, record the date of receipt.
3. Are the exporter and importer named in the CRF/FCVR the same as those listed on the authorised PI/IC?
If no, DETAIN.


4a. Does the free on board (FOB) value of the CRF/FCVR/IDF match the value indicated in the authorised PI?
If no, DETAIN.
4b. Do the item's description and the quantities for each of the products indicated in the CRF/FCVR/IDF match the quantities authorised in the PI?
If no, go to #4c.
If yes, proceed to #5a.
4c. Are the item's description and quantities indicated in the CRF **greater than** those authorised in the PI?
If no, go to #4d.
If yes, DETAIN.
4d. Are the item's description and quantities indicated in the CRF **less than** those authorised in the PI?
If yes, mark the quantities of short-landed items on the PI, write "partial shipment," and proceed to #5a.
5a. Does the shipment require a Certificate of Analysis (COA)?
If no, go to Section C (Physical Examination and Testing).
If yes, go to #5b.
5b. Is the COA present with the consignment?
If no, DETAIN.
5c. Is there a COA for each batch?
If no, DETAIN.
5d. If the consignment contains vaccines, is there a COA from the manufacturer and an approval from the drug regulatory authority of country of origin?
If no, DETAIN.


5e. Is the COA signed and stamped by authorised person(s)?
If no, DETAIN.
5f. Are the reported test results within specified limits? (COA must indicate specifications and results.)
If no, DETAIN.
5g. For products with **more than** 24 months' shelf life, is 60% of their shelf life remaining?
If no, DETAIN.
5h. For products with **less than** 24 months' shelf life, is 80% of their shelf life remaining?
If no, DETAIN.
5i. Do the batch numbers on the unit samples and COAs match?
If no, DETAIN.
5j. Do the expiration dates on the unit samples and the COAs match?
If no, DETAIN.
If yes, proceed to Section C (Physical Examination and Testing) for further verification of the consignment.


C) Physical Examination
1. Indicate the category of product with a check mark in the grey box to the left of the listed categories.
2. Enter the total number of products in the consignment.
3. Enter the total number of pharmaceutical products.
4. Indicate the number of pharmaceutical batches.
5. Does the label show any evidence of tampering?
If no, continue to #6.
If yes, proceed to Section D (Conclusion) and reject.
6. Is the language written on the label and package insert Swahili and/or English?
If no, proceed to Section D (Conclusion) and reject.
If yes, proceed to #7.
7. Do unit samples collected from each batch have tamperproof seals? Are the seals intact?
If either are no, proceed to Section D (Conclusion) and reject.
If both are yes, proceed to #8.



D) Conclusion

Conclude the inspection by releasing, rejecting, or detaining the consignment and writing the reasons for any shipments rejected or detained. The inspector(s) should print his/her name and sign and date the form.

SOP for Inspection of Pharmaceutical Consignments at Ports of Entry (TFDAINS 001)

TANZANIA FOOD AND DRUGS AUTHORITY DIRECTORATE OF INSPECTIONS AND SURVEILLANCE STANDARD OPERATING PROCEDURE				
TITLE: INSPECTION OF PHARMACEUTICAL CONSIGNMENTS AT PORTS OF ENTRY				
SOP NO.: **TFDAINS 001**	**SUPERSEDES:** **None**	**DATE OF ISSUE:** **Nov. 2002**	**EFFECTIVE DATE:** **Nov. 2002**	**NEXT REVIEW DATE:** **June 2006**

Objective

The objective of this SOP is to outline the procedure that drug inspectors must follow at ports of entry to conduct inspection of pharmaceutical consignments entering the country. The instructions outlined in this SOP refer to the POE Consignment Inspection Form.

Scope

This SOP details the procedure for inspecting and screening of drugs at ports of entry before either release to the market or denial of entry to the country.

Responsibility

The Director-General, Director of Inspections and Surveillance, Director of Product Evaluation and Registration, Director of Laboratory Services, Chief Drug Inspector, drug inspectors, and drug laboratory analysts shall ensure implementation of this SOP.

Accountability

The Director of Inspections and Surveillance is accountable for drug inspections at POEs.

Distribution of Forms

The Director-General, Director of Inspections and Surveillance, Director of Product Evaluation and Registration, Director of Laboratory Services, Chief Drug Inspector, drug inspectors, and drug laboratory analysts should get copies. A copy should also be kept in the Master File.

References

1. Pharmacy Board of Tanzania. 2000. *Guidelines for Importation of Pharmaceuticals.*
2. Tanzania Ministry of Health. 1996. *Guidelines for Donations.*
3. TFDA List of Registered Products

Special Instructions

The following forms, may be required to be filled in during the execution of this SOP:

1. POE Consignment Inspection Form
2. Rejection/Detention Form (annexed)
3. Sample Receipt Form (annexed)

The following SOPs may be used, depending on the products contained in the consignment:

1. SOP No. SPD 02-00 Suspicious Sample Surveillance Programme
2. Drug Quality Surveillance SOPs: SPD 02-01 Antimalarials, SPD 03-01 Antibiotics, and SPD 05-01 Antiretrovirals
3. SOP No. TFDAINS 002 for Physical Examination of Pharmaceutical Products

Procedure

The procedure described in this SOP consists of four sections. The sections relate to the POE Consignment Inspection Form, which must be used to record results of inspection, screening, and testing of consignment samples at POEs. Each section clearly indicates the decision(s) that are to be taken by the drug inspector when consignment(s) fail or pass inspection.

The procedure described in this SOP entails that at a POE, the drug inspector must:

1. Obtain the consignment to be inspected and tested (if necessary) from the Tanzania Revenue Authority, Customs and Excise Department (TRA/C&E).

2. Record all the particulars of the consignment on the POE Consignment Inspection Form according to the procedures outlined in this SOP.

Section A: Consignment Information

This section gives information pertaining to the consignment. The following information must be recorded:

1. *Port of entry name:* On the POE Consignment Inspection Form, circle the name of the POE at which the consignment was received. There are 15 official POEs, each of which has an abbreviation made up of three capital letters (Table 1). For the purpose of inspection of pharmaceutical consignments, the Medical Stores Department will be considered as a POE.

Table 1. Ports of Entry with Abbreviations

Port of Entry	Abbreviation
Dar es Salaam Harbour	DRH
Dar es Salaam International Airport	DIA
Holili	HOL
Horohoro	HOR
Kigoma Harbour	KIG
Kilimanjaro International Airport	KIA
Kyela-Mbeya	KYE
Medical Stores Department	MSD
Mtukula-Kagera	MTU
Mtwara Harbour	MTW
Mwanza Airport	MWA
Mwanza Harbour	MWH
Namanaga-Arusha	NAM
Sirari	SIR
Tanga Harbour	TAN
Tunduma-Mbeya	TUN

2. *Registration status of the consignee/importer:* The inspector is required to note whether the consignee/importer is registered by the TFDA. The inspector should circle Y (for yes) or N (for no) and fill in the name of the consignee/importer.

3. *Consignment control type:* The consignment control type is either airway bill (AWB), C21, C29, F89, or R. The inspector shall select the appropriate control type. The inspector should ask the responsible TRA/C&E official for the consignment control type.

4. The most common control type is the R number, which is a number assigned by the TRA/C&E to every consignment entering the country. The R number can be found in the Customs Control Advice document issued by the TRA/C&E. The inspector should ask the responsible TRA/C&E official for the control type number.

~~5.~~ *Date of inspection:* In the space provided, the inspector should record the date on which the inspection was started.

6. *Name of manufacturer and country of origin:* The inspector should record, in the space provided, the name of the firm and the country where the products in the consignment were manufactured.

7. *Commercial nature of the consignment:* The inspector should record in the space provided whether the consignment is a donation by choosing either Y (for yes) or N (for no).

8. *Monetary value of consignment:* The inspector should record, in the space provided, the monetary value of the consignment. This information is obtained from the invoice or from the Final Classification and Valuation Report (FCVR).

9. Currency: The inspector must circle the type of currency in which the monetary value is presented.

Section B: Documentation

The objective of Section B of the form is to enable the inspector to verify the particulars of the consignment and make appropriate decisions before proceeding any further with the inspection.

Item 1a: Examination of the Pro Forma Invoice

Confirm that the consignee has a Pro Forma Invoice (PI) with an original endorsement by the TFDA. If the PI is in order, proceed to item 1b. If the consignee does not have a PI with an original endorsement by the TFDA:

1. Stop the inspection
2. Complete the Rejection/Detention Form
3. Inform the TRA/C&E of the detention and give a copy of the form to the TRA
4. Give a copy of the form to the consignee

Upon resolution of detention issues and on written instructions from the TFDA, the inspector will continue with inspection from where he/she had stopped.

Item 1b: Examination of the Import Certificate (IC)

If the consignment includes controlled drugs, confirm that the consignee has a Import Certificate (IC) with an original endorsement by an authorised official of the TFDA.

If the consignee does not have an IC with an original endorsement by the TFDA:

1. Stop the inspection
2. Complete the Rejection/Detention Form
3. Inform the TRA/C&E of the detention and give a copy of the form to the TRA
4. Give a copy of the form to the consignee

Upon resolution of detention issues by written instructions from the TFDA, the inspector will continue with inspection from where he/she had stopped.

If the consignee has a PI and an IC with an original endorsement by the TFDA, proceed to item 1c.

Item 1c: Importing Country

Check that the products are imported from the sources indicated in the PI/IC. If they are, proceed to item 1d.

Item 1d: Declared POE

Check that the products are being imported through the declared POE. If yes, enter the PI and IC numbers and their issue dates, and proceed to item 2.

Item 2: Examination of the CRF/FCVR/IDF

Obtain from the TRA/C&E the original of the Clean Report of Findings (CRF)/FCVR or Import Declaration Form (IDF). Confirm that the CRF/FCVR/IDF receipt date is within the expiry date of the PI/IC. If not:

1. Circle N (for no) in the space provided
2. Stop the inspection
3. Complete the Rejection/Detention Form
4. Inform the TRA/C&E of the rejection/detention

If the CRF/FCVR receipt date is within the expiry date of the PI/IC, fill in the date the consignment was received, and proceed to item 3.

Item 3: Verification of Exporter and Importer (Consignee)

Confirm that the name(s) and address(es) of the exporter and importer named in the CRF/FCVR/IDF and the PI are the same. If not:

1. Stop the inspection
2. Complete the Rejection/Detention Form
3. Inform the TRA/C&E of the rejection/detention and give a copy of the form to the TRA

If the name(s) and address(es) of the exporter and importer named in the CRF/FCVR/IDF and the PI are the same, proceed to item 4.

Item 4a: Verification of Drug Value

Confirm that the free on board (FOB) value for each of the products indicated in the CRF/FCVR/IDF match the quantities in the endorsed PI.

If the value indicated in the CRF/FCVR/IDF matches the value authorised in the PI, proceed to item 4b.

Item 4b: Quantities

Confirm that the quantities for each of the products indicated in the CRF/FCVR/IDF match the quantities in the endorsed PI. If yes, proceed to item #5. If no, proceed to items 4c and 4d.

Item 4c: Greater Quantities

If the quantities indicated in the CRF/FCVR/IDF are **greater than** amounts authorised in the PI:

1. Stop the inspection
2. Complete the Rejection/Detention Form
3. Inform the TRA/C&E of the rejection/detention and give a copy of the form to the TRA

If not, proceed to item 4c.

Item 4d: Lesser Quantities

If the quantities indicated in the CRF/FCVR/IDF are **less than** amounts authorised in the PI:

1. Stop the inspection
2. Complete the Rejection/Detention Form

3. Inform the TRA/C&E of the rejection/detention and give a copy of the form to the TRA

In these cases, also mark the quantities of short-landed products on the endorsed PI and add the words “partial shipment.”

Item 5: Determination of Acceptable Shelf Life

This item examines the Certificate of Analysis (COA), if required, in the following sequence:

a. Determine if the consignment requires a COA. If not, skip the remainder of item 5 and proceed to Section C.
b. Is the COA present?
c. Is there a COA for each batch?
d. If the consignment contains vaccines, does the shipment include a COA and an approval from the regulatory body of the country of origin?
e. Is the COA signed and stamped by an authorised person(s)?
f. Are the reported tests results within specified limits?
g. For products with more than 24 months’ shelf life, is 60 percent of their shelf life remaining?
h. For products with less than 24 months’ shelf life, is 80 percent of their shelf life remaining?
i. Do the batch numbers on the unit samples and the COAs match?
j. Do the expiration dates on the unit samples and the COAs match?

If the answer to any of the above (except 5a) is “No”:

1. Stop the inspection
2. Complete the Rejection/Detention Form
3. Inform the TRA/C&E of the rejection/detention and give the TRA a copy of the form

If the answer to all of the above is yes (except 5a), proceed to Section C.

Section C: Physical Examination and Testing

Item 1: Categories

Indicate the categories of products. Categories include human medicines, pharmaceutical raw materials, veterinary medicines, medical supplies, medical equipment, and vaccines.

Item 2: Total Number of Products

Enter the number of products in the consignment.

Item 3: Number of Pharmaceutical Products

Enter the number of pharmaceutical products in the consignment.

Item 4: Number of Batches

Enter the number of pharmaceutical batches in the consignment.

Item 5: Labelling

Check if the label shows any evidence of tampering. For example:

1. Entire label or parts of labels have been cut off
2. New labels have been pasted over old ones

3. Label details were erased or painted over and replaced with new details
4. Labels on primary container are missing
5. Labels on secondary containers are missing
6. Label does not bear the name and address of the manufacturer

If the label shows any evidence of tampering:

1. Stop the inspection
2. Complete the Rejection/Detention Form
3. Inform the TRA/C&E of the rejection/detention and give the TRA a copy of the form

If the labels meet the requirements, proceed to item 6.

Item 6: Language on Label

Verify that the language on labels and package inserts is Swahili and/or English.

If the language is not correct or package inserts are not available:

1. Stop the inspection
2. Complete the Rejection/Detention Form
3. Inform the TRA/C&E of the rejection/detention and give the TRA a copy of the form

If the language is Swahili or English and the package inserts are available, proceed to item 7.

Item 7: Seals

Verify that the samples have intact tamperproof seals. If yes, proceed to item 8. If no:

1. Stop the inspection
2. Complete the Rejection/Detention Form
3. Inform the TRA/C&E of the rejection/detention and give the TRA a copy of the form

Item 8: Expiry Dates

Verify the expiration dates on the unit samples.

If any of the unit samples have expired:

1. Stop the inspection
2. Complete the Rejection/Detention Form
3. Inform the TRA/C&E of the rejection/detention and give the TRA a copy of the form

If no, proceed to item 9.

Item 9: Physical Examination

Perform physical examination of the sample(s) in accordance with SOP No. TFDAINS 002 and using the POE Physical Examination Results Form.

If the samples are satisfactory and testing is required, proceed to item 10. If samples do not pass testing, proceed to Section D to conclude the inspection.

Item 10: Surveillance Programme
For each sample required for testing under the surveillance programme, collect the minimum sample quantities indicated in Table 2. For an example of how to determine the number of unopened unit pack(s) for testing, see Table 3.

Table 2. Sampling Plan

Dosage Form	Minimum Sample Size to Be Taken from Each Batch for Testing
Tablets/capsules	100 tablets/capsules
Suppositories/ovules	20 suppositories/ovules
Powders/sachets	20 packets/sachets
Injectables (ampoules)	20 ampoules
Injectables (vials)	20 vials
Eyedrops	6 bottles
Syrups	6 bottles
IV fluids	6 bottles

Table 3. An Example of Sample Size Determination (Based on Table 2: Sampling Plan)

1	2	3	4	5	6
	Description	**Batch No.**	**Unit Pack**	**Quantity per Batch**	**Number of Unit Packs to Be Collected**
1	Quinine sulfate tablets	020717F	T/1,000's	10,000	1
2	Artesunate tablets	BF86	P/12's	3,000	9
3	Sulfadoxine/pyrimethamine tablets	U7MW3	P/3's	10,000	20
4	Quinine injection 600 mg/2 mL	MZ03P	Each	1,000	20

Item 11: Number of Products in Surveillance Programme
Enter the total number of products in this consignment included in the surveillance programme.

Item 12: Number of Batches in Surveillance Programme
Enter the total number of batches in this consignment included in the surveillance programme.

Item 13: Samples for Screening
Take samples for screening according to SOP Nos. SPD 02-01, SPD 03-01, and SPD 05-01.

Test the samples according to the Drug Quality Surveillance Programme's SOPs (SPD 02-01, SPD 03-01, and SPD 05-01). If the sample must be sent to the Drug Quality Control Laboratory (DQCL), pack and ship it according to the packing and shipping SOP, TFDAINS 004.

Section D: Conclusion

This section of the form requires the inspector to reject or accept the consignment. Mark, as appropriate, the rejection or acceptance decision in the space provided on the inspection form and include remarks (if any).

If the consignment is accepted, all supporting documents relating to the released shipment must be stamped "APPROVED FOR RELEASE." If the consignment is rejected, it must be detained in the safe custody of the TRA/C&E and disposed of in the manner and conditions specified in the *Guidelines for Importation of Pharmaceuticals*, paragraph 5.4(ii) on page 10.

To conclude the inspection and testing, the inspector(s) must sign and date the inspection form as appropriate.

Port of Entry Consignment Inspection Form (TFDAINS Form 001)

UNITED REPUBLIC OF TANZANIA
MINISTRY OF HEALTH

TANZANIA FOOD AND DRUGS AUTHORITY
Tel: +255-22-2450512/2450751
FAX: +255-22-2450793
Web site: http//www.tfda.or.tz

PORT OF ENTRY (POE) CONSIGNMENT INSPECTION FORM
(A rejoinder to SOP for Inspection of Pharmaceutical Consignments at Ports of Entry)

Particulars in this checklist must be filled in for every consignment imported into the country.

A) Consignment Information

1. POE Name (circle)	DIA	DRH	MSD	NAM	SIR
	KIA	MWA	MWH	HOR	TAN
	HOL	KIG	TUN	KYE	MTW
	MTU				

2. Is consignee (importer) registered with the TFDA? (Y / N)

Name of Consignee……

3					4	5	6	
Control Type (circle)					**Control Type Number**	**Date of Inspection**	**Name of Manufacturer and Country of Origin**	
R	**AWB**	**C21**	**C29**	**F89**			Manufacturer	Country

7	8	9	
Is the consignment a donation? (Circle)	**Monetary Value of Consignment**	**Currency** (Circle)	
Y / N		U.S. Dollar ($) E.U. Euro (€) U.K. Pound (£) Kenyan Shilling (Ksh) S.A. Rand (R)	Swiss Franc (CHF) Egyptian Pound (£) Tanzanian Shilling (Tsh) Other: (please indicate) ……..

Prepared by:	**Checked by:**	**Approved by:**
Date:	**Date:**	**Date:**

B) Documentation

Observations		Results/Decision (Circle Y for yes or N for no. Unless otherwise specified, if no, write "DETAINED"[2] in right column)			
1a.	Does the consignee have a Pro Forma Invoice (PI) with an original endorsement by the Tanzania Food and Drugs Authority (TFDA)? If yes, proceed to #1b.	**Y**	**N**		
1b.	If the consignment includes controlled drugs, does the consignee have an Import Certificate (IC) with an original endorsement by the authorised official of the TFDA? If yes, proceed to #1c.	**Y**	**N**	**N/A**	
1c.	Are the specified products imported from sources indicated in the PI/IC? If yes, proceed to #1d.	**Y**	**N**		
1d.	Is the consignment being imported through the declared POE?	**Y**	**N**		
	If yes, enter the PI[3] or IC number and date and proceed to #2.	**PI #:**		**IC #:**	
		PI Issue Date:		**IC Issue Date:**	
2.	Is the Clean Report of Findings (CRF)/Final Classification and Valuation Report (FCVR)/Import Declaration Form (IDF) receipt date within the expiry date of the PI/IC? If yes, record the date of receipt and proceed to #3.	**Y**	**N**	**Date Consignment Received at POE:**	
3.	Are the exporter and importer named in the CRF/FCVR the same as those listed in the PI? If yes, proceed to item #4.	**Y**	**N**		
4a.	Does the free on board (FOB) value of the CRF/FCVR/IDF **match** the value indicated in the authorised PI? If yes, proceed to item #4b.	**Y**	**N**		
4b.	Do the item's description and the quantities for each of the products indicated in the CRF/ FCVR **match** the quantities authorised in the PI? If no, see #4c and #4d. If yes, proceed to item #5.	**Y**	**N**		

[2] "DETAINED" means: (a) stop the inspection; (b) complete a Rejection/Detention Form; (c) inform the TRA/C&E of the rejection/detention; (d) give a copy of the Rejection/Detention Form to the TRA. If detention issues are resolved by written instructions from the TFDA, proceed from where the inspection stopped.

[3] Pro Forma Invoice will be valid for six months from date of endorsement by the TFDA.

4c.	Are the item's description and quantities indicated in the CRF **greater than** those authorised in the PI? If no, see #4d. If yes, detain consignment.	**Y**	**N**		
4d.	Are the item's description and quantities indicated in the CRF **less than** those authorised in the PI? If yes, mark the quantities of short-landed items on the PI, write "partial shipment," and proceed to #5a.	**Y**	**N**		
5a.	Does the consignment require a Certificate of Analysis (COA)? If yes, go to #5b. If no, go to Section C (Physical Examination and Testing).	**Y**	**N**		
5b.	Is the COA present with the consignment?	**Y**	**N**		
5c.	Is there COA for each pharmaceutical batch?	**Y**	**N**		
5d.	If the consignment contains vaccines, is there a COA from the manufacturer and an approval from the regulatory authority of the country of origin?	**Y**	**N**	**NA**	
5e.	Is the COA signed and stamped by authorised person(s)?	**Y**	**N**		
5f.	Are the reported test results within specified limits?	**Y**	**N**		
5g.	For products with **more than** 24 months' shelf life, is 60% of their shelf life remaining?	**Y**	**N**	**NA**	
5h.	For the products with **less than** 24 months' shelf life, is 80% of their shelf life remaining?	**Y**	**N**	**NA**	
5i.	Do the batch numbers on the unit samples and the COAs match? If yes, proceed to #5j. If no, detain shipment.	**Y**	**N**		
5j.	Do the expiration dates on the unit samples and the COAs match? If yes, proceed to Section C (Physical Examination and Testing) for further verification of the consignment. If no, detain shipment.	**Y**	**N**		

(C) Physical Examination and Testing

1.	Indicate the categories of products:			
		Human Medicines		
		Pharmaceutical Raw Materials		
		Veterinary Medicines		
		Medical Supplies		
		Medical Equipment		
		Vaccines		
2.	Total number of products in the consignment	Enter #		
3.	Number of pharmaceutical products	Enter #		
4.	Number of pharmaceutical batches	Enter #		
5.	Does the label show any evidence of tampering? If no, proceed to #6. If yes, proceed to Section D (Conclusion) and reject.	**Y**	**N**	
6.	Is the language written on the label and package insert Swahili and/or English? If yes, proceed to #7. If no, proceed to Section D (Conclusion) and reject.	**Y**	**N**	
7.	Do unit samples collected from each batch have tamperproof seals? Are the seals intact? If both are yes, proceed to #8. If either are no, go to Section D (Conclusion) and reject.	**Y**	**N**	
8.	Does the consignment contain expired units? If no, go to #9. If yes, go to Section D (Conclusion) and reject.	**Y**	**N**	
9.	Conduct physical examination for all batches according to SOP No. TFDAINS 002 and using the POE Physical Examination Results Form (TFDAINS Form 002). Do samples pass physical examination? If yes, proceed to #10. If no, go to Section D (Conclusion).	**Y**	**N**	
10.	Does the consignment include products in the surveillance programmes? If yes, go to #11. If no, go to Section D (Conclusion).	**Y**	**N**	
11.	Total number of products in this consignment included in a surveillance programme			
12.	Total number of batches in this consignment included in a surveillance programme			
13.	Take samples for Minilab screening according to the Drug Quality Surveillance Programme's SOPs: SPD 02-01, SPD 03-01, and SPD 05-01			

(D) Conclusion

The consignment as inspected and tested as required is hereby:	*Remarks (if any):*
Released	
Rejected	*Reasons for rejection must be clearly indicated:*
Detained	*Reasons for detainment must be clearly indicated:*

Name(s) of Inspector(s)	**Signature and Date**

SOP for Physical Examination Procedures for Pharmaceutical Products (TFDAINS 002)

TANZANIA FOOD AND DRUGS AUTHORITY DIRECTORATE OF INSPECTIONS AND SURVEILLANCE STANDARD OPERATING PROCEDURE				
TITLE: PHYSICAL EXAMINATION PROCEDURES FOR PHARMACEUTICAL PRODUCTS				
SOP NO.: **TFDAINS 002**	**SUPERSEDES:** **None**	**DATE OF ISSUE:** **Nov. 2002**	**EFFECTIVE DATE:** **Nov. 2002**	**NEXT REVIEW DATE:** **June 2006**

Objective

The objective of this standard operating procedure is to outline the procedures and instructions that drug inspectors must follow when examining physical attributes of sample(s) of pharmaceutical products.

Scope

This SOP details the procedure for physical examination of pharmaceutical products during inspection at ports of entry and at facilities during postmarketing surveillance.

Responsibility

The Director-General, Director of Inspections and Surveillance, Director of Product Evaluation and Registration, Director of Laboratory Services, Chief Drug Inspector, drug inspectors, and drug laboratory analysts shall ensure implementation of this SOP.

Accountability

The Director of Laboratory Services is accountable for the final results.

Distribution

The Director-General, Director of Inspections and Surveillance, Director of Product Evaluation and Registration, Director of Laboratory Services, Chief Drug Inspector, drug inspectors, and drug laboratory analysts should receive copies. A copy should also be kept in the Master File.

References

1. GPHF Minilab manuals
2. Kenyon, A. S. 1999. *Rapid Screening of Tuberculosis Pharmaceuticals by Thin-Layer Chromatography*. St. Louis, MO: U.S. Food and Drug Administration. <http://www.pharmweb.net/pwmirror/library/tlc/TBDRUGS.pdf >
3. World Health Organization (WHO). 1991. *Basic Tests for Pharmaceutical Dosage Forms*. Geneva: WHO.
4. TFDA List of Registered Products
5. *Drug Defect Reference* CD

Special Instructions

The following forms, may need to be filled in during the execution of this SOP,

1. POE Physical Examination Results Form
2. Facility Physical Examination Results Form
3. POE Consignment Inspection Form
4. Drug Dispensing Outlet (Part I, Part II, Dispensary) Inspection Forms
5. Rejection/Detention Form (annexed)
6. Sample Receipt Form (annexed)
7. Confiscation/Quarantine Form (annexed)

The following SOPs may need to be referred to when executing this SOP:

1. SOP No. SPD 02-00 Suspicious Sample Surveillance Programme
2. SOP Nos. SPD 02-01, SPD 03-01, and SPD 05-01: Drug Quality Surveillance Programme

Procedure

The procedure and instructions given in this SOP relate to the POE/Facility Physical Examination Results Forms, which must be used to record results of physical examination of the samples. At POEs, a pass or fail result is captured in Section 4 (Conclusion/Decision) of the POE Physical Examination Results Form. Then this the overall result is transferred to Section D (Conclusion) of the POE Consignment Inspection Form. For postmarketing surveillance at facilities, the overall assessment need only be recorded under Section 4 (Conclusion/Decision) of the Facility Physical Examination Results Form.

Sections 1 and 2: Captures POE/facility and product information.

Sections 3A and 3B: Provides instructions for physical examination of tablets and capsules.

Sections 3C, 3D, and 3E: Outlines the procedures and instructions for physical examination of liquid and semisolid dosage forms (which encompasses injectable and parenteral forms).

Section 4: Captures the conclusion or the final decision after the physical examination of the sample.

Section 5: Indicates whether another batch of the product will be examined.

Section 6: Records the name and signature of the inspector and the date of inspection.

Sections 1, 2, 5, and 6 are self-explanatory. The remaining sections are described below.

Sections 3A and 3B: Physical Examination of Tablet/Capsule Sample

The drug inspector should make sure that the particulars of the tablet/capsule sample have been recorded on the Sample Receipt Form (SRF).

Tests to Be Conducted

The following tests should be conducted and their results and/or observations recorded on the appropriate Physical Examination Results Form.

Odour of the Tablet/Capsule Sample

Determine the odour of the tablet/capsule samples in the following way:

1. Remove/open the container seal (at room temperature and in a room that is free from drafts) and smell the odour of the opened container.

2. Remove any cotton wool or filler material (if present) before tearing open the immediate container[4] before smelling the odour again.

3. Expose the tablets/capsules according to the following chart.

Pack Size (in Tablets/Capsules)	Exposure to Air in Minutes
100 or less	5
101 to 500	10
501 or more	25

4. After exposure to the air at room temperature (for the duration indicated in the above chart in a room that is free from drafts), the contents of a freshly opened container should be odourless.

5. Record the results of this test as pass or fail in the Physical Examination Results Form.

Other Physical Characteristics of the Tablet/Capsule Sample

To determine other characteristics of the tablet/capsule samples, the inspector should:

1. When taking a sample of the tablets/capsules for visual inspection, wear surgical gloves to avoid handling the sample with bare hands.
2. Use a spatula, spoon, or tablet/capsule counter to obtain a sample of the tablets/capsules from the original container.
3. Draw 5 to 25 tablets and place the tablets/capsules on a piece of white paper.
4. Examine one side of the tablet/capsule in ordinary room daylight.
5. With the spatula, turn over the tablet/capsule and examine the other side.
6. Record observations of this test as pass or fail for each characteristic on the Physical Examination Results Form.

[4] Some samples have plastic bags as their immediate containers, which have to be torn to smell the odour.

In addition to odour, the characteristics to note for tablets are:

- **Uniformity of Size:** The tablets should be uniform in size.
- **Uniformity of Shape:** The tablets should be uniform in shape.
- **Uniformity of Colour:** The tablets should be uniform in colour.
- **Coating** (tablets only: can be film-coated, sugar-coated, or enteric-coated): The coating should be uniform. The core of the tablets should be fully covered.
- **Polishing:** The tablets should be uniformly polished and free of powders.
- **Markings** (scoring, letters, etc.): Markings on tablets should be uniform and identical.
- **Breaks:** The tablets should be free of breaks.
- **Cracks:** The tablets should be free of cracks.
- **Splitting:** The tablets should be free of splits.
- **Capping or cavitations of tablets:** The tablets should be free of capping or cavitations.
- **Embedded surface spots:** The tablets should be free of embedded surface spots.
- **Foreign particulate contamination:** The tablets should be free of embedded or adherent foreign matter.

In addition to odour, the characteristics to note for capsules are:

- **Presence of empty capsules** in the case of a sample of capsules: The sample examined should be free of empty capsules.
- **Presence of open or broken capsules:** The sample examined should be free of open or broken capsules.
- **Separate cap and body of a capsule:** The capsules in the sample should be intact.
- **Pinholes:** The capsules should be free of pinholes.
- **Stickiness:** The capsules should not stick together.
- **Extraneous material:** The container or bottle of capsules should be free of extraneous material such as powder.
- **Presence of weak point in body of capsule:** The sample capsules should not show any evidence of weak points in the body.

Sections 3C, 3D, and 3E: Physical Examination of Solution and Suspension Dosage Forms

This section outlines the procedures and instructions for examining physical characteristics of liquid dosage forms (which includes solutions and/or suspensions for oral and parenteral administration). The section is divided into the following subsections:

3C. Solutions
a. Particulate matter
b. Clarity of liquid/solution (including parenterals/injectables)
c. State of primary container
d. Other (specify)

3D. Suspensions
a. Dispersability
b. State of primary container
c. Other (specify)

3E. Suspensions for Parenteral Administration
a. Dispersability
b. Flowability (aqueous)
c. Flowability (non-aqueous)
d. State of primary container
e. Other (specify)

3C. Solutions

Particulate Matter

Method
Invert the container several times or swirl gently. Do not agitate, as agitation will incorporate air into the liquid/solution.

Inference
Liquids (solutions and syrups) should be entirely free from visible foreign particles. Solid foreign particles are usually irregular in shape and will tend to settle to the bottom of the container, whereas lint or threadlike particles may float in the liquid. In contrast, fine air bubbles, which may be seen moving on the surface of the solution, are spherical or oval.

Clarity

Method
Without disturbing the container, examine the container (preferably against a black background) under ordinary light.

Inference
The liquid/solution should be clear and free from turbidity.

State of Primary Container

Method
Physically examine each of the sample primary containers for evidence of damage such as cracks, breaks, tears, or leakage.

Inference
Primary container should not show any evidence of cracks, breaks, tears, or leakage.

3D. Suspensions

Dispersability

Method
For dry powders for reconstitution, reconstitute as directed by the manufacturer. Gently shake the container to obtain a uniform suspension.

Inference
The suspension is easily dispersed. A homogeneous suspension that remains homogeneous for at least three minutes should be obtained.

State of Primary Container

Method
Physically examine each of the sample primary containers for evidence of damage such as cracks, breaks, tears, or leakage.

Inference
Primary container should not show any evidence of cracks, breaks, tears, or leakage.

3E. Suspensions for Parenteral Administration

Dispersability

Method
For dry powders for reconstitution, reconstitute as directed by the manufacturer. Gently shake the container to obtain a uniform suspension.

Inference
The suspension is easily dispersed. A homogeneous suspension that remains homogeneous for at least three minutes should be obtained.

Flowability (Aqueous)

Suspensions in aqueous vehicles, after shaking as above, should flow freely without binding when the contents of the vial are aspirated through a 22-gauge, 1-inch hypodermic needle, using a hypodermic syringe with a suitable volume.

Flowability (Non-aqueous)

Suspensions in nonaqueous vehicles, after shaking as above, should flow freely without binding when the contents of the final containers are aspirated through an 18-gauge, 1.5-inch hypodermic needle using a hypodermic syringe with a suitable volume.

State of Primary Container

Method
Physically examine each of the sample primary containers for evidence of damage such as cracks, breaks, tears, or leakage.

Inference
Primary container should not show any evidence of cracks, breaks, tears, or leakage.

Section 4: Conclusion/Decision

Fill in the results of the tests described above in the space provided in this section.

If the sample passes the physical tests:

- For POEs, fill in Section C, item 9, on the POE Consignment Inspections Form, then complete the rest of the form.

- If an antimalarial, antibiotic, or antiretroviral drug sample must have further testing, refer to SOP No. SPD 02-01, SPD 03-01, or SPD 05-01.

If the sample fails the physical tests:

- For POEs, reject the consignment and fill in Section D (Conclusion) of the POE Consignment Inspection Form.

- For a sample taken for postmarketing surveillance:
    - Collect samples for further testing according to SOP No. SPD 02-00 and quarantine the remaining part of the batch(es) by filling in the Confiscation/Quarantine Form.
    - The quarantined products should be detained until the DQCL completes the evaluation.

To keep a record of the actions, decisions taken, and compliance with POE Consignment Inspection SOP No. TFDAINS 001 and Postmarketing Surveillance SOP No. TFDAINS 003 during inspection, the SOPs have been translated into two forms (the POE Physical Examinations Results Form and the Facility Physical Examinations Results Form). The inspector must fill in the appropriate form when conducting physical examination of pharmaceutical products at POEs and at facilities during postmarketing surveillance.

POE Physical Examination Results Form (TFDAINS Form 002)

UNITED REPUBLIC OF TANZANIA
MINISTRY OF HEALTH

TANZANIA FOOD AND DRUGS AUTHORITY
Tel: +255-22-2450512/2450751
FAX: +255-22-2450793
Web site: http//www.tfda.or.tz

PORT OF ENTRY (POE) PHYSICAL EXAMINATION RESULTS FORM

1. POE Name

POE (circle)	DIA	DRH	MSD	NAM	SIR	KIA	MWA	MWH
	TAN	HOR	HOL	KIG	TUN	KYE	MTU	MTW

Control Type (circle)	R	AWB	C21	C29	F89	
Control Type Number						

2. Product Information

Product Name:		
Batch #:	Date of Manufacture:	Date of Expiry:
Manufacturer:	Country of Manufacturer:	
Product Form/Category (select one)		Tablets (go to Section 3A)
		Capsules (go to Section 3B)
		Liquids: solutions and syrups (go to Section 3C)
		Liquids: suspensions (go to Section 3D)
		Parenterals: solutions and suspensions (go to Section 3E)

3. Test Results and Observations

A) Tablets

	Parameter	Specifications	Status	
			Pass	Fail
1	Odour (immediately on opening the outer container)	No odour, except for flavoured tablets and those with active ingredients normally having characteristic odour		
2	Odour (after exposing the tablets according to recommended plan of exposure)	No odour, except for flavoured tablets and those with active ingredients normally having characteristic odour		
3	Uniformity of size, shape, colour, and coating (visual inspection)	Uniform in size and shape, uniformity of colour and coating		
4	Tablet core fully covered	Uniform coating with core fully covered		
5	Polishing	Uniformly polished and free of adhering fine powders		
6	Markings (scoring, letters, etc.)	Uniform and identical		
7	Breaks, cracks, splitting, capping, and cavitations	Free of breaks, cracks, splitting, capping, and cavitations		
8	Embedded surface spots, foreign particulate contamination	Free of embedded surface spots, foreign particulate contamination		
9	Other (specify)			

B) Capsules

	Parameter	Specifications	Status	
			Pass	Fail
1	Odour (on immediately on opening the outer container)	No odour, except for those with active ingredients normally having characteristic odour		
2	Odour (after exposing the capsules according to recommended plan of exposure)	No odour, except for those with active ingredients normally having characteristic odour		
5	Presence of empty, broken, or separated capsules	Free of empty capsules, no broken capsules		
4	Pinholes in capsules	Free of pinholes in capsules		
5	Stickiness between capsules	Capsules are not sticky		
6	Container/bottle free of powder and/or extraneous material	Container/bottle free of powder and/or extraneous material		
7	Weak point in body of capsule	No weak point in body of capsule		
8	Other (specify)			

C) Liquids: Solutions/Syrups

	Parameter	Specifications	Status	
			Pass	Fail
1	Particulate matter	Should be entirely free from foreign particles		
2	Clarity	Should be clear and free of turbidity		
3	State of primary container	Should not show any evidence of cracks, breaks, tears, or leakage		
4	Other (specify)			

D) Suspensions

	Parameter	Specifications	Status	
			Pass	Fail
1	Dispersability	Easily dispersed to obtain a homogeneous suspension upon moderate shaking for 20 seconds and remain homogeneous for 3 minutes		
2	State of primary container	Should not show any evidence of cracks, breaks, tears, and leakage		
3	Other (specify)			

E) Solutions/Suspensions

	Parameter	Specifications	Status	
			Pass	Fail
1	Clarity	Should be clear and free of turbidity		
2	Dispersability	Easily dispersed to obtain a homogeneous suspension upon moderate shaking for 20 seconds and remain homogenous for at least 3 minutes		
3	Flowability (aqueous)	Aqueous injectable suspensions should flow freely without binding when the contents of vial/ampoule are aspirated through a 22-gauge, 1-inch hypodermic needle, using a hypodermic syringe with a suitable volume		
4	Flowability (non-aqueous)	Non-aqueous injectable suspensions should flow freely without binding when the contents of the vial/ampoule are aspirated through an 18-gauge, 1.5-inch hypodermic needle, using a hypodermic syringe with a suitable volume		
5	State of primary container	Should not show any evidence of cracks, breaks, tears, or leakage		
6	Other (specify)			

4. Conclusion/Decision

STATUS: The sample as visually inspected (tick as appropriate)		*Remarks (if any):*
	Pass	
	Fail	

5. Is there any other batch for physical examination? Y / N (circle one)

If yes, return to Section 2, Product Information, and fill in the remainder of the form for the new batch. If no, go to #6.

6. Name of Inspector: Signature:

	Date:	

Note: SOP No. TFDAINS 002 requires the inspector to skip physical examination for suppositories, pessaries, creams/ointments, and solutions packaged in opaque containers (e.g., eyedrops).

Prepared by:	**Checked by:**	**Approved by:**
Date:	**Date:**	**Date:**

Facility Physical Examination Results Form (TFDAINS Form 003)

UNITED REPUBLIC OF TANZANIA
MINISTRY OF HEALTH

TANZANIA FOOD AND DRUGS AUTHORITY
Tel: +255-22-2450512/2450751
FAX: +255-22-2450793
Web site: http//www.tfda.or.tz

FACILITY PHYSICAL EXAMINATION RESULTS FORM

1. General Information

Facility Type (circle)	**Warehouse**	**Wholesale/ Retail**	**Retail Part I**	**DLDB (Part II)/ DLDM**	**Hospital**	**Health Centre**	**Dispensary**
Name of Facility							

2. Product Information

Product Name:			
Batch #:	**Date of Manufacture:**	**Date of Expiry:**	
Manufacturer:			
Country of Manufacturer:			
Product Form/Category (select one)			Tablets (go to Section 3A)
			Capsules (go to Section 3B)
			Liquids: solutions and syrups (go to Section 3C)
			Liquids: suspensions (go to Section 3D)
			Parenterals: solutions and suspensions (go to Section 3E)

3. Test Results and Observations

A) Tablets

	Parameter	Specifications	Status	
			Pass	Fail
1	Odour (immediately on opening the outer container)	No odour, except for flavoured tablets and those with active ingredients normally having characteristic odour		
2	Odour (after exposing the tablets according to recommended plan of exposure)	No odour, except for flavoured tablets and those with active ingredients normally having characteristic odour		
3	Uniformity of size, shape, colour, and coating (visual inspection)	Uniform in size and shape, uniformity of colour and coating		
4	Tablet core fully covered	Uniform coating with core fully covered		
5	Polishing	Uniformly polished and free of adhering fine powders		
6	Markings (scoring, letters, etc.)	Uniform and identical		
7	Breaks, cracks, splitting, capping, and cavitations	Free of breaks, cracks, splitting, capping, and cavitations		
8	Embedded surface spots, foreign particulate contamination	Free of embedded surface spots, foreign particulate contamination		
9	Other (specify)			

B) Capsules

	Parameter	Specifications	Status	
			Pass	Fail
1	Odour (on immediately on opening the outer container)	No odour, except for those with active ingredients normally having characteristic odour		
2	Odour (after exposing the capsules according to recommended plan of exposure)	No odour, except for those with active ingredients normally having characteristic odour		
5	Presence of empty, broken, or separated capsules	Free of empty capsules, no broken capsules		
4	Pinholes in capsules	Free of pinholes in capsules		
5	Stickiness between capsules	Capsules are not sticky		
6	Container/bottle free of powder and/or extraneous material	Container/bottle free of powder and/or extraneous material		
7	Weak point in body of capsule	No weak point in body of capsule		
8	Other (specify)			

C) Liquids: Solutions/Syrups

	Parameter	Specifications	Status	
			Pass	Fail
1	Particulate matter	Should be entirely free from foreign particles		
2	Clarity	Should be clear and free of turbidity		
3	State of primary container	Should not show any evidence of cracks, breaks, tears, or leakage		
4	Other (specify)			

D) Suspensions

	Parameter	Specifications	Status	
			Pass	Fail
1	Dispersability	Easily dispersed to obtain a homogeneous suspension upon moderate shaking for 20 seconds and remain homogeneous for 3 minutes		
2	State of primary container	Should not show any evidence of cracks, breaks, tears, and leakage		
3	Other (specify)			

E) Solutions/Suspensions

	Parameter	Specifications	Status	
			Pass	Fail
1	Clarity	Should be clear and free of turbidity		
2	Dispersability	Easily dispersed to obtain a homogeneous suspension upon moderate shaking for 20 seconds and remain homogenous for at least 3 minutes		
3	Flowability (aqueous)	Aqueous injectable suspensions should flow freely without binding when the contents of vial/ampoule are aspirated through a 22-gauge, 1-inch hypodermic needle, using a hypodermic syringe with a suitable volume		
4	Flowability (non-aqueous)	Non-aqueous injectable suspensions should flow freely without binding when the contents of the vial/ampoule are aspirated through an 18-gauge, 1.5-inch hypodermic needle, using a hypodermic syringe with a suitable volume		
5	State of primary container	Should not show any evidence of cracks, breaks, tears, or leakage		
6	Other (specify)			

4. Conclusion/Decision

STATUS: The sample as visually inspected (tick as appropriate)		*Remarks (if any):*
	Pass	
	Fail	

5. Is there any other batch for physical examination? Y / N (circle one)

If yes, return to Section 2, Product Information, and fill in the remainder of the form for the new batch. If no, go to #6.

6. Names of Inspector: Signature:

(a)		
(b)	**Date:**	

Note: SOP No. TFDAINS 002 requires the inspector to skip physical examination for suppositories, pessaries, creams/ointments, and solutions packaged in opaque containers (e.g., eyedrops).

Prepared by:	**Checked by:**	**Approved by:**
Date:	**Date:**	**Date:**

Chapter 3. Drug Surveillance and Testing Programme

In this chapter, the SOPs for the drug surveillance and testing programme are detailed. The chapter includes the sampling and test procedures using the German Pharma Health Fund (GPHF) Minilab methods. (The test methods are elaborated in detail in Part II of this handbook: *The Use of Minilab Procedures for Verification of Identity and Drug Content*.)

After obtaining the test results, the inspector should report the results using the format shown on the appropriate Screening Certificate. A decision tree that will guide the decision-making process after each test is performed is also included.

Four antimalaria drugs have been included in the first phase of the surveillance programme. These drugs are artesunate, quinine hydrochloride, quinine sulfate/bisulfate, and sulfadoxine/pyrimethamine. The second phase of the programme includes the following six antibiotics: amoxicilline, ampicillin, ciprofloxacin, co-trimoxazole, erythromycin, and metronidazole. Recently, the surveillance programme has been expanded to include antiretroviral drugs. Other drug categories may be included in this programme in the future.

SOP for Suspicious Sample Surveillance Programme (SPD 02-00)

TANZANIA FOOD AND DRUGS ADMINISTRATION DIRECTORATE OF INSPECTIONS AND SURVEILLANCE STANDARD OPERATING PROCEDURE				
TITLE: SUSPICIOUS SAMPLE SURVEILLANCE PROGRAMME				
SOP NO.: **SPD 02-00**	**SUPERSEDES:** **None**	**DATE OF ISSUE:** **Nov. 2002**	**EFFECTIVE DATE:** **Nov. 2002**	**NEXT REVIEW DATE:** **June 2006**

Objective

The objective of this standard operating procedure is to outline the procedures drug inspectors must follow when collecting samples that appear suspicious.

Scope

This SOP details the procedures for collecting suspicious samples at any point in the distribution system. If possible, collected samples should be in unopened containers and within their expiry date.

Responsibility

The Director-General, Director of Inspections and Surveillance, Director of Laboratory Services, Chief Drug Inspector, drug inspectors, and drug laboratory analysts shall ensure implementation of this SOP.

Accountability

The Director of Inspections and Surveillance is accountable for the implementation of this SOP.

Distribution

The Director-General, Director of Inspections and Surveillance, Director of Laboratory Services, Chief Drug Inspector, drug inspectors, and drug laboratory analysts should get copies. A copy should also be kept in the Master File.

References

1. World Health Organisation (WHO) Expert Committee on Specifications for Pharmaceutical Preparations. 1999. *Guidelines for Inspection of Drug Distribution Channels.* 35th Report. WHO Technical Report Series No. 885, Annex 6. Geneva: WHO.
2. World Health Organisation (WHO). 1999. *Guidelines for the Development of Measures to Combat Counterfeit Drugs.* WHO/EDM/QSM/99.1. Geneva: WHO.
3. GPHF Minilab manuals

4. Kenyon, A. S. 1999. *Rapid Screening of Tuberculosis Pharmaceuticals by Thin-Layer Chromatography.* St. Louis, MO: U.S. Food and Drug Administration. <http://www.pharmweb.net/pwmirror/library/tlc/TBDRUGS.pdf >
5. TFDA List of Registered Products

Special Instructions

The following forms may need to be filled in during the execution of this SOP:

1. POE Physical Examination Results Form
2. Facility Physical Examination Results Form
3. POE Screening Certificate
4. Facility Screening Certificate
5. Sample Receipt Form (annexed)
6. Confiscation/Quarantine Form (annexed)

Procedure

The procedure described in this SOP requires the drug inspector to collect and screen all suspicious samples using GPHF Minilab procedures (if possible). Samples that require further testing should be sent to the TFDA DQCL. For each suspicious sample to be sent for further testing, collect sample(s) as indicated in Table 4 below. If these amounts are not available, collect what is available.

Table 4. Preferred Sample Size from Each Batch

Dosage Form	Preferred Sample Size from Each Batch
Tablets/capsules	100 tablets/capsules
Suppositories/ovules	20 suppositories/ovules
Powders/sachets	20 packets/sachets
Injectables (ampoules)	20 ampoules
Injectable (vials)	20 vials
Eyedrops	6 bottles
Syrups	6 bottles
IV Fluids	6 bottles

For an example of how to determine the number of unopened unit pack(s) for testing, see Table 5 below.

Table 5. Example of Sample Size Determination

Description	Batch No.	Unit Pack	Number of Unit Packs to Be Collected
Aspirin tablets	020717F	T/1,000's	1
Clotrimazole pessary	BF86	P/6's	4
Dextrose IV solution	U7MW3	B/24 × 100 mL	6

After the sample is collected:

1. Complete a Sample Receipt Form for each sample collected.

2. Explain details of the sample on the continuation page of the SRF.

3. Assign and mark each sample with a number from the respective SRF. The following sample numbering system is recommended: Date, month, year, region abbreviation, inspection number (REG sequence number); for example, 150502ARU1 = Inspection number 1 conducted in the Arusha Region on May 15, 2002. See Table 6 for inspection site abbreviations.

Table 6. Inspection Sites and Abbreviations

Inspection Site	Inspection Site Abbreviation
Arusha Region	ARU
Dar es Salaam Region (including MSD)	DAR
Dar es Salaam Airport	DIA
Dar es Salaam Harbour	DRH
Kilimanjaro Region (Moshi and vicinity)	KIL
Mara Region	MAR
Medical Stores Department Headquarters	MSD
Mwanza Region	MWA
Namanga Port of Entry	NAM
Sirari Port of Entry	SIR

Samples that require further testing should be sent to the TFDA DQCL in accordance with chain of custody, packaging, and shipping SOP No. TFDAINS 004.

SOP for Drug Quality Surveillance Programme: Antimalarials (SPD 02-01)

TANZANIA FOOD AND DRUGS AUTHORITY DIRECTORATE OF INSPECTIONS AND SURVEILLANCE STANDARD OPERATING PROCEDURE				
TITLE: DRUG QUALITY SURVEILLANCE PROGRAMME: ANTIMALARIALS **Artesunate, quinine hydrochloride, quinine sulfate/bisulfate, and sulfadoxine/pyrimethamine** ***(Refers to POE Consignment Inspection Form)***				
SOP NO.: **SPD 02-01**	**SUPERSEDES:** **None**	**DATE OF ISSUE:** **Nov. 2002**	**EFFECTIVE DATE:** **Nov. 2002**	**NEXT REVIEW DATE:** **June 2006**

Objective

The purpose of this standard operating procedure, SOP No. SPD 02-01, is to describe how to conduct testing and follow-up action for the antimalarials listed above in the title box. Instructions contained in this SOP must be followed when conducting testing of these products. The instructions refer to the POE Consignment Inspection Form and the Drug Dispensing Outlet (Part I, Part II, Dispensary) Inspection Forms for postmarketing surveillance.

Scope

This SOP details the procedure for testing of antimalarials collected at ports of entry and for postmarketing surveillance.

Responsibility

The Director-General, Director of Inspections and Surveillance, Director of Product Evaluation and Registration, Director of Laboratory Services, Chief Drug Inspector, drug inspectors, and drug laboratory analysts shall ensure implementation of this SOP.

Accountability

The Director of Inspections and Surveillance is accountable for the implementation of this SOP.

Distribution

The Director-General, Director of Inspections and Surveillance, Director of Product Evaluation and Registration, Director of Laboratory Services, Chief Drug Inspector, drug inspectors, and drug laboratory analysts should receive copies.

References

1. GPHF Minilab manuals
2. Kenyon, A. S. 1999. *Rapid Screening of Tuberculosis Pharmaceuticals by Thin-Layer Chromatography.* St. Louis, MO: U.S. Food and Drug Administration. <http://www.pharmweb.net/pwmirror/library/tlc/TBDRUGS.pdf >
3 World Health Organization (WHO). 1991. *Basic Tests for Pharmaceutical Dosage Forms.* Geneva: WHO.
4. TFDA List of Registered Products
5. *Drug Defect Reference* CD

Special Instructions

The following forms may need to be filled in during execution of this SOP:

1. POE Physical Examination Results Form
2. Facility Physical Examination Results Form
3. POE Consignment Inspection Form
4. Drug Dispensing Outlet Inspection Forms
5. Rejection/Detention Form (annexed)
6. Sample Receipt Form (annexed)
7. Confiscation/Quarantine Form (annexed)

Sampling and Testing Procedures

The procedure described in this SOP consists of two sections. The sections relate to the POE Consignment Inspection Form and the POE/Facility Physical Examination Forms. These forms must be used to record results of testing of consignment samples at POEs and samples collected for the purpose of postmarketing surveillance. Each section of the forms clearly indicates the tests and the pass-or-fail decision(s) to be made by the designated official of the TFDA responsible for the inspection and/or testing of the drugs.

Sampling

After assessing the need to take samples for testing, the inspector shall follow the sampling plan summarised in Tables 4 and 5.

Table 7. Preferred Sample Size from Each Batch

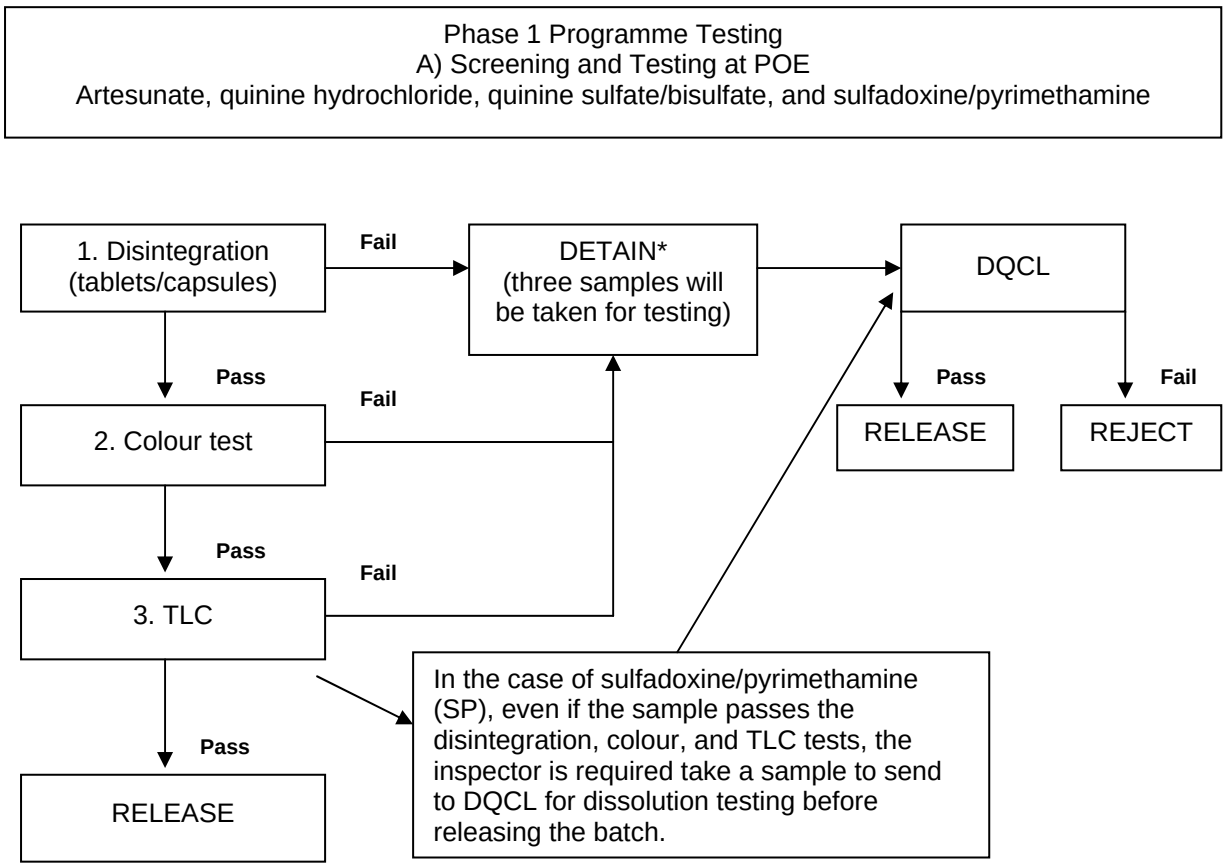
Dosage Form	Minimum Sample Size
Tablets/capsules	100 tablets/capsules
Suppositories/ovules	20 suppositories/ovules
Powders/sachets	20 packets/sachets
Injectables (ampoules)	20 ampoules
Injectables (vials)	20 vials
Eyedrops	6 bottles
Syrups	6 bottles
IV fluids	6 bottles

Table 8. Example of Sample Size Determination (Based on Sampling Plan Shown in Table 7)

Description	Batch Number	Unit Pack	Number of Unit Packs to Be Collected
Quinine bisulfate tablets	020717F	T/500's	1
Clotrimazole pessary	BP86	P/6's	4
Ciprofloxacin injection	U7MW3	24's x 100 mL	6
Artesunate tablets	02F12	P/6's	17

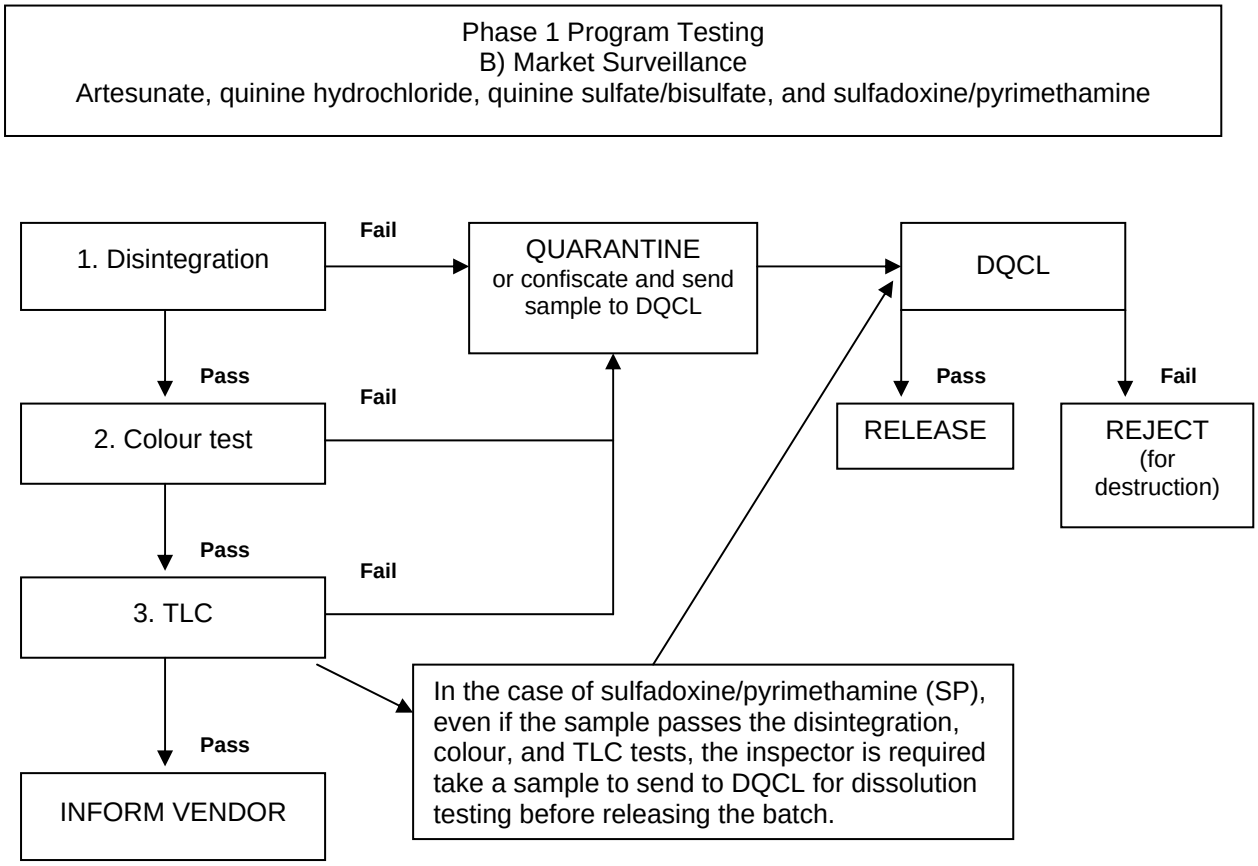
Testing

For each sample taken at a POE, the tests and decision making should be done according to the following flowchart.



***Note:** Detain for a maximum of 10 working days; thereafter, effect conditional release. "Conditional release" means that the consignee is authorised to clear the consignment from the port of entry but not to distribute or sell the consignment until written approval is received from the TFDA.

For samples collected during postmarketing surveillance, the tests and decision making should be done according to the following flowchart.



Checked by:	**Approved by:**

The results of the screening tests should be reported using the appropriate Screening Certificate, depending on whether the samples were obtained as part of a POE or drug dispensing outlet inspection.

SOP for Drug Quality Surveillance Programme: Antibiotics (SPD 03-01)

TANZANIA FOOD AND DRUGS AUTHORITY DIRECTORATE OF INSPECTIONS AND SURVEILLANCE STANDARD OPERATING PROCEDURE				
TITLE: DRUG QUALITY SURVEILLANCE PROGRAMME: ANTIBIOTICS **Amoxicilline, ampicillin, ciprofloxacin, co-trimoxazole, erythromycin, and metronidazole** ***(Refers to POE Consignment Inspection Form)***				
SOP NO.: **SPD 03-01**	**SUPERSEDES:** **None**	**DATE OF ISSUE:** **Oct. 2003**	**EFFECTIVE DATE:** **Nov. 2003**	**NEXT REVIEW DATE:** **June 2006**

Objective

The purpose of this standard operating procedure, SOP No. SPD 03-01, is to describe how to conduct testing and follow-up action for the antibiotics listed in the title box. Instructions contained in this document must be followed when conducting testing of these products. The instructions refer to the POE Consignment Inspection Form and the Drug Dispensing Outlets (Part I, Part II, Dispensary) Inspection Forms.

Scope

This SOP details the procedure for testing of antibiotics collected at ports of entry and for postmarketing surveillance.

Responsibility

The Director-General, Director of Inspections and Surveillance, Director of Product Evaluation and Registration, Director of Laboratory Services, Chief Drug Inspector, drug inspectors, and drug laboratory analysts shall ensure implementation of this SOP.

Accountability

The Director of Inspections and Surveillance is accountable for the implementation of this SOP.

Distribution

The Director-General, Director of Inspections and Surveillance, Director of Product Evaluation and Registration, Director of Laboratory Services, Chief Drug Inspector, drug inspectors, and drug laboratory analysts should receive copies.

References

1. GPHF Minilab manuals
2. Kenyon, A. S. 1999. *Rapid Screening of Tuberculosis Pharmaceuticals by Thin-Layer Chromatography*. St. Louis, MO: U.S. Food and Drug Administration. <http://www.pharmweb.net/pwmirror/library/tlc/TBDRUGS.pdf >
3. World Health Organization (WHO). 1991. *Basic Tests for Pharmaceutical Dosage Forms*. Geneva: WHO.
4. TFDA List of Registered Products
5. *Drug Defect Reference* CD

Special Instructions

The following forms may need to be filled in during execution of this SOP:

1. POE Physical Examination Results Form
2. Facility Physical Examination Results Form
3. POE Consignment Inspection Form
4. Drug Dispensing Outlet (Part I, Part II, Dispensary) Inspection Forms
5. Rejection/Detention Form (annexed)
6. Sample Receipt Form (annexed)
7. Confiscation/Quarantine Form)(annexed)

Sampling and Testing Procedures

The procedure described in this SOP consists of two sections. The sections relate to the POE Consignment Inspection Form, the Drug Dispensing Outlet (Part I, Part II, Dispensary) Inspection Forms, and the POE/Facility Physical Examination Forms. These forms must be used to record results of testing of consignment samples at POEs and samples collected for the purpose of postmarketing surveillance. Each section of the forms clearly indicates the tests and the pass-or-fail decision(s) to be made by the designated official of the TFDA responsible for the inspection and/or testing of the drugs.

Sampling

After assessing the need to take samples for testing, the inspector shall follow the sampling plan presented in Tables 6 and 7.

Table 9. Minimum Sample Size to Be Taken from Each Batch for Testing

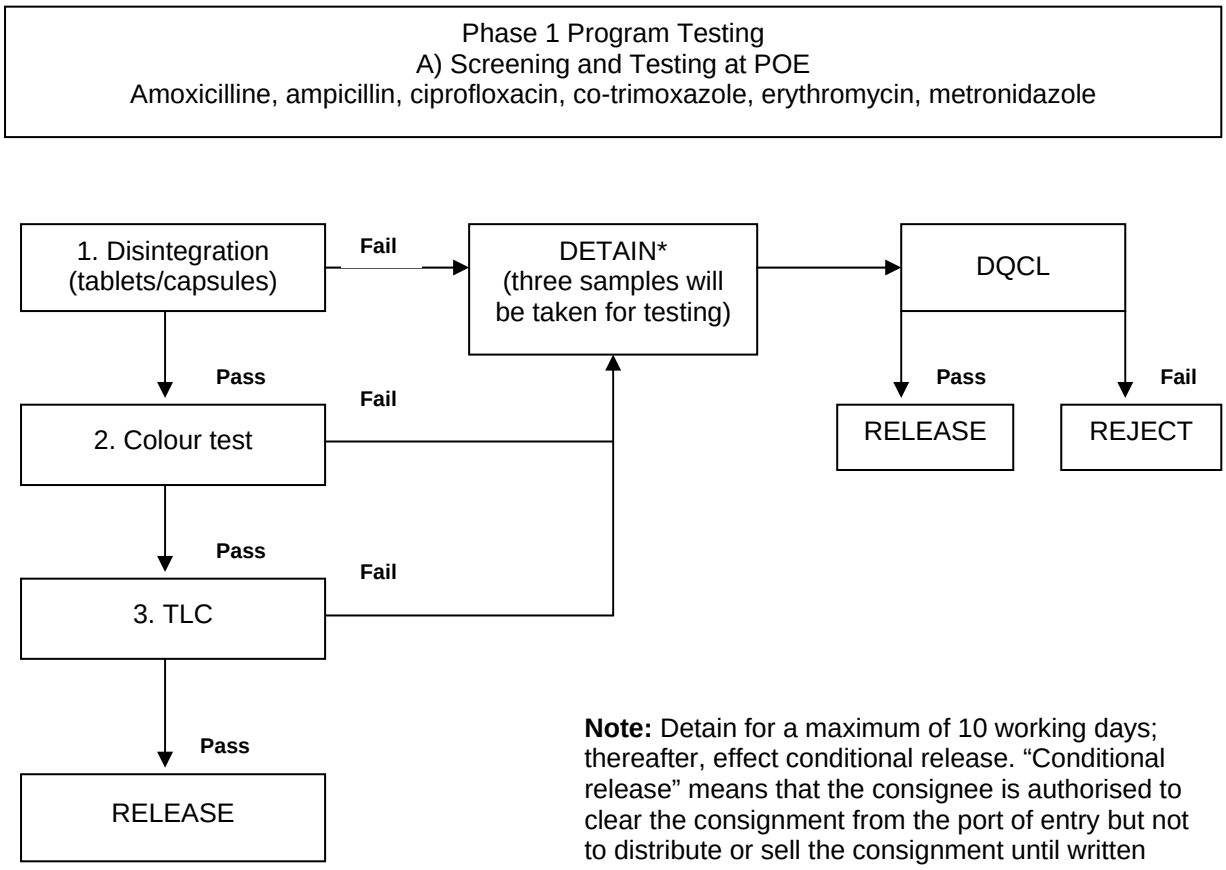
Dosage Form	Minimum Sample Size
Tablets/capsules	100 tablets/capsules
Suppositories/ovules	20 suppositories/ovules
Powders/sachets	20 packets/sachets
Injectables (ampoules)	20 ampoules
Injectables (vials)	20 vials
Eyedrops	6 bottles
Syrups	6 bottles
IV fluids	6 bottles

Table 10. Example of Sample Size for Different Products

Description	Batch Number	Unit Pack	Number of Unit Packs to Be Collected
Quinine hydrochloride	020717F	T/500's	500
Clotrimazole pessary	BP86	P/6's	4
Ciprofloxacin injection 100 mL	U7MW3	B/24's × 100 mL	6
Artesunate tablets	02F12	P/6's	17

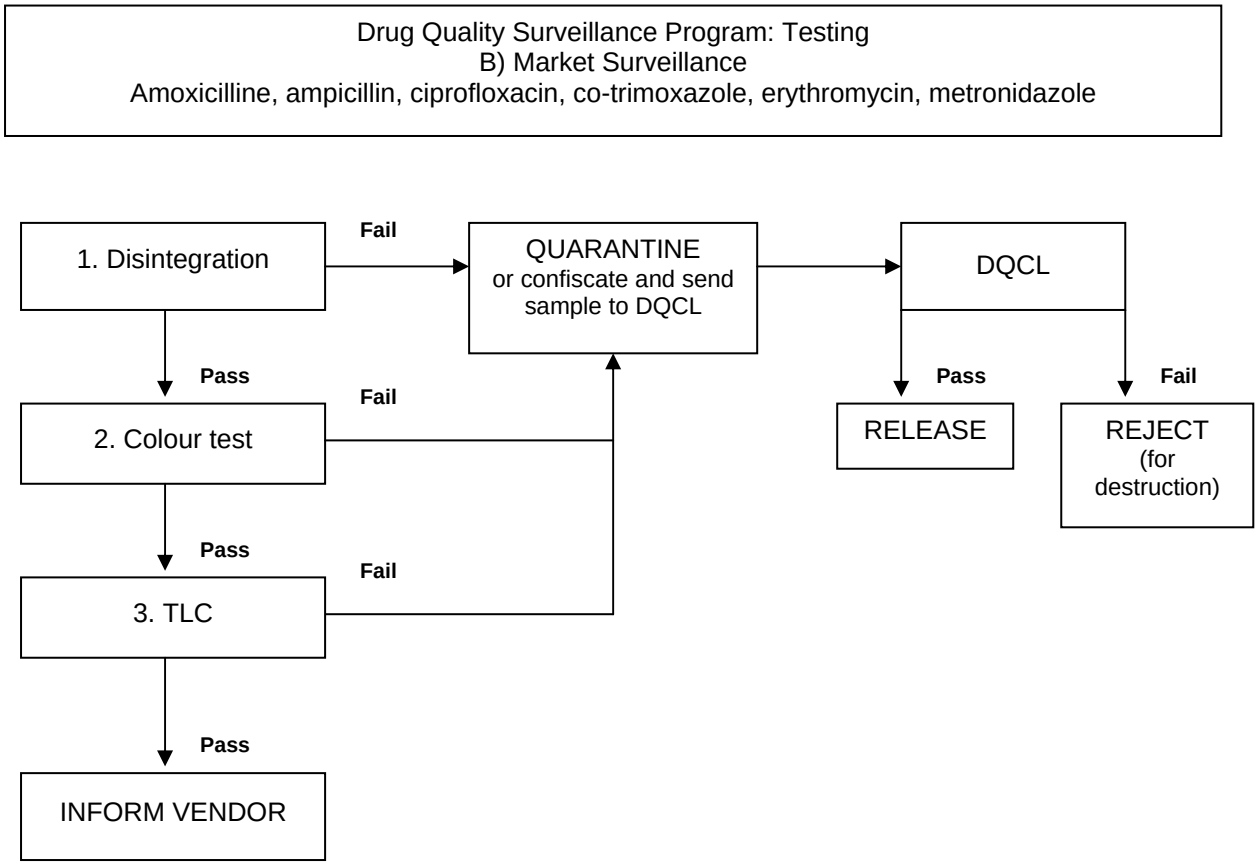
Testing

For each sample taken at a POE, the tests and decision making should be done according to the following flowchart.



Note: Detain for a maximum of 10 working days; thereafter, effect conditional release. “Conditional release” means that the consignee is authorised to clear the consignment from the port of entry but not to distribute or sell the consignment until written approval is received from the TFDA.

For samples collected during postmarketing surveillance, the tests and decision making should be done according to the following flowchart.



The results of the screening tests should be reported using the appropriate Screening Certificate (POE Screening Certificate or Facility Screening Certificate), depending on whether the samples were obtained as part of a POE or drug dispensing outlet inspection.

SOP for Drug Quality Surveillance Programme: Antiretrovirals (SPD 05-01)

TANZANIA FOOD AND DRUGS AUTHORITY DIRECTORATE OF INSPECTIONS AND SURVEILLANCE STANDARD OPERATING PROCEDURE				
TITLE: DRUG QUALITY SURVEILLANCE PROGRAMME: ANTIRETROVIRALS **Didanosine, indinavir, lamivudine, zidovudine, nevirapine, and stavudine** ***(Refers to POE Consignment Inspection Form)***				
SOP NO.: **SPD 05-01**	**SUPERSEDES:** **None**	**DATE OF ISSUE:** **February 2005**	**EFFECTIVE DATE:** **March 2005**	**NEXT REVIEW DATE:** **June 2006**

Objective

SOP No. SPD 05-01 describes how to conduct testing and follow-up actions for the above-cited products. Instructions contained in this document must be followed when conducting testing of these products.

Scope

This SOP describes the procedure for testing of drugs collected at POEs and for postmarketing surveillance.

Responsibility

The Director-General, Director of Inspections and Surveillance, Director of Product Evaluation and Registration, Director of Laboratory Services, Chief Drug Inspector, drug inspectors, and drug laboratory analysts shall ensure implementation of this SOP.

Accountability

The Director of Inspections and Surveillance is accountable for the implementation of this SOP.

Distribution

The Director-General, Director of Inspections and Surveillance, Director of Product Evaluation and Registration, Director of Laboratory Services, Chief Drug Inspector, drug inspectors, and drug laboratory analysts should receive copies.

References

1. GPHF Minilab manuals
2. Kenyon, A. S. 1999. *Rapid Screening of Tuberculosis Pharmaceuticals by Thin-Layer Chromatography*. St. Louis, MO: U.S. Food and Drug Administration. <http://www.pharmweb.net/pwmirror/library/tlc/TBDRUGS.pdf >
3. World Health Organization (WHO). 1991. *Basic Tests for Pharmaceutical Dosage Forms*. Geneva: WHO.

4. TFDA List of Registered Products
5. *Drug Defect Reference* CD

Special Instructions

The following forms may need to be filled in during the execution of this SOP:

1. POE Physical Examination Results Form
2. Facility Physical Examination Results Form
3. Rejection/Detention Form (annexed)
4. Sample Receipt Form (annexed)
5. Confiscation/Quarantine Form (annexed)

The following SOPs may need to be referred to when executing this SOP:

1. SOP No. SPD 02-00 Suspicious Sample Surveillance Programme

Sampling and Testing Procedures

The procedures described in this SOP consist of two sections. The sections relate to the POE Consignment Inspection Form and the POE and Facility Physical Examination Forms. These forms must be used to record results of testing of consignment samples at the POE and samples collected for the purpose of market surveillance. Each section of the forms clearly indicates the tests and the pass/fail decision(s) to be made by the designated official of the TFDA responsible for inspection and/or testing of the drugs.

Sampling

After assessing the need to take samples for testing, the inspector shall adhere to the following sampling plan.

Table 11. Sampling Plan

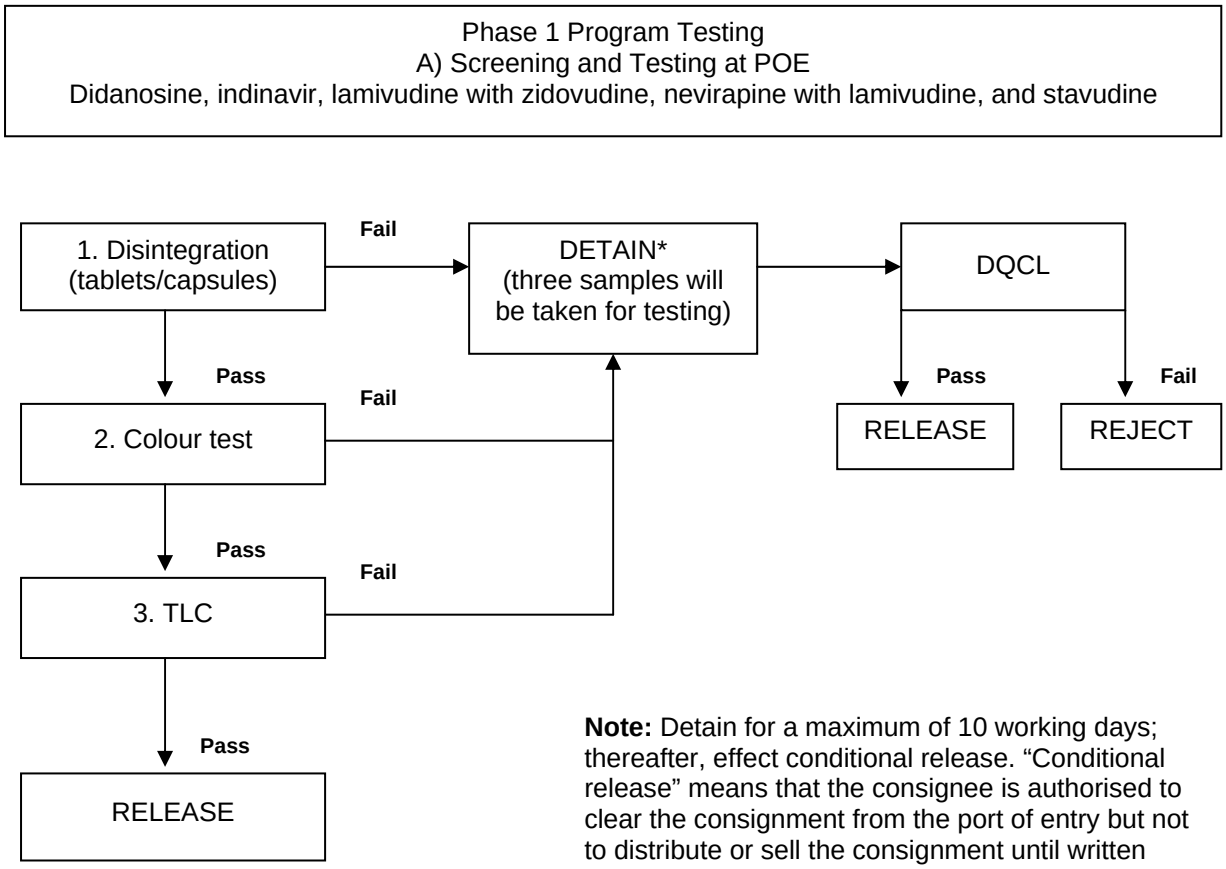
Dosage Form	Minimum Sample Size to Be Taken from Each Batch for Testing
Tablets/capsules	100 tablets/capsules
Suppositories/ovules	20 suppositories/ovules
Powders/sachets	20 packets/sachets
Injectables (ampoules)	20 ampoules
Injectables (vials)	20 vials
Eyedrops	6 bottles
Syrups	6 bottles
IV fluids	6 bottles

Table 12. Example of Sample Size for Different Products

Description	Batch Number	Unit Pack	Number of Unit Packs to Be Collected
Didanosine 500 mg tablets	020717F	T/500's	500
Lamuvidine syrup	BP86	B/100 mL	6 bottles

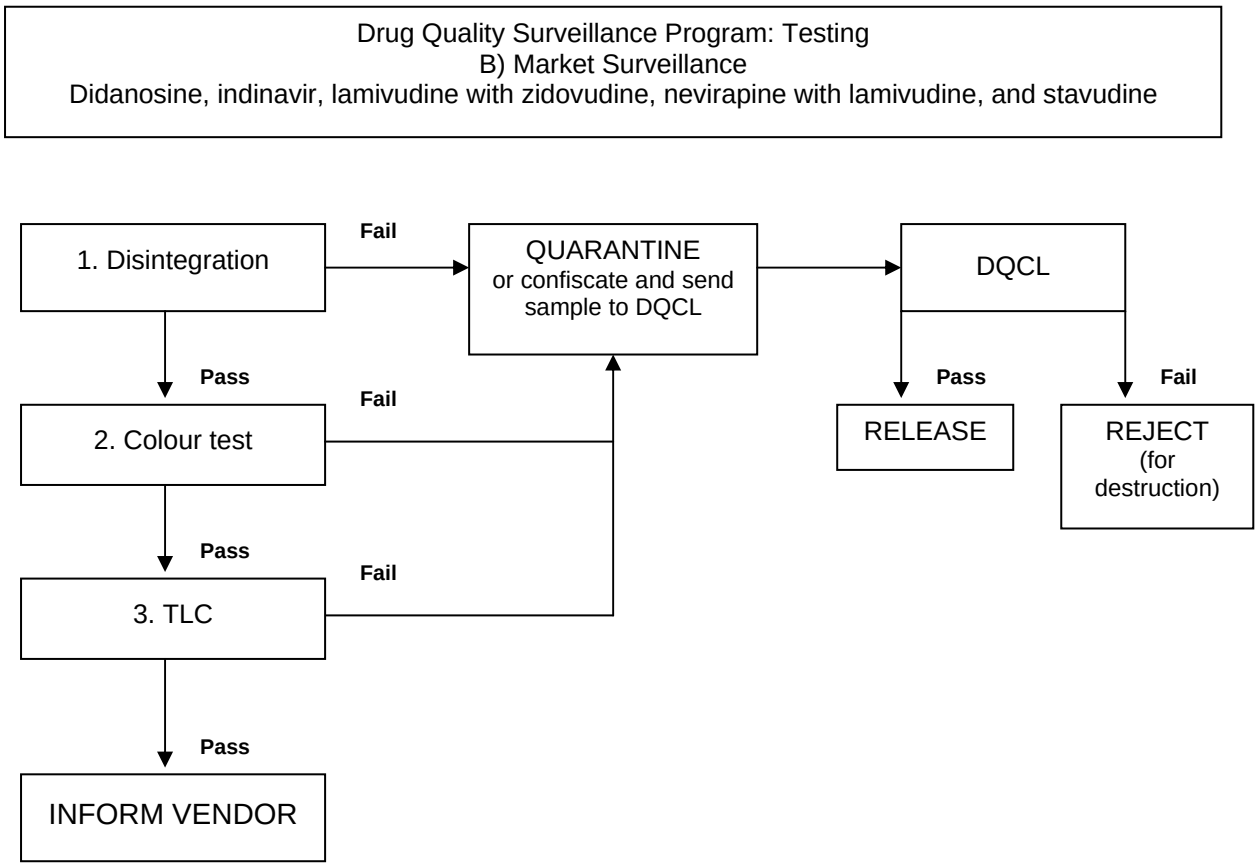
Testing

For each sample taken at the POE, the tests should be done and the indicated decisions made according to the following flowchart.



Note: Detain for a maximum of 10 working days; thereafter, effect conditional release. "Conditional release" means that the consignee is authorised to clear the consignment from the port of entry but not to distribute or sell the consignment until written approval is received from the TFDA.

For samples collected during postmarketing surveillance, tests should be done and the indicated decisions made according to the following flowchart.



Note: The results of the screening tests should reported using the appropriate screening certificate.

POE Screening Certificate

UNITED REPUBLIC OF TANZANIA
MINISTRY OF HEALTH

TANZANIA FOOD AND DRUGS AUTHORITY
Tel: +255-22-2450512/2450751
FAX: +255-22-2450793
Web site: http//www.tfda.or.tz

POE SCREENING CERTIFICATE

POE (circle)	DIA	DRH	MSD	NAM	SIR						
	KIA	MWA	MWH	HOR	TAN						
	HOL	KIG	TUN	KYE	MTW						
	MTU										
Date Sample Collected											
Control Type (circle)	**R**	**AWB**	**C21**	**C29**	**F89**						
Control Type Number											
Name of Importer/Consignee											
PRODUCT (circle one)	Amoxicilline Ampicillin Artesunate Ciprofloxacin Co-trimoxazole	Didanosine Erythromycin Indinavir Lamivudine Metronidazole	Nevirapine Quinine Stavudine Sulfadoxine/pyrimethamine Zidovudine								
Dosage Form (circle one)	Tablet	Capsule	Syrup	Suspension	Injection	Infusion					
	Lozenge	Pessary	Caplet	Suppository	Eyedrops	Eardrops					
	Ointment	Cream	Gel	Other (specify)							
Batch Number											
Date of Manufacture											
Expiry Date											
Manufacturer											
Country of Manufacture											
Label Claim											
Date of Analysis											

Prepared by:	**Checked by:**	**Approved by:**
Date:	**Date:**	**Date:**

TEST	RESULTS	
	Pass	Fail
Visual		
Disintegration		
Colour reaction		
Thin-layer chromatography		
If SP, date sent to TFDA		
FINAL RESULTS (circle)	PASS / FAIL	
COMMENTS		
ACTION TAKEN		

Screening done by: ……..
Signature: ……....
Date: ……....

Facility Screening Certificate

UNITED REPUBLIC OF TANZANIA
MINISTRY OF HEALTH

TANZANIA FOOD AND DRUGS AUTHORITY
Tel: +255-22-2450512/2450751
FAX: +255-22-2450793
Web site: http//www.tfda.or.tz

FACILITY SCREENING CERTIFICATE

Facility Type (circle)	**Warehouse**	**Wholesale/ Retail Part I**	**Retail Part I**	**DLDB (Part II)/ DLDM**	**Hospital**	**Health Centre**	**Dispensary**
Name of Facility							
Date Sample Collected							
PRODUCT (circle one)	Amoxicilline Ampicillin Artesunate Ciprofloxacin Co-trimoxazole	Didanosine Erythromycin Indinavir Lamivudine Metronidazole			Nevirapine Quinine Stavudine Sulfadoxine/pyrimethamine Zidovudine		
Dosage Form (circle one)	Tablet	Capsule	Syrup	Suspension	Injection	Infusion	
	Lozenge	Pessary	Caplet	Suppository	Eyedrops	Eardrops	
	Ointment	Cream	Gel	Other (specify)			
Batch Number							
Date of Manufacture							
Expiry Date							
Manufacturer							
Country of Manufacture							
Label Claim							

Prepared by:	**Checked by:**	**Approved by:**
Date:	**Date:**	**Date:**

TESTS	RESULTS	
	Pass	Fail
Visual		
Disintegration		
Colour reaction		
Thin-layer chromatography		
If SP, date sent to TFDA		
FINAL RESULTS (circle)	PASS / FAIL	
COMMENTS		
ACTION TAKEN		

Screening done by: ……..
Signature: ……....
Date: ……....

Chapter 4. Postmarketing Surveillance Programme, Inspection of Drug Dispensing Outlets, and Chain of Custody

Surveillance of quality of drugs is one way of ensuring that drugs of questionable quality are removed from the market.

During postmarketing surveillance, inspectors shall conduct systematic inspections (according to established procedures) of drug outlets (part II retail shops, part I pharmacies, wholesalers, dispensaries, and hospitals). The aim is to ensure that these facilities meet the required minimum standards, are operating legally, and do not stock drugs of questionable quality.

As the collected samples may be used as evidence in a court of law, sample handling and transferring must be done according to the procedures outlined in the SOP for chain of custody (TFDAINS 004).

This chapter describes issues pertaining to the inspection of drug dispensing outlets, collection of suspicious drug samples from such outlets, and chain of custody.

Postmarketing Surveillance and Chain of Custody of Samples

Introduction

The chain of custody is the list of individuals who have had access to the collected sample materials. The chain begins with the first person to assume custody of the materials. Individuals who handle the secured materials but who do not compromise the seals or closures are not part of the chain. (Common Carrier employees who ship the secured materials are not part of the chain.)

Types of Collections

- Adverse reaction samples—generally compromised samples—have seals that have been broken; these materials include products associated with unexpected illnesses or deaths.
- Products reported to be ineffective—generally a group of findings, not a single incident.
- Suspicious samples—generally in unopened containers.
- Labelling or containers that seem incorrect.
- Routine surveillance samples—generally in unopened containers.

Purpose of Maintaining the Chain

- The collected materials may be used as evidence in a legal proceeding and must be protected to have status in court.
- The collected materials are not a tourist site—only individuals with a need to access the material should do so.

Breaks in the Chain

- Any actual or potential unrecorded access to the material breaks the chain. Materials must be either under seal or under strict control at all times.
- Any unauthorised person who accesses the secured material (i.e., breaks security) ends the chain.
- The chain is maintained to document who had access to the evidence.

The End of the Chain

- The chain status ends after it is determined the evidence will not be used in a legal proceeding.
- The collected materials are property of the government and should be destroyed at the conclusion of the findings.
- Apart from documenting handling fraud, the chain has no status after the sample is destroyed or taken out of active inventory.

Law Enforcement

- The food and drug laws are commerce laws, not criminal laws.
- If you uncover possible criminal violations of the law, abandon your investigation and turn the matter over to criminal investigators.
- DON'T EVER PUT YOUR LIFE IN JEOPARDY!

It is impossible to move from an unregulated marketplace to a regulated marketplace overnight. In a free society, it will take years before all players understand and accept compliance as the proper way to do business.

Remember, your job is to help protect the health of the people by assuring that products you regulate comply with the required standards, and to help protect the integrity of the marketplace so that a conscientious person can compete.

> "The right quality and uniformity are foundations of commerce, prosperity and peace."
>
> W. E. Deming

> "The commitment to quality must begin with the highest level of institutional management and extend from there to all other levels in the organization."
>
> W. E. Deming

SOP for Postmarketing Surveillance Programme: Dispensing Outlets Inspection (TFDAINS 003)

TANZANIA FOOD AND DRUGS AUTHORITY DIRECTORATE OF INSPECTIONS AND SURVEILLANCE STANDARD OPERATING PROCEDURE				
TITLE: POSTMARKETING SURVEILLANCE PROGRAMME: DISPENSING OUTLETS INSPECTION				
SOP NO.: **TFDAINS 003**	**SUPERSEDES:** **None**	**DATE OF ISSUE:** **Nov. 2002**	**EFFECTIVE DATE:** **Nov. 2002**	**NEXT REVIEW DATE:** **June 2006**

Objective

The purpose of this standard operating procedure is to outline the procedures drug inspectors must follow when undertaking inspection of dispensing outlets. Dispensing outlets in this context include, but are not limited to, pharmaceutical warehouses, wholesalers (including the Medical Stores Department), pharmacy (part I drug) shops, part II drug shops, hospitals, health centres, and dispensaries.

Scope

This SOP details the procedures for conducting inspection of the above-cited outlets. The SOP covers the following areas: general particulars of the premises, type of inspection being conducted, personnel, general condition of the premises, security of premises, storage conditions, availability of ancillary items, record-keeping and documentation, product labelling examination, sample collection for further testing, reference materials available at the premises, any other relevant observations made by the inspectors, recommendations made by the inspectors, owner/officer in charge of premises, declaration/acceptance of findings, and observations of inspectors and the name(s) and signature(s) of inspector(s) who conducted the inspection. Inspection findings and observations must be recorded in the appropriate Drug Dispensing Outlets Inspection Form.

Responsibility

The Director-General, Director of Inspections and Surveillance, Director of Laboratory Services, Chief Drug Inspector, drug inspectors, and drug laboratory analysts shall ensure implementation of this SOP.

Accountability

The Director of Inspections and Surveillance is accountable for the implementation of this SOP.

Distribution

The Director-General, Director of Inspections and Surveillance, Director of Laboratory Services, Chief Drug Inspector, drug inspectors, and drug laboratory analysts should get copies.

References

1. World Health Organisation (WHO) Expert Committee on Specifications for Pharmaceutical Preparations. 1999. *Guidelines for Inspection of Drug Distribution Channel*s. 35th Report. WHO Technical Report Series No. 885, Annex 6. Geneva: WHO.
2. WHO. 1999. *Guidelines for the Development of Measures to Combat Counterfeit Drugs.* WHO/EDM/QSM/99.1. Geneva: WHO.
3. GPHF Minilab manuals
4. World Health Organization (WHO). 1991. *Basic Tests for Pharmaceutical Dosage Forms*. Geneva: WHO.
5. Kenyon, A. S. 1999. *Rapid Screening of Tuberculosis Pharmaceuticals by Thin-Layer Chromatography*. St. Louis, MO: U.S. Food and Drug Administration. <http://www.pharmweb.net/pwmirror/library/tlc/TBDRUGS.pdf >
6. *Drug Defect Reference* CD
7. TFDA List of Registered Products

Special Instructions

The following forms may need to be filled in during the execution of this SOP:

1. Drug Dispensing Outlet Inspection Forms (TFDAINS Forms 004–009)
2. Sample Receipt Form (annexed)
3. Confiscation/Quarantine Form (annexed)

Procedure

Preparation

Inspectors must prepare themselves for the inspection by collecting all the tools needed to conduct the inspection judiciously and thoroughly. Preparation for inspection of the premises should include an introduction to the person in charge.

Introduction to Person in Charge of Premises

Upon reaching the premises where the inspection is to take place, the inspection must begin with the introduction of the inspector(s) to the person in charge of or responsible for the premises. Inspector(s) must present their credentials and a notice describing the purpose of the inspection to the individual in charge.

Conducting the Inspection

Inspectors should conduct the inspection systematically using the appropriate Drug Dispensing Outlet Inspection Forms (TFDAINS Forms 004–009) and record accordingly their findings and observations.

The following instructions refer to the Drug Dispensing Outlet Inspection Forms.

1. General Particulars of the Outlet

1.1 This subsection requires the inspector to circle the region where the outlet is located.

1.2 This subsection requires the inspector to write the name of the outlet being inspected.

1.3 This subsection requires the inspector to circle the type of outlet being inspected. The following forms are available for recording the inspectional findings:

- Inspection Form for Pharmacies/Wholesalers (TFDAINS Form 004)
- Abbreviated Inspection Form for Pharmacies/Warehouses (TFDAINS Form 005)
- Inspection Form for Hospitals, Health Centres, and Dispensaries (TFDAINS Form 006)
- Abbreviated Inspection Form for Hospitals, Health Centres, and Dispensaries (TFDAINS Form 007)
- Inspection Form for Duka la Dawa Baridi and Muhimu(TFDAINS Form 008)
- Abbreviated Inspection Form for Duka la Dawa Baridi and Muhimu (TFDAINS Form 009)

1.4 This subsection requires the inspector to write the mailing address of the outlet in the space provided.

1.5 This subsection requires the inspector to write the physical location/address of the outlet in the space provided.

1.6 This subsection requires the inspector to write the telephone number of the outlet in the space provided.

1.7 This subsection requires the inspector to write the fax number of the outlet in the space provided.

1.8 This subsection requires the inspector to write the e-mail address of the outlet in the space provided.

1.9 This subsection requires the inspector to write the premises licence number in the space provided.

1.10 Ascertain if the licence is valid (Y) or not (N).

1.11 Indicate whether the original licence is displayed (Y) or not (N).

1.12 This subsection requires the inspector to fill in the name of the pharmacist in charge of the facility in the case of Part I retail; wholesale pharmacies or warehouses; and hospitals, health centres, or dispensaries.

1.13 This subsection requires the inspector to fill in the pharmacist registration number.

1.14 This subsection requires the inspector to indicate whether the pharmacist's Certificate of Registration is displayed (Y) or not (N).

1.15 This subsection requires the inspector to write the date of inspection of the outlet in the space provided.

1.16 This subsection requires the inspector to write the date of the last inspection of the outlet in the space provided.

1.17 This subsection requires the inspector to write the name of the owner of the outlet in the space provided.

1.18 This subsection requires the inspector to ascertain whether the owner is a pharmacist, and if not, whether the owner has a valid contract with a registered pharmacist.

2. Personnel

This section requires the inspector to collect information on the status and qualifications of personnel at the facility being inspected. The inspector should ascertain and record the following particulars:

2.1 For the person responsible/in-charge of the premises

2.1.1 Name
2.1.2 Qualification
2.1.3 Position or title

2.2 For sales staff

2.2.1 Name
2.2.2 Qualification(s)

3. Type of Inspection

This section requires the inspector to circle the type of inspection being conducted and whether postmarketing surveillance is performed. Definitions of the categories/types of inspection are given in Chapter 1.

Note: If the purpose of the inspection is postmarketing surveillance, the inspector should skip the sections dealing with the general conditions of the premises, security of premises, storage conditions, ancillary items, record-keeping and documentation, and reference materials. The major focus of the postmarketing surveillance inspection shall be on physical examination of the products, including labels; ascertaining the legality of the products on stock; and/or taking samples of suspicious products for the surveillance programme.

4. General Condition of the Premises

Inspectors should be familiar with the requirements/standards set by the TFDA in respect to:

- Warehouses for the storage of pharmaceuticals
- Wholesale outlets
- Retail outlets (Part I)
- Retail outlets (Part II)
- Hospitals/health centres/dispensaries

This section requires the inspector to ascertain and record the appropriateness of the premises for the intended purpose in respect to:

4.1.1 Layout
4.1.2 Size/number of rooms
4.1.3 Hygiene
4.1.4 State of repair
4.1.5 Ventilation and cooling system
4.1.6 Lighting
4.1.7 Display of drugs
4.1.8 Utilities: water, handwash basins, WC

In case of nonconformity to any of the above, explain the reason in the space provided on the form. If the space provided on this form is not enough, use the separate continuation pages that are attached to the form.

5. Security of Premises

The inspector must ascertain and record the security of the premises in respect to:

5.1.1 External perimeter security structures (fencing, gates, walls, windows, etc.)
5.1.2 Special secure cupboards for restricted (controlled) drugs
5.1.3 Accessibility to unauthorised person(s)
5.1.4 Documents/record-keeping

In case of nonconformity to any of the above, explain the reason in the space provided on the form. If the space provided on this form is not enough, use the separate continuation pages that are attached to the form.

6. Storage Conditions

This section requires the inspector to ascertain and record the suitability of the storage conditions for the intended purpose in respect to:

6.1.1 Durability of floor and ease of cleaning
6.1.2 Prevention of infestation by vermin and pests
6.1.3 Adequate shelving
6.1.4 Pallets
6.1.5 Execution of stock rotation on the basis of first expiry, first out (FEFO)
6.1.6 Storage of returned/recalled/expired/quarantined goods
6.1.7 Availability and appropriateness of cold rooms or refrigerators for the storage of vaccines and/or biologicals

In case of nonconformity to any of the above, explain the reason in the space provided on the form. If the space provided in this form is not enough, use the separate continuation pages that are attached to the form.

7. Ancillary Items

If the facility does compounding, this section requires the inspector to ascertain and record the availability and suitability of ancillary items for the intended purpose in respect to the following items:

7.1.1. Hotplate(s) or any other source of heat
7.1.2. Weighing balance(s) and weights
7.1.3. Dispensing measures (measuring cylinders, beakers, etc.)
7.1.4. Source of clean and safe water
7.1.5. Mortar and pestle, spatula, and dispensing tray

In case of nonconformity to any of the above, explain the reason in the space provided on the form. If the space provided on this form is not enough, use the separate continuation pages that are attached to the form.

8. Record-Keeping and Documentation

This section requires the inspector to ascertain and record the suitability of record-keeping and documentation for intended use in respect to:

8.1.1. Prescription Book
8.1.2. Poison Book
8.1.3. Controlled Drugs Register
8.1.4. Written procedures for maintenance of cold-chain product
8.1.5. Import Permit
8.1.6. Ledger Book or an appropriate inventory control system
8.1.7. TFDA-endorsed Pro Forma Invoices
8.1.8. Receipts/invoices
8.1.9. Copies of delivery notes
8.1.10. Accuracy of record-keeping
8.1.11 Check if the physical stock of the narcotic/psychotropic drugs match those on the Register
8.1.12 Ensure that the prescriptions for narcotic/psychotropic drugs are written by qualified personnel and are kept according to regulations
8.1.13. Endorsement of entries by authorised person(s)
8.1.14. Written procedures for handling returned, recalled, and/or expired drugs
8.1.15 Written procedures for dealing with complaints and/or adverse reaction reports

In case of nonconformity to any of the above, explain the reason in the space provided on the form. If the space provided in this form is not enough, use the separate continuation pages that are attached to the form.

9. Reference Materials

This section requires the inspector to ascertain and record the availability of appropriate reference materials kept at the facility, including the following basic required materials:

9.1.1 *Tanzania National Formulary* (current edition)

9.1.2 *Tanzania Pharmaceutical Handbook*

9.1.3 Tanzanian Food, Drug and Cosmetics Act 2003 and its corresponding regulations and guidelines

9.1.4 Standard treatment guidelines

9.1.5 National essential drugs list

9.1.6 Current list of registered drugs

9.1.7 Pharmaceuticals and Poisons Act 1978 and its corresponding regulations and guidelines

9.1.8 *Good Dispensing Manual* (Swahili/English versions)

9.1.9 *British National Formulary*

9.1.10 *British Veterinary Codex*

In case of nonconformity to any of the above, explain the reason in the space provided on the form. If the space provided in this form is not enough, use the separate continuation pages that are attached to the form.

10. Legality of Stocked Products

This section requires the inspector to determine whether there are unregistered or unauthorised products stocked on the premises.

11. Product Label Examination

This section requires the inspector to examine the labels of the products in stock and evaluate them in respect to:

11.1.1. Language of labels and package inserts
11.1.2. Any signs of tampering on the labels
11.1.3 Labelling requirements

In case of nonconformity to any of the above, explain in the space provided on the form. If the space provided in this form is not enough, use the separate continuation pages that are attached to the form.

12. Samples for Examination

This section requires the inspector to take samples of drugs in the surveillance programme and/or suspicious samples for screening and testing in accordance with SPD 02-00, SPD 02-01, SPD 03-01, or SPD 05-01, as appropriate.

13. Other Observations

This section requires the inspector to record any other observations in the space provided in the form. If the space provided in this form is not enough, use the separate continuation pages that are attached to the form.

14. Recommendations

This section requires the inspector to make recommendations based on the findings of the inspection. The recommendation should be written in the space provided on the form. If the space provided in this form is not enough, use the separate continuation pages that are attached to the form.

15. Owner's/In-Charge Declaration

This section requires the inspector to give a copy of his/her findings and other observations to the owner or person in charge. The owner or the person in charge of the premises should read the copy and then write his/her name in the space provided and sign and date the declaration.

16. Name(s) and Signature(s) of Inspector(s)

This section requires the inspector to testify that the findings and other observations he/she made are true and correct by writing his/her name in the space provided and signing and dating the inspection form to conclude the inspection.

Drug Dispensing Outlet Inspection Form for Retail Pharmacies and Wholesalers (TFDAINS Form 004)

UNITED REPUBLIC OF TANZANIA
MINISTRY OF HEALTH

TANZANIA FOOD AND DRUGS AUTHORITY
Tel: +255-22-2450512/2450751
FAX: +255-22-2450793
Web site: http//www.tfda.or.tz

PART I DRUG DISPENSING OUTLET INSPECTION FORM (RETAIL PHARMACIES AND WHOLESALERS)

1. General

1.1	Region where the facility is situated (circle one on the list below)				
Arusha Dar es Salaam Dodoma Iringa	Kagera Kigoma Kilimanjaro Lindi	Manyara Mara Mbeya Morogoro Mtwara	Mwanza Pwani Rukwa Ruvuma Shinyanga	Singida Tabora Tanga	
1.2	Name of Outlet:				
1.3	Type: (circle) Warehouse Wholesale Wholesale/Retail (Part I) Retail Part I				
1.4 Mailing Address: ……..……..... ……..……..... 1.6	Telephone Number:	1.5 Physical Address/Location: Street/Ward……..... District……..... 1.7	Fax Number:		
1.8	E-mail Address:				
1.9	Premises Licence Number:	1.10	Is the licence valid? Y / N	1.11	Is the original licence displayed? Y / N
1.12	Name of Pharmacist in Charge:	1.13	Pharmacist Registration Number:	1.14	Is the Certificate of Registration displayed? Y / N
1.15	Date of Inspection:	1.16	Date of Last Inspection:		
1.17	Ownership/Name of Proprietor(s):				
1.18	If the owner is not a pharmacist, does he/she have a valid contract with a registered pharmacist? Y/ N/ NA				

Prepared by:	**Checked by:**	**Approved by:**
Date:	**Date:**	**Date:**

2. Personnel

2.1 Responsible Staff (other than the pharmacist in charge)

2.1.1	Name:	
2.1.2	Qualification:	
2.1.3	Position/Title:	

2.2 Sales Person(s)

2.2.1	Name	2.2.2	Qualifications
1.			
2.			
3.			

3. Type of Inspection

3.1. Circle one: Announced/Unannounced	3.2 Circle one: Routine, Concise, Follow-up, Special, Investigative	3.3 Postmarketing surveillance done? Y / N If yes, go to #10. If no, go to #4.

4. General Condition of Premises

4.1	Is the premises appropriate for the intended purpose in respect to: (please indicate Y for yes [pass] or N for no [fail])				
		Warehouse	**Wholesale**	**Wholesale/ Retail**	**Retail Part I**
4.1.1	Layout (display, dispensing, and storage room accessible and well secured against unauthorised entry)				
4.1.2	Size/number of rooms (warehouse and stores: enough space to minimise mix-ups; retail: separate rooms for display, dispensing, and storage)				
4.1.3	Hygiene (clean and free from debris)				
4.1.4	State of repair (no cracks or crevices on the floor, smooth painted walls)				
4.1.5	Ventilation and cooling system (working and provides suitable temperatures for drug storage)				
4.1.6	Lighting (adequate to enable reading of labels)				
4.1.7	Display of drugs (only OTC drugs are displayed)				
4.1.8	Utilities: water, handwash basins, WC				
4.2	In case of nonconformity, explain: If space provided is not enough, please use continuation page(s).				

5. Security of Premises

5.1	Are the premises secure in respect to:				
		Warehouse	**Wholesale**	**Wholesale/Retail**	**Retail Part I**
5.1.1	External perimeter security (fencing, gates, walls, windows, etc.)				
5.1.2	Special secure cupboards for restricted (controlled) drugs				
5.1.3	Accessibility to unauthorised person(s)				
5.1.4	Documents/records-keeping				
5.2	In case of nonconformity, explain: If space provided is not enough, please use continuation page(s).				

6. Storage Conditions

6.1	Are the storage conditions suitable for the intended purpose in respect to:				
		Warehouse	**Wholesale**	**Wholesale/ Retail**	**Retail Part I**
6.1.1	Durability of floor and ease of cleaning				
6.1.2	Prevention of infestation by vermin and pests				
6.1.3	Adequate shelving (no medicines are kept on the floor)				
6.1.4	Pallets				
6.1.5	Execution of stock rotation/FEFO				
6.1.6	Storage of returned/recalled/ expired/quarantined goods				
6.1.7	Cold rooms/refrigerators for the storage of vaccines and/or biologicals				
6.2	In case of nonconformity, explain: If space provided is not enough, please use continuation page(s).				

7. Ancillary Items

7.1	Does the facility do compounding? If yes, go to #7.2. If no, go to 8.	Y / N (circle)			
7.2	Are suitable ancillary items available for the intended purpose in respect to the follow items:				
		Warehouse	**Wholesale**	**Wholesale/Retail**	**Retail Part I**
7.2.1	Hotplate or any other source of heat				
7.2.2	Weighing balance(s) and weights				
7.2.3	Dispensing measures (measuring cylinders, beakers, etc.)				
7.2.4	Source of clean and safe water				
7.2.5	Mortar and pestle, spatula, and dispensing tray				
7.3	In case of nonconformity, explain: If space provided is not enough, please use continuation page(s).				

8. Record-Keeping and Documentation

8.1	Are record-keeping and documentation suitable for the intended use in respect to:				
		Warehouse	**Wholesale**	**Wholesale/Retail**	**Retail Part I**
8.1.1	Prescription Book				
8.1.2	Poison Book				
8.1.3	Controlled Drugs Register				
8.1.4	Written procedures for maintenance of cold-chain product				
8.1.5	Import Permit				
8.1.6	Ledger Book or an appropriate inventory control system				
8.1.7	TFDA-endorsed Pro Forma Invoices				
8.1.8	Receipts/invoices				
8.1.9	Copies of delivery notes				
8.1.10	Accuracy of record-keeping				
8.1.11	Do the physical quantities of narcotic/psychotropic drugs match those on the Register?				
8.1.12	Are the prescriptions for narcotic/psychotropic drugs written by duly qualified medical personnel and properly kept?				
8.1.13	Endorsement of entries by authorised person(s)				
8.1.14	Written procedures for handling returned, recalled, and/or expired drugs				

8.1.15	Written procedures for dealing with complaints and/or adverse reaction reports				
8.2	In case of nonconformity, explain: If space provided is not enough, please use continuation page(s).				

9.0 Reference Materials

9.1	Are appropriate reference material(s) available?				
		Warehouse	**Wholesale**	**Wholesale/Retail**	**Retail Part I**
9.1.1	*Tanzania National Formulary* (TNF)				
	Indicate edition of TNF				
9.1.2	*Tanzania Pharmaceutical Handbook*				
9.1.3	Tanzanian Food, Drug and Cosmetics Act 2003 and its corresponding regulations and guidelines				
9.1.4	Standard treatment guidelines				
9.1.5	National essential drugs list				
9.1.6	Current list of registered drugs				
9.1.7	Pharmaceuticals and Poison Act 1978 and its corresponding regulations and guidelines				
9.1.8	*Good Dispensing Manual* (Swahili/English versions)				
9.1.9	*British National Formulary*				
9.1.10	*British Veterinary Codex*				
9.2	In case of nonconformity, explain: If space provided is not enough, please use continuation page(s).				

10. Legality of Stocked Products

Note: In case of nonconformity, stop the inspection, confiscate the products, and fill in the Confiscation/Quarantine Form.

	Yes	No	Number of Products Confiscated
10.1 Are there unregistered products stocked on the premises?			
10.2 Are there unauthorised products in stock?			

11. Product Label Examination

11.1	Closely examine the products in stock and evaluate the labels in respect to:				
		Warehouse	**Wholesale**	**Wholesale/Retail**	**Retail Part I**
11.1.1	Language of labels and package inserts				
11.1.2	Any signs of tampering				
11.1.3	Labelling requirements				
11.2	In case of nonconformity, explain: If space provided is not enough, please use continuation page(s).				

12. Samples for Examination

12.1	Conduct physical examination on pharmaceutical products stocked in the facility according to SOP No. TFDAINS 002 and take samples of batches of antimalaria and antibiotic drugs included in the drug quality surveillance programme for GPHF Minilab screening. For suspicious antimalarials and antibiotics, take samples in accordance with SPD 02-00, SPD 02-01, SPD 03-01, or SPD 05-01, as appropriate.	
12.2	Number of batches of products sampled under the surveillance programme	
12.3	Number of batches of suspicious products sampled	

13. Any Other Observations

If space provided is not enough, please use continuation page(s).

14. Recommendations

Name and Address of Facility:	
Items requiring attention:	Actions agreed to be taken and timeline:

15. Owner's/In-charge Declaration

I/we, ……..……., the in-charge/owner of the said premises, certify the information and observations made on this sheet during the inspection of the premises to be true and correct.

Signature: …….....	Date: …….....

16.	**Name(s) of Inspector(s):**	**Signature(s) of Inspector(s)**
1.	……	
2.	……	
3.	……	
Date:		

Abbreviated Drug Dispensing Outlet Inspection Form for Retail Pharmacies and Wholesalers (TFDAINS Form 005)

UNITED REPUBLIC OF TANZANIA
MINISTRY OF HEALTH

TANZANIA FOOD AND DRUGS AUTHORITY
Tel: +255-22-2450512/2450751
FAX: +255-22-2450793
Web site: http//www.tfda.or.tz

ABBREVIATED PART I DRUG DISPENSING OUTLET INSPECTION FORM (RETAIL PHARMACIES AND WHOLESALERS)

1. General

1.1	Region where the facility is situated (circle one on the list below)				
Arusha Dar es Salaam Dodoma Iringa	Kagera Kigoma Kilimanjaro Lindi	Manyara Mara Mbeya Morogoro Mtwara	Mwanza Pwani Rukwa Ruvuma Shinyanga	Singida Tabora Tanga	
1.2	Name of Outlet:				
1.3	Type: (circle) Warehouse Wholesale Wholesale/Retail (Part I) Retail Part I				
1.4 Mailing Address: ……..…….. ……..……....		1.5 Physical Address/Location: Street/Ward……..... District……....			
1.6	Telephone Number:	1.7	Fax Number:		
1.8	E-mail Address:				
1.9	Premises Licence Number:	1.10	Is the licence valid? Y / N	1.11	Is the original licence displayed? Y / N
1.12	Name of Pharmacist in Charge:	1.13	Pharmacist Registration Number:	1.14	Is the Certificate of Registration displayed? Y / N
1.15	Date of Inspection:	1.16	Date of Last Inspection:		
1.17	Ownership/Name of Proprietor(s):				
1.18	If the owner is not a pharmacist, does he/she have a valid contract with a registered pharmacist? Y/ N/ NA				

Prepared by:	**Checked by:**	**Approved by:**
Date:	**Date:**	**Date:**

2. Personnel

2.1 Responsible Staff (other than the pharmacist in charge)

2.1.1	Name:	
2.1.2	Qualification:	
2.1.3	Position/Title:	

2.2 Sales Person(s)

2.2.1	Name	2.2.2	Qualifications
1.			
2.			
3.			

3. Type of Inspection

3.1. Circle one: Announced/Unannounced	3.2 Circle one: Routine, Concise, Follow-up, Special, Investigative	3.3 Postmarketing surveillance done? Y / N If yes, go to #10. If no, go to #4.

4. Legality of Stocked Products

Note: In case of nonconformity, stop the inspection, confiscate the products, and fill in the Confiscation/Quarantine Form.

	Yes	**No**	**Number of Products Confiscated**
4.1 Are there unregistered products stocked on the premises?			
4.2 Are there unauthorised products in stock?			

5. Product Label Examination

5.1	Closely examine the products in stock and evaluate the labels in respect to:				
		Warehouse	**Wholesale**	**Wholesale/Retail**	**Retail Part I**
5.1.1	Language of labels and package inserts				
5.1.2	Any signs of tampering				
5.1.3	Labelling requirements				
5.2	In case of nonconformity, explain: If space provided is not enough, please use continuation page(s).				

6. Samples for Examination

6.1	Conduct physical examination on pharmaceutical products stocked in the facility according to SOP No. TFDAINS 002 and take samples of batches of antimalaria and antibiotic drugs included in the drug quality surveillance programme for GPHF Minilab screening. For suspicious antimalarials and antibiotics, take samples in accordance with SPD 02-00, SPD 02-01, SPD 03-01, or SPD 05-01, as appropriate.	
6.2	Number of batches of products sampled under the surveillance programme	
6.3	Number of batches of suspicious products sampled	

7. Any Other Observations

If space provided is not enough, please use continuation page(s).

8. Recommendations

Name and Address of Facility:	
Items requiring attention:	Actions agreed to be taken and timeline:

9. Owner's/In-charge Declaration

I/we, ……..……., the in-charge/owner of the said premises, certify the information and observations made on this sheet during the inspection of the premises to be true and correct.

Signature: …….....	Date: …….....

10.	Name(s) of Inspector(s):	Signature(s) of Inspector(s)
1.	……	
2.	……	
3.	……	
Date:		

Drug Dispensing Outlet Inspection Form for Hospitals, Health Centres, and Dispensaries (TFDAINS Form 006)

UNITED REPUBLIC OF TANZANIA
MINISTRY OF HEALTH

TANZANIA FOOD AND DRUGS AUTHORITY
Tel: +255-22-2450512/2450751, FAX: +255-22-2450793
Web site: http//www.tfda.or.tz

DISPENSARY INSPECTION FORM
(HOSPITALS, HEALTH CENTRES, AND DISPENSARIES)

1. General

1.1	Region where the facility is situated (circle one on the list below)			
Arusha Dar es Salaam Dodoma Iringa	Kagera Kigoma Kilimanjaro Lindi	Manyara Mara Mbeya Morogoro Mtwara	Mwanza Pwani Rukwa Ruvuma Shinyanga	Singida Tabora Tanga
1.2	Name of Outlet:			
1.3	Type: (circle) Hospital Health Centre Dispensary			
1.4 Mailing Address: …… ……		1.5 Physical Address/Location: Street/Ward……..... District……..... ……		

1.6	Telephone Number:	1.7	Fax Number:		
1.8	E-mail Address:				
1.9	Premises Licence Number:	1.10	Is the licence valid? Y / N	1.11	Is the original licence displayed? Y / N
1.12	Name of Pharmacist in Charge:	1.13	Pharmacist Registration Number:	1.14	Is the Certificate of Registration displayed? Y / N
1.15	Date of Inspection:	1.16	Date of Last Inspection:		
1.17	Ownership/Name of Proprietor(s):				

Prepared by:	**Checked by:**	**Approved by:**
Date:	**Date:**	**Date:**

2. Personnel

2.1 Responsible Staff (other than the pharmacist in charge)

2.1.1	Name:	
2.1.2	Qualification:	
2.1.3	Position/Title:	

2.2 Other Dispensary Staff

2.2.1	Name	2.2.2	Qualifications
1.			
2.			
3.			

3. Type of Inspection

3.1. Circle one: Announced/Unannounced	3.2 Circle one: Routine, Concise, Follow-up, Special, Investigative	3.3 Postmarketing surveillance done? Y / N If yes, go to #10. If no, go to #4.

4. General Condition of Premises

4.1	Is the premises appropriate for the intended purpose in respect to: (please indicate Y for yes [pass] or N for no [fail])			
		Hospital	**Health Centre**	**Dispensary**
4.1.1	Layout (display, dispensing, and storage room accessible and well secured against unauthorised entry)			
4.1.2	Size/number of rooms (warehouse and stores: enough space to minimise mix-ups; retail: separate rooms for display, dispensing, and storage)			
4.1.3	Hygiene (clean and free from debris)			
4.1.4	State of repair (no cracks or crevices on the floor, smooth painted walls)			
4.1.5	Ventilation and cooling system (working and provides suitable temperatures for drug storage)			
4.1.6	Lighting (adequate to enable reading of labels)			
4.1.7	Display of drugs (only OTC drugs are displayed)			
4.1.8	Utilities: water, handwash basins, WC			
4.2	In case of nonconformity, explain: If space provided is not enough, please use continuation page(s).			

5. Security of Premises

5.1	Are the premises secure in respect to:			
		Hospital	**Health Centre**	**Dispensary**
5.1.1	Special secure cupboards for restricted (e.g., narcotic and psychotropic) drugs			
5.1.2	Do unauthorised persons have access to the secure storage areas?			
5.1.3	Documents/records-keeping			
5.2	In case of nonconformity, explain: If space provided is not enough, please use continuation page(s).			

6. Storage Conditions

6.1	Are the storage conditions suitable for the intended purpose in respect to:			
		Hospital	**Health Centre**	**Dispensary**
6.1.1	Durability of floor and ease of cleaning			
6.1.2	Prevention of infestation by vermin and pests			
6.1.3	Adequate shelving (no medicines are kept on the floor)			
6.1.4	Pallets			
6.1.5	Execution of stock rotation/ FEFO			
6.1.6	Storage of returned/recalled/ expired/quarantined goods			
6.1.7	Cold rooms/refrigerators for the storage of vaccines and/or biologicals			
6.2	In case of nonconformity, explain: If space provided is not enough, please use continuation page(s).			

7. Ancillary Items

7.1	Does the facility do compounding? If yes, go to #7.2. If no, go to 8.	Y / N (circle)		
7.2	Are suitable ancillary items available for the intended purpose in respect to the follow items:			
		Hospital	**Health Centre**	**Dispensary**
7.2.1	Hotplate or any other source of heat			
7.2.2	Weighing balance(s) and weights			
7.2.3	Dispensing measures (measuring cylinders, beakers, etc.)			
7.2.4	Source of clean and safe water			
7.2.5	Mortar and pestle, spatula and dispensing tray			
7.3	In case of nonconformity, explain: If space provided is not enough, please use continuation page(s).			

8. Record-Keeping and Documentation

8.1	Are record-keeping and documentation suitable for the intended use in respect to:			
		Hospital	**Health Centre**	**Dispensary**
8.1.1	Prescription Book			
8.1.2	Poison Book			
8.1.3	Controlled Drugs Register			
8.1.4	Written procedures for maintenance of cold chain product			
8.1.5	Import Permit			
8.1.6	Ledger Book or an appropriate Inventory Control System			
8.1.7	TFDA-endorsed Pro Forma Invoices			
8.1.8	Receipts/Invoices			
8.1.9	Copies of delivery notes			
8.1.10	Accuracy of record-keeping			
8.1.11	Do the physical quantities of narcotic/psychotropic drugs match those on the Register?			
8.1.12	Are the prescriptions for narcotic/psychotropic drugs written by duly qualified medical personnel and properly kept?			
8.1.13	Endorsement of entries by authorised person(s)			
8.1.14	Written procedures for handling returned, recalled, and/or expired drugs			

8.1.15	Written procedures for dealing with complaints and/or adverse reaction reports			
8.2	In case of nonconformity, explain: If space provided is not enough, please use continuation page(s).			

9.0 Reference Materials

9.1	Are appropriate reference material(s) available?			
		Hospital	**Health Centre**	**Dispensary**
9.1.1	*Tanzania National Formulary* (TNF)			
	Indicate edition of TNF			
9.1.2	*Tanzania Pharmaceutical Handbook*			
9.1.3	Tanzanian Food, Drug and Cosmetics Act 2003 and its corresponding regulations and guidelines			
9.1.4	Standard treatment guidelines			
9.1.5	National essential drugs list			
9.1.6	Current list of registered drugs			
9.1.7	Pharmaceuticals and Poison Act 1978 and its corresponding regulations and guidelines			
9.1.8	*Good Dispensing Manual* (Swahili/English versions)			
9.1.9	*British National Formulary*			
9.1.10	*British Veterinary Codex*			
9.2	In case of nonconformity, explain: If space provided is not enough, please use continuation page(s).			

10. Legality of Stocked Products

Note: In case of nonconformity, stop the inspection, confiscate the products, and fill in the Confiscation/Quarantine Form.

	Yes	No	Number of Products Confiscated
10.1 Are there unregistered products stocked on the premises?			
10.2 Are there unauthorised products in stock?			

11. Product Label Examination

11.1	Closely examine the products in stock and evaluate the labels in respect to:			
		Hospital	**Health Centre**	**Dispensary**
11.1.1	Language of labels and package inserts			
11.1.2	Any signs of tampering			
11.1.3	Labelling requirements			
11.2	In case of nonconformity, explain: If space provided is not enough, please use continuation page(s).			

12. Samples for Examination

12.1	Conduct physical examination on pharmaceutical products stocked in the facility according to SOP No. TFDAINS 002 and take samples of batches of antimalaria and antibiotic drugs included in the drug quality surveillance programme for GPHF Minilab screening. For suspicious antimalarials or antibiotics, take samples in accordance with SPD 02-00, SPD 02-01, SPD 03-01, or SPD 05-01, as appropriate.	
12.2	Number of batches of products sampled under the screening programme	
12.3	Number of batches of suspicious products sampled	

13. Any Other Observations

If space provided is not enough, please use continuation page(s).

14. Recommendations

Name and Address of Facility:	
Items requiring attention:	Actions agreed to be taken and timeline:

15. Owner's/In-charge Declaration

I/we, ……..……., the in-charge/owner of the said premises, certify the information and observations made on this sheet during the inspection of the premises to be true and correct.

Signature: …….....	Date: …….....

16.	**Name(s) of Inspector(s):**	**Signature(s) of Inspector(s)**
1.	……	
2.	……	
3.	……	
Date:		

Abbreviated Drug Dispensing Outlet Inspection Form for Hospitals, Health Centres, and Dispensaries (TFDAINS Form 007)

UNITED REPUBLIC OF TANZANIA
MINISTRY OF HEALTH

TANZANIA FOOD AND DRUGS AUTHORITY
Tel: +255-22-2450512/2450751
FAX: +255-22-2450793
Web site: http//www.tfda.or.tz

ABBREVIATED DISPENSARY INSPECTION FORM (HOSPITALS, HEALTH CENTRES, AND DISPENSARIES)

1. General

1.1	Region where the facility is situated (circle one on the list below)			
Arusha Dar es Salaam Dodoma Iringa	Kagera Kigoma Kilimanjaro Lindi	Manyara Mara Mbeya Morogoro Mtwara	Mwanza Pwani Rukwa Ruvuma Shinyanga	Singida Tabora Tanga
1.2	Name of Outlet:			
1.3	Type: (circle) Hospital Health Centre Dispensary			
1.4 Mailing Address: ……..…….. ……..……..		1.5 Physical Address/Location: Street/Ward……..... District……..... ……..		
1.6	Telephone Number:	1.7	Fax Number:	
1.8	E-mail Address:			
1.9	Premises Licence Number:	1.10	Is the licence valid? Y / N	1.11 Is the original licence displayed? Y / N
1.12	Name of Pharmacist in Charge:	1.13	Pharmacist Registration Number:	1.14 Is the Certificate of Registration displayed? Y / N
1.15	Date of Inspection:	1.16	Date of Last Inspection:	
1.17	Ownership/Name of Proprietor(s):			

Prepared by:	**Checked by:**	**Approved by:**
Date:	**Date:**	**Date:**

2. Personnel

2.1 Responsible Staff (other than the pharmacist in charge)

2.1.1	Name:	
2.1.2	Qualification:	
2.1.3	Position/Title:	

2.2 Other Dispensary Staff

2.2.1	Name	2.2.2	Qualifications
1.			
2.			
3.			

3. Type of Inspection

3.1. Circle one: Announced/Unannounced	3.2 Circle one: Routine, Concise, Follow-up, Special, Investigative	3.3 Postmarketing surveillance done? Y / N If yes, go to #10. If no, go to #4.

4. Legality of Stocked Products

Note: In case of nonconformity, stop the inspection, confiscate the products, and fill in the Confiscation/Quarantine Form.

	Yes	**No**	**Number of Products Confiscated**
4.1 Are there unregistered products stocked on the premises?			
4.2 Are there unauthorised products in stock?			

5. Product Label Examination

5.1	Closely examine the products in stock and evaluate the labels in respect to:			
		Hospital	**Health Centre**	**Dispensary**
5.1.1	Language of labels and package inserts			
5.1.2	Any signs of tampering			
5.1.3	Labelling requirements			
5.2	In case of nonconformity, explain: If space provided is not enough, please use continuation page(s).			

6. Samples for Examination

6.1	Conduct physical examination on pharmaceutical products stocked in the facility according to SOP No. TFDAINS 002 and take samples of batches of antimalaria and antibiotic drugs included in the drug quality surveillance programme for GPHF Minilab screening. For suspicious antimalarials and antibiotics, take samples in accordance with SPD 02-00, SPD 02-01, SPD 03-01, or SPD 05-01, as appropriate.	
6.2	Number of batches of products sampled under the surveillance programme	
6.3	Number of batches of suspicious products sampled	

7. Any Other Observations

If space provided is not enough, please use continuation page(s).

8. Recommendations

Name and Address of Facility:	
Items requiring attention:	Actions agreed to be taken and timeline:

9. Owner's/In-charge Declaration

I/we, ……..……., the in-charge/owner of the said premises, certify the information and observations made on this sheet during the inspection of the premises to be true and correct.

Signature: …….....	Date: …….....

10.	Name(s) of Inspector(s):	Signature(s) of Inspector(s)
1.	……	
2.	……	
3.	……	
Date:		

Drug Dispensing Outlet Inspection Form for Duka la Dawa Baridi and Muhimu (TFDAINS Form 008)

UNITED REPUBLIC OF TANZANIA
MINISTRY OF HEALTH

TANZANIA FOOD AND DRUGS AUTHORITY
Tel: +255-22-2450512/2450751
FAX: +255-22-2450793
Web site: http//www.tfda.or.tz

PART II DRUG DISPENSING OUTLET INSPECTION FORM (DUKA LA DAWA BARIDI AND MUHIMU)

1. General

1.1	Region where the facility is situated (circle one on the list below)			
Arusha Dar es Salaam Dodoma Iringa	Kagera Kigoma Kilimanjaro Lindi	Manyara Mara Mbeya Morogoro Mtwara	Mwanza Pwani Rukwa Ruvuma Shinyanga	Singida Tabora Tanga
1.2	Name of Outlet:			
1.3	Type: (circle) Duka la Dawa Muhimu Duka la Dawa Baridi			
1.4 Mailing Address: ……..…….. ……..……..		1.5 Physical Address/Location: Street/Ward……..... District……....		
1.6	Telephone Number:	1.7	Fax Number:	
1.8	E-mail Address:			
1.9	Premises Licence Number:	1.10	Is the licence valid? Y / N	1.11 Is the original licence displayed? Y / N
1.12	Name of Pharmacist in Charge:	1.13	Pharmacist Registration Number:	1.14 Is the Certificate of Registration displayed? Y / N
1.15	Date of Inspection:	1.16	Date of Last Inspection:	
1.17	Ownership/Name of Proprietor(s):			

Prepared by:	**Checked by:**	**Approved by:**
Date:	**Date:**	**Date:**

2. Personnel

2.1 Responsible Staff

2.1.1	Name:	
2.1.2	Qualification:	
2.1.3	Position/Title:	

2.2 Sales Persons

Are all sales persons qualified to operate a Duka la Dawa Baridi/Muhimu? Y / N (circle one)			
2.2.1	Name	2.2.2	Qualifications
1.			
2.			
3.			

3. Type of Inspection

3.1. Circle one: Announced/Unannounced	3.2 Circle one: Routine, Concise, Follow-up, Special, Investigative	3.3 Postmarketing surveillance done? Y / N If yes, go to #9. If no, go to #4.

4. General Condition of Premises

4.1	Is the premises appropriate for the intended purpose in respect to: (please indicate Y for yes [pass] or N for no [fail])		
		Duka la Dawa Baridi	**Duka la Dawa Muhimu**
4.1.1	Layout		
4.1.2	Size/number of rooms		
4.1.3	Hygiene (clean and free from debris)		
4.1.4	State of repair (no cracks or crevices on the floor, smooth painted walls)		
4.1.5	Ventilation and cooling system (working and provides suitable temperatures for drug storage)		
4.1.6	Lighting (adequate to enable reading of labels)		
4.1.7	Display of drugs		
4.1.8	Utilities: water, handwash basins, WC		
4.2	In case of nonconformity, explain: If space provided is not enough, please use continuation page(s).		

5. Security of Premises

5.1	Are the premises secure in respect to:		
		Duka la Dawa Baridi	**Duka la Dawa Muhimu**
5.1.1	External perimeter security (e.g., fencing, gates, walls, windows)		
5.1.2	Do unauthorised persons have access to the secure storage areas?		
5.1.3	Documents/records-keeping		
5.2	In case of nonconformity, explain: If space provided is not enough, please use continuation page(s).		

6. Storage Conditions

6.1	Are the storage conditions suitable for the intended purpose in respect to:		
		Duka la Dawa Baridi	**Duka la Dawa Muhimu**
6.1.1	Durability of floor and ease of cleaning		
6.1.2	Prevention of infestation by vermin and pests		
6.1.3	Adequate shelving		
6.1.4	Pallets		
6.1.5	Execution of stock rotation/ FEFO		
6.1.6	Storage of returned/recalled/ spoiled/expired/quarantined goods		
6.1.7	Cold rooms/refrigerators for the storage of vaccines and/or biologicals		
6.2	In case of nonconformity, explain: If space provided is not enough, please use continuation page(s).		

7. Record-Keeping and Documentation

7.1	Are record-keeping and documentation suitable for the intended use in respect to:		
		Duka la Dawa Baridi	**Duka la Dawa Muhimu**
7.1.1	Prescription Book		
7.1.2	Poison Book (for Duka la Dawa Muhimus only)		
7.1.3	Ledger Book or an appropriate Inventory Control System		
7.1.4	Receipts/Invoices		
7.1.5	Copies of delivery notes		
7.1.6	Accuracy of record-keeping		
7.1.7	Legality of the source(s) of supplies		
7.1.8	Written procedures for handling returned, recalled, and/or expired drugs		
7.1.9	Written procedures for dealing with complaints and/or adverse reaction reports		
7.2	In case of nonconformity, explain: If space provided is not enough, please use continuation page(s).		

8. Reference Materials

8.1	Are appropriate reference material(s) available?		
		Duka la Dawa Baridi	**Duka la Dawa Muhimu**
8.1.1	*Tanzania National Formulary* (TNF)		
	Indicate edition of TNF		
8.1.2	*Tanzania Pharmaceutical Handbook*		
8.1.3	Tanzanian Food, Drug and Cosmetics Act 2003 and its corresponding regulations and guidelines		
8.1.4	*Good Dispensing Manual* (Swahili/English versions)		
8.2	In case of nonconformity, explain: If space provided is not enough, please use continuation page(s).		

9. Legality of Stocked Products

Note: In case of nonconformity, stop the inspection, confiscate the products, and fill in the Confiscation/Quarantine Form.

	Yes	No	Number of Products Confiscated
9.1 Are there unregistered products stocked on the premises?			
9.2 Are there unauthorised products in stock?			

10. Product Label Examination

10.1	Closely examine the products in stock and evaluate the labels in respect to:		
		Duka la Dawa Baridi	**Duka la Dawa Muhimu**
10.1.1	Language of labels and package inserts		
10.2	In case of nonconformity, explain: If space provided is not enough, please use continuation page(s).		

11. Samples for Examination

11.1	Conduct physical examination on pharmaceutical products stocked in the facility according to SOP No. TFDAINS 002 and take samples of batches of antimalaria and antibiotic drugs included in the drug quality surveillance programme for GPHF Minilab screening. For suspicious antimalarials and antibiotics, take samples in accordance with SPD 02-00, SPD 02-01, SPD 03-01, or SPD 05-01, as appropriate.	
11.2	Number of batches of products sampled under the surveillance programme	
11.3	Number of batches of suspicious products sampled	

12. Any Other Observations

If space provided is not enough, please use continuation page(s).

13. Recommendations

Name and Address of Facility:	
Items requiring attention:	Actions agreed to be taken and timeline:

14. Owner's/In-charge Declaration

I/we, ……..……., the in-charge/owner of the said premises, certify the information and observations made on this sheet during the inspection of the premises to be true and correct.

Signature: …….....	Date: …….....

15.	**Name(s) of Inspector(s):**	**Signature(s) of Inspector(s)**
1.	……	
2.	……	
3.	……	
Date:		

Abbreviated Drug Dispensing Outlet Inspection Form for Duka la Dawa and Muhimu (TFDAINS Form 009)

UNITED REPUBLIC OF TANZANIA
MINISTRY OF HEALTH

TANZANIA FOOD AND DRUGS AUTHORITY
Tel: +255-22-2450512/2450751
FAX: +255-22-2450793
Web site: http//www.tfda.or.tz

ABBREVIATED PART II DRUG DISPENSING OUTLET INSPECTION FORM (DUKA LA DAWA BARIDI AND MUHIMU)

1. General

1.1	Region where the facility is situated (circle one on the list below)			
Arusha Dar es Salaam Dodoma Iringa	Kagera Kigoma Kilimanjaro Lindi	Manyara Mara Mbeya Morogoro Mtwara	Mwanza Pwani Rukwa Ruvuma Shinyanga	Singida Tabora Tanga
1.2	Name of Outlet:			
1.3	Type: (circle) Duka la Dawa Muhimu Duka la Dawa Baridi			
1.4 Mailing Address: ……..…….. ……..……..		1.5 Physical Address/Location: Street/Ward……..... District……..... ……..		
1.6	Telephone Number:	1.7	Fax Number:	
1.8	E-mail Address:			
1.9	Premises Licence Number:	1.10	Is the licence valid? Y / N	1.11 Is the original licence displayed? Y / N
1.12	Name of Pharmacist in Charge:	1.13	Pharmacist Registration Number:	1.14 Is the Certificate of Registration displayed? Y / N
1.15	Date of Inspection:	1.16	Date of Last Inspection:	
1.17	Ownership/Name of Proprietor(s):			

Prepared by:	**Checked by:**	**Approved by:**
Date:	**Date:**	**Date:**

2. Personnel

2.1 Responsible Staff

2.1.1	Name:	
2.1.2	Qualification:	
2.1.3	Position/Title:	

2.2 Sales Persons

Are all sales persons qualified to operate a Duka la Dawa Baridi/Muhimu? Y / N (circle one)			
2.2.1	Name	2.2.2	Qualifications
1.			
2.			
3.			

3. Type of Inspection

3.1. Circle one: Announced/Unannounced	3.2 Circle one: Routine, Concise, Follow-up, Special, Investigative	3.3 Postmarketing surveillance done? Y / N If yes, go to #9. If no, go to #4.

4. Legality of Stocked Products

Note: In case of major nonconformity, stop inspection, confiscate the products, and fill in the confiscation forms.

	Yes	**No**	**Number of Products Confiscated**
4.1 Are there unregistered products stocked on the premises?			
4.2 Are there unauthorised products in stock?			

5. Product Label Examination

5.1	Closely examine the products on stock and evaluate the labels in respect to:		
		Duka la Dawa Baridi	**Duka la Dawa Muhimu**
5.1.1	Language of labels and package inserts		
5.2	In case of nonconformity, explain: If space provided is not enough, please use continuation page(s).		

6. Samples for Examination

6.1	Conduct physical examination on pharmaceutical products stocked in the facility according to SOP No. TFDAINS 002 and take samples of batches of antimalaria and antibiotic drugs included in the drug quality surveillance programme for GPHF Minilab screening. For suspicious antimalarials and antibiotics, take samples in accordance with SPD 02-00, SPD 02-01, SPD 03-01, or SPD 05-01, as appropriate.	
6.2	Number of batches of products sampled under the surveillance programme	
6.3	Number of batches of suspicious products sampled	

7. Any Other Observations

If space provided is not enough, please use continuation page(s).

8. Recommendations

Name and Address of Facility:	
Items requiring attention:	Actions agreed to be taken and timeline:

9. Owner's/In-charge Declaration

I/we, ……..……., the in-charge/owner of the said premises, certify the information and observations made on this sheet during the inspection of the premises to be true and correct.

Signature: …….....	Date: …….....

10.	**Name(s) of Inspector(s):**	**Signature(s) of Inspector(s)**
1.	……	
2.	……	
3.	……	
Date:		

SOP for Chain of Custody, Packing, and Shipping Procedures (TFDAINS 004)

TANZANIA FOOD AND DRUGS ADMINISTRATION DIRECTORATE OF INSPECTIONS AND SURVEILLANCE STANDARD OPERATING PROCEDURE				
TITLE: CHAIN OF CUSTODY, PACKING, AND SHIPPING PROCEDURES				
SOP NO.: **TFDAINS 004**	**SUPERSEDES:** **None**	**DATE OF ISSUE:** **Nov. 2002**	**EFFECTIVE DATE:** **Nov. 2002**	**NEXT REVIEW DATE:** **June 2006**

Objective

The objective of this standard operating procedure is to describe the procedures drug inspectors must follow to establish chain of custody and to package and ship samples to official examination points.

Scope

This SOP details how to maintain a chain of custody system and how to package and ship all types of samples to the DQCL or other examination points.

Responsibility

The Director-General, Director of Inspections and Surveillance, Director of Laboratory Services, Chief Drug Inspector, drug inspectors, and drug laboratory analysts shall ensure implementation of this SOP.

Accountability

The Director of Inspections and Surveillance is accountable for the implementation of this SOP.

Distribution

The Director-General, Director of Inspections and Surveillance, Director of Laboratory Services, Chief Drug Inspector, drug inspectors, and drug laboratory analysts should get copies. A copy should also be kept in the Master File.

Special Instructions

The following forms may need to be filled in during the execution of this SOP's Chain of Custody Control Form:

1. POE Consignment Inspection Form
2. Dispensing Outlets Inspection Forms (TFDAINS Forms 004–009)
3. Rejection/Detention Form (annexed)
4. Sample Receipt Form (annexed)
5. Confiscation/Quarantine Form (annexed)

The following SOPs may be consulted during the execution of this SOP:

1. SOP No. SPD 02-00 Suspicious Sample Surveillance Programme
2. SOP No. SPD 02-01 Drug Quality Surveillance Programme: Antimalarials
3. SOP No. SPD 03-01 Drug Quality Surveillance Programme: Antibiotics
4. SOP No. SPD 05-01 Drug Quality Surveillance Programme: Antiretrovirals

This SOP is divided into four sections. Section A covers the chain of custody control mechanism and form. Instructions for packaging samples are given in Section B. Instructions for sealing the samples is given in Section C. Maintenance of chain of custody records is covered in Section D.

Procedure

The procedures in this SOP describe how the drug inspector establishes chain of custody and packages and ships samples for examination. Samples collected through surveillance programmes and those that require examination must be shipped under strict chain of custody procedures in order to protect the legal integrity of the sample. This SOP also describes how other official staff members are to maintain the chain of custody through to the final destruction of the sample. The collecting inspector must maintain the collected samples under control at all times until the sealing operation is complete.

Section A: Chain of Custody Control Form

1. Sample collections: For routine surveillance programmes, only unopened containers with intact safety seals should be collected. Products associated with adverse events may be collected "as is," with a description of the collection circumstances noted on the continuation page(s) of the Chain of Custody Control Form.

2. Complete the Chain of Custody Control Form for each batch of samples collected. The collecting inspector should keep unsealed samples under complete control at all times (e.g., in a secure, locked area) when not in the inspector's immediate possession. The completed Chain of Custody Control Form and any continuation pages should be folded and placed in a business-size envelope.

Section B: Packaging

1. The label on the bottom of the sample bag (Figure 1) should be filled out using a ballpoint pen or other indelible ink marker, and the collecting inspector should fill in the seal number on the paper tape seal.

Sample Number:
Trade/Generic Name:
Manufacturer's Name:
Lot Number:
Consignee:
Inspector Name (printed):
Surveillance Programme:

Figure 1. Label on Bottom of Sample Bag

2. The sample(s) should be placed in the labelled sample bag, and the top of the bag should be folded over two or three times with half-inch folds.

3. The completed paper tape seal should be glued over the folded centre of the bag so that opening the bag breaks the seal.

4. The envelope containing the Chain of Custody Control Form should be stapled through the fold, thereby closing the bag and attaching the envelope.

5. For samples that are too large to fit in the sample bag:
   a. Complete the required information on the bottom of the bag.
   b. Wrap the container on two axes with the completed seal. Opening the container should break the seal.
   c. Attach the completed sample bag and chain of custody envelope to the sample container. Larger samples may be packaged in other containers using the same labelling as on the bottom of the sample bag. That container should also have paper tape seals glued over any possible opening sites so that the seal is broken if the container is opened.

Section C: Sealed Sample Shipment

The sealed samples should be placed in appropriate shipping containers for forwarding to their examination point. The shipping containers should be filled with crumpled paper or other packing material to prevent damage to the samples.

Section D: Chain of Custody Record Maintenance

1. The individual who breaks the seal and opens the bag should complete the Chain of Custody Control Form and keep the samples secure during the examination period.

2. Any transfers of the sample(s) to other individuals should be documented either through resealing before forwarding or by documentation on the continuation page.

3. The sample should then be returned under seal to the sample custodian for retention until it is destroyed.

4. After the examination has been concluded and all legal actions have been completed, the sample custodian should complete the destruction portion of the Chain of Custody Control Form and forward the form to his/her supervisor for approval of the destruction of the remaining portion of the sample(s). The destruction should be done in accordance with TFDA regulations.

PART II

Chapter 5. The Use of the German Pharma Health Fund Minilab for Verification of Identity and Content of Drugs

General Introduction

Quality assurance of pharmaceutical products, whether locally manufactured or imported, is of prime importance in any health care system; lack of quality assurance endangers the lives of citizens. Many developing countries, like Tanzania, do not have well-established pharmaceutical industries and rely mostly on imported drugs; such countries often do not have good quality assurance systems. As such, these countries are at the risk of being supplied with substandard products that will endanger the lives of their citizens. Thus, affordable but reliable methods for quality assurance are urgently required to ensure that both locally manufactured and imported products meet the prescribed standards and thus are safe for human use.

The TFDA, in collaboration with MSH through the SEAM Program and the School of Pharmacy at MUCHS, has developed a training programme to prepare drug inspectors to monitor the quality of drugs entering the Tanzanian market. Initially, the programme enrolled inspectors involved in POE inspections. The programme has been further expanded to train more inspectors and also to include other drug categories in addition to antimalaria drugs

Of the many methods for checking the quality of drugs, thin-layer chromatography (TLC) has been selected because of its simplicity, cost-effectiveness, and adaptability to field conditions. This document, therefore, is designed to guide inspectors through the basic principles of TLC and the practical aspects of quality control of currently used antimalarial drugs by TLC using the German Pharma Health Fund Minilab kit (GPHF Minilab). Along with analysis by TLC, inspectors will also carry out visual inspection, disintegration testing, and colour reactions of the products being analyzed.

Introduction to Chromatography

Objectives

- Describe the basic principles underlying chromatographic analysis
- Classify the different chromatographic methods

Chromatography is a physicochemical technique that is used primarily for the separation of components of a given sample, in which the individual components are distributed between two different phases, one of which is stationary while the other moves (is mobile). The stationary phase may be a solid or liquid supported on a solid or gel, and may be packed in a column, spread as a layer, or distributed as a film. Thus, a chromatographic system basically consists of three components: a stationary phase, a mobile phase, and an inert support or matrix.

Chromatography was described in 1903 by botanist Mikhail Tswett, who separated coloured plant pigments by using chalk. The term "chromatography" comes from two Greek words: *chromatos* meaning "colour" and *grapha* which means "drawing." Originally, the technique was limited to separation of coloured components; however, with the development of various detection methods, chromatography is now applied for colourless compounds as well.

Classification of Chromatographic Techniques

Chromatographic techniques have been classified in various ways. Classification may be based on the nature of stationary and mobile phases, mechanism or principle behind the technique, or mode of laboratory operation.

Classification Based on the Nature of the Two Phases

Based on the nature of the stationary and mobile phases, chromatographic techniques can be classified as shown in Table 13.

Table 13. Classification of Chromatographic Techniques According to Nature of Two Phases

Stationary Phase	Mobile Phase	Type	Example
Solid	Liquid	Liquid-solid chromatography	TLC, high-performance liquid chromatography (HPLC), column chromatography (CC)
Solid	Gas	Gas-solid chromatography	Not practical
Liquid	Liquid	Liquid-liquid chromatography	CC, HPLC, paper chromatography (PC), counter current chromatography (CCC)
Liquid	Gas	Gas-liquid chromatography	Gas-liquid chromatography (GLC)

Classification Based on Mechanism (Principle) of Separation

Adsorption Chromatography (e.g., TLC, CC)

Adsorption chromatography, the oldest chromatographic technique, was developed by Mikhail Tswett. It involves separation of drugs based on their differential strength of adsorption to the surface of a finely powdered adsorbent (stationary phase). Some of its characteristics include:

- Binding involves weak non-ionic forces (e.g., H-bonding, van der Waals interactions)
- Hydroxyl (OH) and aromatic groups generally tend to enhance binding
- Stationary phase is always a solid
- Mobile phase may be a liquid or gas; in practical terms, gas is not a very good mobile phase

Partition Chromatography (e.g., PC, HPLC)

With this technique, separation is based on differential solubility of solutes in two partially immiscible solvents (i.e., mobile and stationary phases). The mobile phase flows in contact with the stationary phase, which is sorbed to a solid support.

Ion Exchange Chromatography

This type involves ionic exchange between an external liquid phase and an ionic solid phase.

Gel Permeation (Gel Filtration, Size Exclusion) Chromatography

Separation is based on molecular size.

Electrophoresis

Electrophoresis involves migration of charged particles in an electric field. Separation is according to the charge of the solute.

Affinity Chromatography

This type depends on specific reversible binding of a molecule with a particular ligand.

Classification Based on Form of Preparation (Laboratory Operation)

Chromatography may also be classified based on the type of laboratory operation used to achieve separation of different species in a mixture. Examples of this type of classification are listed below.

- Column chromatography (e.g., gravity CC, flash chromatography): the stationary phase is bonded to a vertical column, and the mobile phase percolates the stationary phase by means of gravity
- Planar chromatography: the stationary phase is bonded to a plate to form a thin layer (e.g., TLC)
- Paper chromatography: uses paper as a support for stationary phase
- Counter-current chromatography: liquid-liquid partition methods that do not need a solid support
- HPLC: the mobile phase is pumped under pressure through a short, tightly packed column to achieve faster separation

Thin-Layer Chromatography

Objectives

- Describe the basic principles of TLC
- List the various steps involved in the TLC technique
- Determine Rf values

Thin-layer chromatography has been known for more than 100 years, but it was not until the 1950s that Egon Stahl developed it to become a method of wide applicability. TLC is a liquid-solid planar chromatographic technique in which the stationary phase consists of a finely divided polar adsorbent material in the form of a uniform thin layer bonded onto a plate. After a mixture of drugs in the form of a solution is applied to the plate, the plate is placed in a developing chamber; then, in the mobile phase, the drugs will move across the plate because the solvent moves up the plate by capillary action. The separation of the drugs is dependent on their solubility and the affinity between the two phases. The substances being separated/analyzed are eventually detected on the chromatogram by ultraviolet (UV) light and chemical reactions.

TLC is primarily a separation technique, but under controlled conditions it can be useful as an analytical tool for identification and quantification of substances, detection of impurities and degradation products of drugs, and monitoring of chemical reactions. Although sensitivity and resolution are lower in TLC than in HPLC and GLC, some of the advantages of TLC over other chromatographic methods include:

- The apparatus used in TLC is cheap and simple.
- Several samples can be analyzed simultaneously.
- There is great flexibility in terms of stationary and mobile phases.
- No detection problems occur in the case of non-elution, thermal instability, or masking by solvent, as is the case with HPLC and GLC, because the applied substance remains on the plate.

TLC may be performed as normal or reversed phase chromatography. In the normal phase in TLC, the stationary phase is more polar than the mobile phase. Thus, the mobile phase consists of an organic solvent or mixture of organic solvents, and is less polar than the stationary phase. In reversed phase systems, the stationary phase is less polar than the mobile phase. The mobile phase is a mixture of water with an organic solvent. The stationary phase consists of an adsorbent that has been bonded with an organic substrate, such as long-chain hydrocarbons or aliphatic acids (e.g., C_{18}).

Some Terminology Used in TLC

Adsorbent: A substance that causes passing molecules or ions to adhere to the surface of its particles

Analyte/sample: A mixture that is being separated or analyzed (e.g., drugs)

Chromatogram: A developed TLC plate with substance spots at various positions

Chromatoplate: TLC plate

Detection/Location/Visualisation: The process of locating (making visible) the substances being analyzed on the chromatoplate after development

Development: The process of separating the sample mixture by the ascending migration of solvent in the adsorbent layer

Eluent: The solvent (mobile) phase that removes substances from the stationary phase

Eluotropic series: List of solvents arranged according to their elution power

Elution: Removal of a compound from a column or stationary phase

Elution power: Ability to remove compounds from the stationary phase

Mobile phase: A solvent that flows through the stationary phase by capillary action, dissolving and carrying with it the substances that are being separated or analyzed

Origin/start: A position about 2 cm from the bottom of a TLC plate, at which sample spots are applied; it may be marked as a line

Rf value: "Retardation factor" or "ratio-to-front" (i.e., a ratio of distance travelled by a substance from the origin to distance travelled by the solvent from the origin)

Solvent front: The highest position (front line) reached by the solvent on a chromatoplate after development

Stationary phase: A solid substance that is coated on glass, plastic, or aluminium plates and adsorbs molecules to be separated

Standard TLC Conditions

Stationary Phase

The stationary phase consists of a thin layer of appropriate adsorbent bonded onto a suitable support, which may be a glass, plastic, or aluminium plate. Binding to the plate is assured by mixing the adsorbent with a binding agent, such as calcium sulfate. Plates may be prepared in the laboratory or purchased from a reliable supplier.

Adsorbents are porous materials of a different chemical nature that are made into finely divided particles so that they provide a large surface area for effective separation. Commonly used adsorbents include silica gel and alumina. Silica gel is hydrated silicic acid with polar functional groups on the surface, which adsorbs polar molecules. It is the most widely used adsorbent for TLC and CC.

In this course, precoated silica gel TLC plates with a binder and fluorescent indicator (silica gel GF_{254}) are used.

Mobile Phase

The mobile phase is the transport medium, the choice of which will depend on the substances to be separated and the adsorbent to be used. The mobile phase has two functions:

- First, it must displace the solute (drug) from the adsorbent to make it able to migrate across the TLC plate. Thus, it must have *elution power*. In normal phase TLC, elution power increases with the increasing polarity of the mobile phase (Figure 2).

- Second, it must help to separate a mixture of drugs, excipients, and impurities so that they can be deposited at different positions on the chromatoplate and have different Rf values.

The solvent may be made up of one component or a mixture of two or more solvents (i.e., a solvent system). The solvents to be used in this course are able to perform the two functions for the specified drugs being analyzed, and most are mixtures.

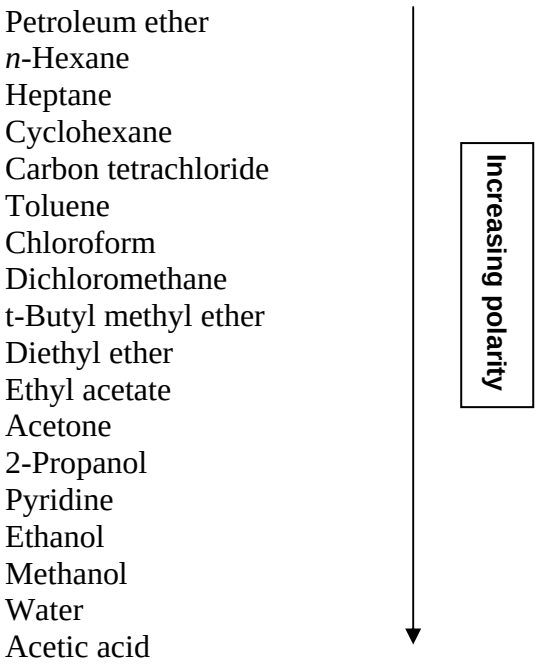


Figure 2. Eluotropic Series

Separation Chamber

The separation chamber is a container, usually made of glass, into which the mobile phase and a loaded TLC plate are placed in order to effect separation or analysis. A glass jar that closes tightly can prevent the loss of mobile phase and, hence, prevent poor results (see Preparation of Mobile Phase below).

Methodology

The TLC technique involves the following procedures:

- Preparation of plates
- Preparation of mobile phase
- Application of samples and standards
- Development
- Detection of analytes

Preparation of Plates

Plates may be prepared in the laboratory or purchased. For this course and the analytical work you will be performing at your stations using the GPHF Minilab kit, precoated plates have been supplied. The plates provided are of analytical standard with a layer thickness of 250 μm and a size of 5 × 10 cm.

Preparation of Mobile Phase

The specified mobile phase has to be thoroughly mixed and placed in the development chamber at a depth of 5 to 10 mm. For reproducible results, the chamber must be saturated with the mobile phase by lining it with a filter paper before running the chromatogram. Presaturation prevents evaporation of the mobile phase, which would adversely affect the separation and position and shape of spots. When developing the chromatoplate, a concave solvent front indicates that the chamber is not well saturated. This must be avoided.

Application of Samples and Standards

- Samples and standards must be dissolved in a suitable solvent, preferably a volatile solvent with low polarity, to reduce diffusion of sample. Polar solvents are strongly adsorbed to the layer, leading to marked irregularities and distortion of spots as the mobile phase passes up the thin layer.

- The starting line (origin) is drawn lightly with a pencil, not a pen. A pen has organic ink, which would be taken up with the solvent when the chromatoplate is being developed. The pencil should be soft to avoid scratching the plate, which would distort the separation of substances. The starting line is drawn parallel to and about 1.5 cm from the bottom of the plate; this distance ensures that the line does not touch the solvent in the developing chamber. If the line touches the solvent, the applied substances would be washed down into the mobile phase and a reliable chromatogram would not be obtained.

- On the line, spotting positions may be marked lightly with a pencil about 1 cm apart. Since the plate may run more than one sample, each spot must be properly labelled with the pencil.

- Samples may be applied (spotted) by using a micropipette, capillary tube, or calibrated microsyringe. For this course, 2 μL capillary tubes will be used for the purpose. Usually about 1 to 10 μL of each sample is spotted on the starting line, but in this course only 2 μL of each sample and standard will be spotted.

- The spotting device must be extremely small in order to obtain spots not more than 4 mm in diameter. When large spots are applied, poor resolution results and spots will be too close to each other.

- Only a small amount of sample should be applied (about 10 μg) because overloading leads to spreading of spots with possible tailing and other effects, resulting in erratic Rf values.

- Where the necessary sample may be loaded in portions, a little is applied and allowed to dry. Then more may be applied.

- Much care must be taken when spotting samples. The microcapillary tube should just touch the TLC plate, so as to avoid making a hole on the thin layer. A hole obstructs solvent flow, which distorts the moving spots, possibly leading to poor resolution by preventing separation of substances with close Rf values.

- After all spots are applied, they should be allowed to dry completely before the plate is placed in the developing jar. This is because the presence of sample solvent, especially water and other polar solvents, will drastically alter chromatographic properties, leading to unreliable results.

Development (Running the Chromatogram)

A loaded TLC plate must be in contact with the mobile phase for separation to occur. The plate is placed in a vertical position in the developing chamber saturated with the solvent, with the lower edge immersed in the mobile phase. A pair of tweezers (forceps) may be used to hold the plate to avoid contamination of the plate with hand oils.

The TLC plate may be developed with one or multiple solvents and on one or two dimensions, perpendicular to each other. In this course, one-dimensional, ascending development will be applied. Development occurs when the mobile phase moves up the plate by capillary action. It is allowed to proceed until the solvent front is close to the top edge of the plate (i.e., about three-quarters the height of the plate). Spots are separated depending on how strongly they are adsorbed to the stationary phase and their distribution coefficients in the mobile phase. Polar molecules are strongly adsorbed to the stationary phase, will move slowly, and will be at lower positions on the plate. Nonpolar molecules are more soluble in the relatively less polar mobile phase; they will move faster, and their spots will be at a higher position on the chromatogram.

Detection/Location/Visualisation of Analytes

After development, the plate is taken out of the jar and dried prior to detection of the separated substances. Spots on the developed chromatogram may be located by using various methods. Coloured components are visible in daylight. However, most organic substances are colourless and need other means of detection, some of which are nondestructive, while others are destructive.

Nondestructive Detection Methods

On examination of a plate containing a fluorescent indicator under short-wave UV light (254 nm), absorbing compounds appear as dark spots on a green background. Examination of the plate under long-wave UV light (365 nm) will reveal naturally fluorescent compounds. Any spots visualised under UV should be marked lightly with a pencil.

Detection of substances that cannot be detected by UV light is achieved by using chemical reagents, which produce various colours with the substances. The reagents are used in the form of a spray or vapour. A good hood is necessary when sprays are used. Exposure to iodine vapour is one of the nondestructive detection methods that uses chemical reagents.

Destructive Detection Methods

Destructive detection methods change the substances being analyzed. For example, concentrated sulfuric acid is very useful for locating various substances. Plates are sprayed or dipped in the reagent, then heated at about 120°C. Separated substances are charred and appear as dark or dark-brown spots.

In this phase of this course, antimalarials will be analyzed. Examination of chromatograms with UV light (254 nm and 365 nm) will be done for all substances. In addition, all plates will be exposed to iodine vapour. Substances being analyzed appear as brown spots. The spots disappear quickly when exposed to the atmosphere; hence, they have to be traced with a pencil immediately after exposure to iodine. In the case of artesunate products, plates will also be exposed to dilute sulfuric acid in methanol, since artesunate is not visible under UV light and may not be visible in iodine vapour.

Evaluation and Documentation of Chromatograms

Evaluation

Evaluation of chromatograms is done by determination of Rf values and visual examination of spots.

Determination of Rf Values

Rf value, a “retardation factor” or “ratio-to-front,” is determined by measuring the distances moved by the spot and the solvent. The Rf value is equal to the distance of the spot centre from the start divided by the distance of the solvent front from the start. Thus, for substances A and B in Figure 3, Rf values are calculated as RfA = dA/dS and RfB = dB/dS.

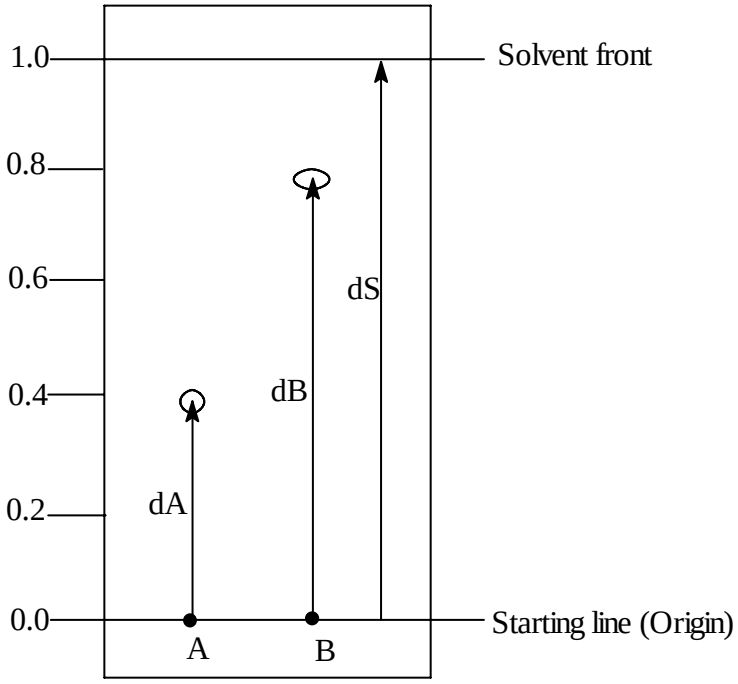


Figure 3. Representation of Chromatogram

Rf values range between 0.00 and 1.00. To avoid the use of decimal points, Rf values are multiplied by 100. The values become hRf values and range between 0 and 100.

Note the following:

- Rf values serve as a guideline only, since they vary depending on a number of factors.
- When a drug sample is run alongside a reference standard, the Rf value will be the same if both products contain the same compound.

Visual Evaluation

Visual evaluation is important both qualitatively and quantitatively. Thus, for a given drug to be accepted as being of good quality and as being the same drug contained in a given dosage unit, it must correspond to the standards provided in terms of travel distances, colour, and sizes of the spots on the chromatogram. Therefore, it is important to carefully:

- Compare the spot sizes (quantitative ratios). The spot size (area) is proportional to the amount of substance being analyzed. If the spot of a given drug being analyzed is smaller than that of the standard applied at the same concentration, then the given drug is of poor quality, containing less of the active ingredient than expected. When a suitable colour reaction is carried out on the chromatogram, spot density can be determined with a densitometer. Spot density is also proportional to the amount of substance applied. For the purpose of our training and practical field work, the densitometer will not be utilised; instead, spots will be evaluated in terms of spot sizes and visual colour intensity.
- Compare the distances moved by various components. This will give the Rf values, which are especially useful qualitatively for identification purposes. By comparison of

distances travelled or Rf values, you can tell whether the drug being analyzed is the same as the given reference standard.

- Compare various properties (e.g., fluorescence or fluorescence quenching). This is also important qualitatively. For a given drug to be the same as the reference standard, its spot must appear similar to the reference spot when examined under UV light.
- Compare colours after exposing the plate to a chemical reagent and heating it, where this is indicated. This is useful both qualitatively and quantitatively.

Documentation

TLC chromatograms may be traced on paper and coloured according to the colour of spots. Photographs of chromatograms may also be taken. However, this is not necessary for this particular training and field work.

The GPHF Minilab

One of the most reliable, simple, and relatively easy and cheap techniques for quality assurance is thin-layer chromatography. The German Pharma Health Fund, which is a not-for-profit organisation, developed a kit that can be used for quality screening of pharmaceutical products being imported and those already on the market. The GPHF Minilab kit is equipped with all the materials needed for carrying out TLC, disintegration tests, and colour reactions for most essential drugs.

The GPHF Minilab can be easily used to monitor the quality of drugs in various places, without the need for complicated methods and complex pieces of equipment. The kit contains all requirements for testing several samples of the essential drugs included in the materials provided. Details of TLC analysis have also been provided under each drug monograph, and the general details are described below.

Verification of Identity and Drug Content via TLC

Principle

Drugs are extracted from tablets and capsules with an appropriate solvent, as specified in the monograph and determined by TLC with reference to an authentic reference standard.

Equipment and Reagents

1. 10 mL vials
2. Aluminium foil
3. Filter paper
4. Funnel
5. Glass microcapillary tubes of 2 µL filling capacity
6. Hotplate
7. Label tape
8. Laboratory glass bottles with a filling capacity of 25 to 100 mL
9. Marker pen

10. Merck TLC aluminium plates precoated with silica gel 60 GF_{254}, size 5 × 10 cm
11. Pencil
12. Pestle
13. Reference and sample tablets
14. Ruler
15. Safety pipette filler
16. Scissors
17. Set of straight pipettes (1 to 25 mL)
18. Solvents for extraction
19. Solvents for mobile phase
20. TLC developing chamber (jar)
21. UV light of 254 nm
22. UV light of 365 nm

Preparation of the Stock Standard Solution

The preparation of a stock standard solution requires a whole reference tablet containing a stated amount of drug, which is crushed prior to extraction, the precise procedure being as follows. Wrap a tablet in aluminium foil and crush it to a fine powder using a pestle. Empty the contents of the aluminium foil over a laboratory glass bottle of appropriate capacity and wash down all residual solid material with an appropriate volume of solvent using a straight pipette. Close the bottle and shake it for about three minutes until most of the solids are dissolved. Allow the solution to stand for another five minutes until the undissolved residue settles below the clear supernatant liquid. This solution should be labelled as "Drug Stock Standard Solution"; it contains a known concentration of the drug per millilitre. Freshly prepare the standard solution for each test.

Preparation of the Working Standard Solution 100 Percent (Upper Working Limit)

Using a pipette, add a stated volume of the clear stock standard solution into an appropriate vial and add a stated volume of diluting solvent. Close and shake the vial. The solution obtained should be labelled as "Drug Working Standard Solution 100%" and contain a known amount of the drug per millilitre. This higher working standard solution represents a drug product of good quality containing 100 percent of the drug.

Preparation of the Working Standard Solution 80 Percent (Lower Working Limit)

Pipette a given volume of the stock standard solution into an appropriate vial and add a stated volume of a specified solvent. Close and shake the vial. The solution obtained should be labelled as "Drug Working Standard Solution 80%" and contain a known amount of drug per millilitre. This is more dilute than the 100 percent working standard solution and thus represents a drug product of poor quality containing just 80 percent of the amount of drug stated on the product's label. In the current investigation, this drug level represents the lower acceptable limit for a given product.

Preparation of the Stock Sample Solution from a Drug Product Claiming a Stated Potency per Unit

The preparation of a stock sample solution requires a whole tablet or capsule from an appropriate drug product sampled in the field. The drug is extracted completely from the sample using the same procedure as for the authentic reference standard: a tablet is wrapped in aluminium foil and crushed to a fine powder prior to transfer into a laboratory glass bottle of a specified capacity. Powder obtained from a capsule should be transferred directly into the laboratory glass bottle, finally putting the empty cap and body shells into the bottle as well. Add a specified volume of appropriate solvent using a straight pipette, close the bottle, and shake it for about three minutes until most of the solids are dissolved. Allow the solution to stand for another five minutes until the undissolved residue settles below the clear supernatant liquid. This solution should be labelled as “Drug Stock Sample Solution”; it contains a known amount of total drug per millilitre. Freshly prepare the sample solution for each test.

Preparation of the Working Sample Solution

Pipette a specified volume of the stock sample solution into an appropriate vial and add a given volume of solvent. Close and shake the vial. The solution obtained should be labelled as “Drug Working Sample Solution.” The expected concentrations of both drug compounds in the working sample solution should match the concentration of drug of the higher working standard solution produced previously.

Spotting

Mark an origin line parallel to and about 1.5 cm from the bottom edge of the chromatoplate and apply 2 µL of each test and standard solution as shown in Figure 4 using the microcapillary pipettes supplied.

Up to five spots can be placed on a plate. Check the uniformity of all spots using UV light of 254 nm. All spots should be circular in shape and equally spaced across the origin line. Although their intensity may differ, their diameter never should. Different intensities are due to residual amounts of tablet and capsule excipients or different drug concentrations in the sample solutions. A difference in spot size, however, is due to poor spotting. Repeat this step if homogeneous spotting is not achieved the first time.

Development

Using a pipette, add a given volume of mobile phase into the jar being used as the TLC developing chamber. Close the chamber and mix thoroughly. Line the chamber’s wall with filter paper and wait for about 15 minutes to ensure saturation of the chamber with solvent vapour. Carefully place the loaded TLC plate into the jar. Close the jar and develop the chromatoplate for about 15 minutes, or until the solvent front has moved about three-quarters of the length of the plate. Remove the plate from the chamber, mark the solvent front, and allow any excess solvent to evaporate, using a hotplate if necessary.

Detection

Dry off all residual solvent, when necessary using the supplied hotplate. Observe the chromatoplate obtained with UV light of 254 nm using the battery-driven fluorescent lamp

supplied. Also observe the plate in daylight after iodine staining or application of any other specified reagent.

Observations Made at 254 nm

The presence of a drug is indicated by a principal spot representing individual drug components at different travel distances. Do not release the batch unless all expected spots are visible. Additional strong spots generated by the test solution indicate drug degradation, especially when associated with a smaller principal spot. Some fainter spots emerging near or on the origin line of the chromatoplate are normally caused by auxiliary agents incorporated in the tablet or capsule formulation.

Run No. 1:
Standard drug's upper working limit representing 100% of total drug

Run No. 2:
A drug product of good quality

Run No. 3:
A drug product of poor quality

Run No. 4:
Standard drug's lower working limit representing 80% of total drug

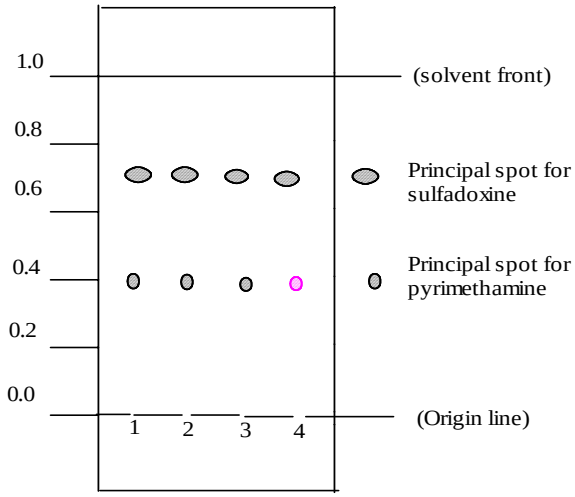


Figure 4. Chromatoplate of SP Observed with UV Light at 254 nm

Observations Made in Daylight after Staining with Iodine or Any Other Specified Reagent

Only the spots reacting with iodine or any other specified reagent become visible for further evaluation of quantities present in the sample.

Results and Actions to Be Taken

The principal spots in the chromatogram obtained with the test solution must correspond in terms of colour, size, shape, and travel distance to those in the chromatograms obtained with the lower and higher standard solutions. This result must be obtained for each method of detection. If this is not achieved, repeat the run from scratch with a second sample. If that sample passes, do a third run. Reject the batch if the drug content cannot be verified by the third run. For a second opinion, refer additional samples to a fully equipped drug quality control laboratory. Retain samples and put the batch in quarantine until a final decision on rejection or release has been made.

Examples of Minilab Procedures for the Verification of Identity and Drug Content of Three Antimalarials

Analysis of Artesunate Tablets

Extraction Medium

- Methanol

Stock Standard Solution

ARTESUNATE STOCK STANDARD SOLUTION (5 mg/mL)
▪ Grind a 50 mg reference tablet and wash down the powder completely with 10 mL of methanol into a 25 mL glass bottle ▪ Close the bottle ▪ Shake the bottle for three minutes ▪ Let the bottle stand for five minutes until all insoluble material settles ▪ Label the bottle as "Artesunate Stock Standard Solution"

Working Standard Solution

ARTESUNATE WORKING STANDARD SOLUTION 100% = 5.0 mg/mL	**ARTESUNATE WORKING STANDARD SOLUTION 80% = 4.0 mg/mL**
▪ Artesunate working standard solution does not need any further dilution	▪ Pipette into a 10 mL vial ▪ 4 mL of stock standard solution ▪ Add 1 mL of methanol ▪ Close, shake, and label it as "Artesunate Working Standard Solution 80%"

Stock Sample Solution

ARTESUNATE STOCK SAMPLE SOLUTION (5 mg/mL) Produced from a 50 mg tablet or capsule	**ARTESUNATE STOCK SAMPLE SOLUTION (5 mg/mL) Produced from a 100 mg tablet or capsule**	**ARTESUNATE STOCK SAMPLE SOLUTION (5 mg/mL) Produced from a 200 mg tablet or capsule**
▪ Grind a 50 mg tablet and wash down the powder completely with 10 mL of methanol into a 25 mL glass bottle ▪ For capsules: open and transfer powder plus cap and body shells into a 25 mL glass bottle and add 10 mL of methanol	▪ Grind a 100 mg tablet and wash down the powder completely with 20 mL of methanol into a 25 mL glass bottle ▪ For capsules: open and transfer powder plus cap and body shells into a 25 mL glass bottle and add 20 mL of methanol	▪ Grind a 200 mg tablet and wash down the powder completely with 40 mL of methanol into a 50 mL glass bottle ▪ For capsules: open and transfer powder plus cap and body shells into a 50 mL glass bottle and add 40 mL of methanol
▪ Close the bottle ▪ Shake the bottle for three minutes ▪ Let the bottle stand for five minutes until all insoluble material settles ▪ Label the bottle as "Artesunate Stock Sample Solution"	▪ Close the bottle ▪ Shake the bottle for three minutes ▪ Let the bottle stand for five minutes until all insoluble material settles ▪ Label the bottle as "Artesunate Stock Sample Solution"	▪ Close the bottle ▪ Shake the bottle for three minutes ▪ Let the bottle stand for five minutes until all insoluble material settles ▪ Label the bottle as "Artesunate Stock Sample Solution"

Working Sample Solution

ARTESUNATE WORKING SAMPLE SOLUTION 100% = 5.0 mg/mL
▪ Artesunate stock sample solution prepared from either unit dosage form requires no further dilution

Preparation of Developing Chamber

PROCEDURE	SOLVENT	AMOUNT
▪ Pipette into the developing chamber (jar)	Ethylacetate	18 mL
▪ Add	Acetone	4 mL
▪ Add	Glacial acetic acid	0.1 mL (precisely)
▪ Close the developing chamber (jar) and mix thoroughly ▪ Line the chamber's wall with filter paper ▪ Wait for about 15 minutes for chamber saturation; use this time to perform spotting (next step)		

Spotting

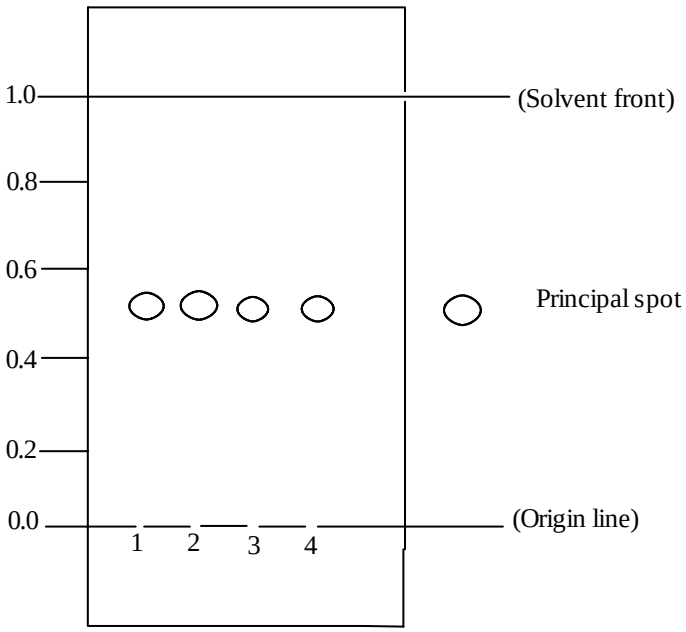
LOADING THE TLC PLATE WITH SAMPLE SOLUTION
▪ Mark an origin line about 1.5 cm from the bottom edge (with pencil) ▪ Apply 2 µL of each working standard solution ▪ Apply 2 µL of each working sample solution (up to five samples will fit on the plate) ▪ Wait until all spots are dry ▪ Check the uniformity of all spots with UV light of 254 nm

Development

- Carefully place the loaded plate into the developing chamber and close the jar
- Wait until the solvent front has moved three-quarters of the length of the plate (developing time, about 15 minutes)
- Remove the plate
- Mark the solvent front
- Air dry the plate or use hotplate if necessary

Detection

- Observe the chromatoplate (Figure 5) in daylight after staining with sulfuric acid
- Observe the plate in daylight after iodine staining
- Compare the result with the description in the manual



- Run no. 1 = 2.0 µL of artesunate 100% standard solution
- Run no. 2 = 2.0 µL of sample solution of a high-quality product
- Run no. 3 = 2.0 µL of sample solution of a poor-quality product
- Run no. 4 = 2.0 µL of artesunate 80% standard solution

Figure 5. Final Chromatoplate for Artesunate

Analysis of Quinine Preparations

Extraction Medium

- Aqueous methanol

Stock Standard Solution

QUININE STOCK STANDARD SOLUTION (10 mg/mL)
▪ Grind a 300 mg reference tablet and wash down the powder completely with 3 mL of water into a 50 mL glass bottle ▪ Close the bottle ▪ Shake the bottle for one minute ▪ Add 27 mL of methanol ▪ Close the bottle ▪ Shake the bottle for three minutes ▪ Let the bottle stand for five minutes until all insoluble material settles. The solution will not be clear; rather, it will appear hazy. ▪ Label the bottle as "Quinine Stock Standard Solution"

Working Standard Solution

QUININE WORKING STANDARD SOLUTION 100% = 1.25 mg/mL	**QUININE WORKING STANDARD SOLUTION 80% = 1.0 mg/mL**
▪ Pipette into a 10 mL vial ▪ Add 1 mL of hazy stock standard solution ▪ Add 7 mL of methanol ▪ Close, shake, and label as "Quinine Working Standard Solution 100%"	▪ Pipette into a 10 mL vial ▪ Add 1 mL of hazy stock standard solution ▪ Add 9 mL of methanol ▪ Close, shake, and label as "Quinine Working Standard Solution 80%"

Stock Sample Solution

QUININE STOCK SAMPLE SOLUTION (10 mg/mL) produced from a product with 100 mg/mL or unit	**QUININE STOCK SAMPLE SOLUTION (10 mg/mL) produced from a product with 200 mg/mL or unit**	**QUININE STOCK SAMPLE SOLUTION (10 mg/mL) produced from a product with 250 mg/mL or unit**
Oral preparations ▪ Grind a 100 mg tablet and wash down the powder completely with 1 mL of water into a 25 mL glass bottle, shake for one minute, then add 9 mL of methanol ▪ For capsules: open and transfer powder plus cap and body shells into a 25 mL glass bottle and add 1 mL of water, shake for one minute, then add 9 mL of methanol ▪ Close the bottle ▪ Shake the bottle for three minutes ▪ Let the bottle stand for five minutes until all insoluble material settles ▪ Label the bottle as "Quinine Stock Sample Solution"	**Oral preparations** ▪ Grind a 200 mg tablet and wash down the powder completely with 2 mL of water into a 25 mL glass bottle, shake for one minute, then add 18 mL of methanol ▪ For capsules: open and transfer powder plus cap and body shells into a 25 mL glass bottle and add 2 mL of water, shake for one minute, then add 18 mL of methanol ▪ Close the bottle ▪ Shake the bottle for three minutes ▪ Let the bottle stand for five minutes until all insoluble material settles ▪ Label the bottle as "Quinine Stock Sample Solution"	**Oral preparations** ▪ Grind a 250 mg tablet and wash down the powder completely with 2 mL of water into a 25 mL glass bottle, shake for one minute, then add 23 mL of methanol ▪ For capsules: open and transfer powder plus cap and body shells into a 25 mL glass bottle and add 2 mL of water, shake for one minute, then add 23 mL of methanol ▪ Close the bottle ▪ Shake the bottle for three minutes ▪ Let the bottle stand for five minutes until all insoluble material settles ▪ Label the bottle as "Quinine Stock Sample Solution"

Parenterals ▪ Pipette 1 mL of injection fluid into 25 mL bottle ▪ Add 9 mL of methanol and shake	**Parenterals** ▪ Pipette 1 mL of injection fluid into 50 mL bottle ▪ Add 19 mL of methanol and shake	**Parenterals** ▪ Pipette 1 mL of injection fluid into 50 mL bottle ▪ Add 24 mL of methanol and shake

QUININE STOCK SAMPLE SOLUTION (10 mg/mL) produced from a product with 300 mg/mL or unit	**QUININE STOCK SAMPLE SOLUTION (10 mg/mL) produced from a product with 500 mg/mL or unit**
Oral preparations ▪ Grind a 300 mg tablet and wash down the powder completely with 3 mL of water into a 50 mL glass bottle, shake for one minute, then add 27 mL of methanol ▪ For capsules: open and transfer powder plus cap and body shells into a 50 mL glass bottle and add 3 mL of water, shake for one minute, then add 27 mL of methanol ▪ Close the bottle ▪ Shake the bottle for three minutes ▪ Let the bottle stand for five minutes until all insoluble material settles ▪ Label the bottle as "Quinine Stock Sample Solution" **Parenterals** ▪ Pipette 1 mL of injection fluid into 50 mL bottle ▪ Add 29 mL of methanol and shake	**Oral preparations** ▪ Grind a 500 mg tablet and wash down the powder completely with 3 mL of water into a 100 mL glass bottle, shake for one minute, then add 47 mL of methanol ▪ For capsules: open and transfer powder plus cap and body shells into a 100 mL glass bottle and add 3 mL of water, shake for one minute, then add 47 mL of methanol ▪ Close the bottle ▪ Shake the bottle for three minutes ▪ Let the bottle stand for five minutes until all insoluble material settles ▪ Label the bottle as "Quinine Stock Sample Solution" **Parenterals** ▪ Pipette 1 mL of injection fluid into 100 mL bottle ▪ Add 49 mL of methanol and shake

Working Sample Solution

QUININE WORKING SAMPLE SOLUTION 100% = 1.25 mg/mL
▪ Pipette into a 10 mL vial ▪ Add 1 mL of hazy stock sample solution ▪ Add 7 mL of methanol ▪ Close, shake, and label as "Quinine Working Sample Solution"

Preparation of Developing Chamber

PROCEDURE	**SOLVENT**	**AMOUNT**
▪ Pipette into the developing chamber (jar) ▪ Add	Methanol Concentrated ammonia solution	20 mL 0.5 mL
▪ Close the developing chamber (jar) and mix thoroughly ▪ Line the chamber's wall with filter paper ▪ Wait for about 15 minutes for chamber saturation: use this time to perform spotting (next step)		

Spotting

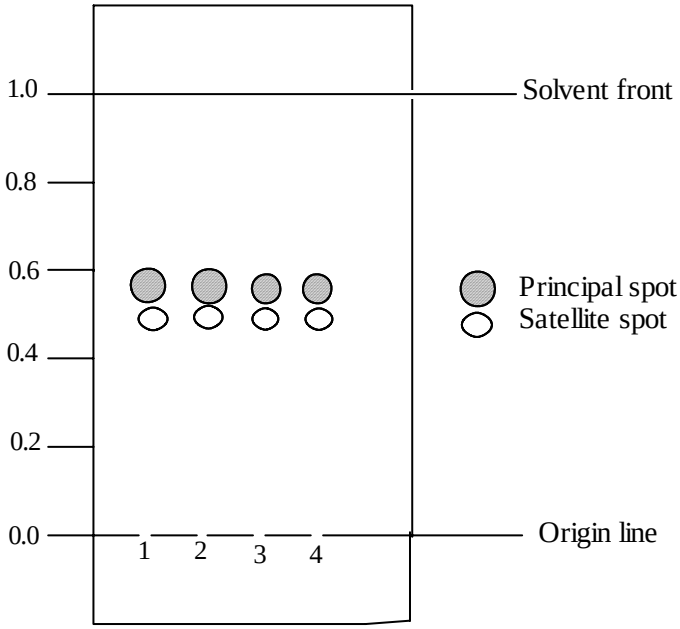
LOADING THE TLC PLATE WITH SAMPLE SOLUTION
▪ Mark an origin line about 1.5 cm from the bottom edge (with pencil) ▪ Apply 2 µL of each working standard solution ▪ Apply 2 µL of each working sample solution (up to five samples will fit on the plate) ▪ Wait until all spots are dry ▪ Check the uniformity of all spots with UV light of 254 nm

Development

- Carefully place the loaded plate into the developing chamber and close the jar
- Wait until the solvent front has moved three-fourths of the length of the plate (developing time, about 20 minutes)
- Remove the plate
- Mark the solvent front
- Air dry the plate or use hotplate if necessary

Detection

- Observe the chromatoplate (Figure 6) with UV light of 254 nm
- Observe the plate with UV light of 365 nm
- Observe the plate in daylight after iodine staining
- Compare the result with the description in the manual



- Run no. 1 = 2.0 µL of quinine 100% standard solution
- Run no. 2 = 2.0 µL of sample solution of a high-quality product
- Run no. 3 = 2.0 µL of sample solution of a poor-quality product
- Run no. 4 = 2.0 µL of quinine 80% standard solution

Figure 6. Final Chromatoplate for Quinine Observed at 254 nm

Analysis of Sulfadoxine/Pyrimethamine Tablets

Extraction Medium

- Methanol

Stock Standard Solution

SULFADOXINE/PYRIMETHAMINE STOCK STANDARD SOLUTION (25.0/1.25 mg/mL)
▪ Grind a 500/25 mg reference tablet and wash down the powder completely with 20 mL of methanol into a 25 mL glass bottle ▪ Close the bottle ▪ Shake the bottle for three minutes ▪ Let the bottle stand for five minutes until all insoluble material settles below the supernatant liquid ▪ Label the bottle as "Sulfadoxine/Pyrimethamine Stock Standard Solution"

Working Standard Solution

SULFADOXINE/PYRIMETHAMINE WORKING STANDARD SOLUTION 100% (6.25/0.3125 mg/mL)	**SULFADOXINE/PYRIMETHAMINE WORKING STANDARD SOLUTION 80% (5.00/0.25 mg/mL)**
▪ Pipette into a 10 mL vial ▪ Add 1 mL of stock standard solution ▪ Add 3 mL of methanol ▪ Close, shake, and label as "Sulfadoxine/Pyrimethamine Working Standard Solution 100%"	▪ Pipette into a 10 mL vial ▪ Add 1 mL of stock standard solution ▪ Add 4 mL of methanol ▪ Close, shake, and label as "Sulfadoxine/Pyrimethamine Working Standard Solution 80%"

Stock Sample Solution

SULFADOXINE/PYRIMETHAMINE STOCK SAMPLE SOLUTION (25.0/1.25 mg/mL) produced from a product claiming a potency of 500 + 25 mg of total compounds
▪ Tablets: Grind one and wash down the powder completely with 20 mL of methanol into a 25 mL glass bottle ▪ Capsules: Open one and transfer powder plus cap and body shells into a 25 mL glass bottle and add 20 mL of methanol
▪ Close and shake the bottle for three minutes ▪ Let the bottle stand for five minutes until all insoluble material settles below the supernatant ▪ Label the bottle as "Sulfadoxine/Pyrimethamine Stock Sample Solution"

Working Sample Solution

SULFADOXINE/PYRIMETHAMINE WORKING SAMPLE SOLUTION 100% (6.25/0.3125 mg/mL)
▪ Pipette into a 10 mL vial ▪ Add 1 mL of stock sample solution ▪ Add 3 mL of methanol ▪ Close, shake, and label as "Sulfadoxine/Pyrimethamine Working Sample Solution"

Preparation of Developing Chamber

PROCEDURE	SOLVENT	AMOUNT
▪ Pipette into the developing chamber ▪ Add	 Ethylacetate Methanol	 15 mL 5 mL
▪ Close the developing chamber (jar) and mix thoroughly ▪ Line the chamber's wall with filter paper ▪ Wait about 15 minutes for chamber saturation; use this time to perform spotting (next step)		

Spotting

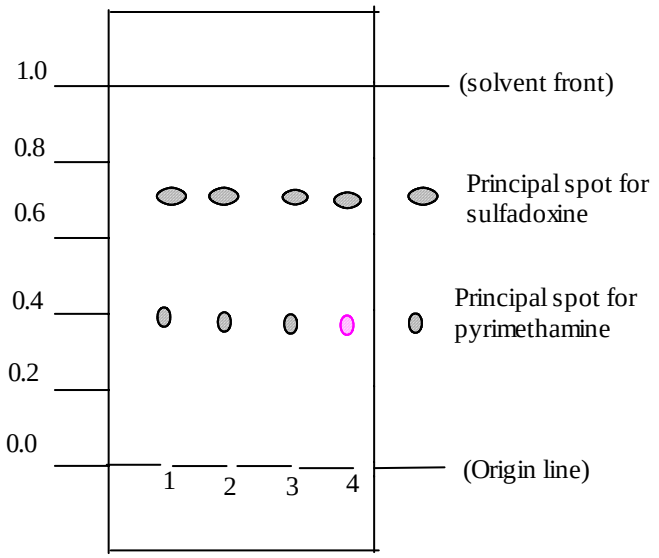
LOADING THE TLC PLATE WITH WORKING STANDARD AND SAMPLE SOLUTIONS
▪ Mark an origin line about 1.5 cm from the bottom edge using a pencil ▪ Apply 2 µL of each working standard solution ▪ Apply 2 µL of each working sample solution between the lower and higher reference standard (up to three samples will fit on the plate) ▪ Wait until all spots are dry ▪ Check the uniformity of all spots with UV light of 254 nm

Development

▪ Carefully place the loaded plate into the developing chamber and close the jar ▪ Wait until the solvent front has moved three-fourths of the length of the plate (developing time, about 15 minutes) ▪ Remove the plate ▪ Mark the solvent front using a pencil ▪ Air dry the plate or use hotplate if necessary

Detection

▪ Observe the chromatoplate (Figure 7) with UV light of 254 nm ▪ Expose the plate to iodine vapour for about one minute ▪ Observe the plate in daylight during and after iodine staining ▪ Compare the result with the description in the manual



- Run no. 1 = 2.0 µL of sulfadoxine/pyrimethamine 100% standard solution
- Run no. 2 = 2.0 µL of sample solution of a high-quality product
- Run no. 3 = 2.0 µL of sample solution of a poor-quality product
- Run no. 4 = 2.0 µL of sulfadoxine/pyrimethamine 80% standard solution

Figure 7. Final Chromatoplate for SP

Visual Inspection

Beginner's Summary

For documentation purposes during the visual inspection of pharmaceutical products, write down all product particulars using the appropriate Screening Certificate.

General Screening

Drug products from particularly cheap sources; drug products with missing or incorrect accompanying documents; drug products with defective dosage forms or packaging; and drug products with incomplete, damaged, or missing labels or with labels written in a foreign language should be subjected to disintegration and identity tests. If they pass, they should be further scrutinised using TLC to determine drug content and gross degradation. Repeat the examination with two other samples to eliminate anomalous results. Should a product not pass all tests, ask for a second opinion and refer an additional sample to a fully equipped drug quality control laboratory. Keep some retained samples in a safe place for future investigations.

Inspection of Packaging Material

Tablets and capsules can be presented in single-unit or multi-unit dose containers such as blister packs or bottles. Patient packs may contain just 10 or 20 tablets, whereas bulk packs may contain 1,000 or more tablets. On reception, the container should be properly sealed and labelled and be without defects and damage. Seals should not have been violated. A strong smell when the container is opened often indicates drug degradation (in products containing flavours or drug substances with a characteristic odour, such as penicillins, odour does not necessarily mean drug degradation). Excessive powder or pieces of tablets at the bottom of the container indicates the presence of abraded and broken tablets or crushed and opened capsules. Another deleterious effect, excessive moisture uptake, is indicated by fused tablets and capsules or by recrystallised drug substance on the solid formulation itself or on the container.

Inspection of Labels

Both the immediate container and the carton should have a durable label fixed on them. Labels may be replaced by printed handwriting, but it must be legible and indelible. At a minimum, the label should provide (1) the name of the drug, (2) the drug's strength, (3) the number of unit doses in the container, (4) the manufacturer's or distributor's name and full address, (5) the batch or lot number, (6) the expiry date, and (7) the storage conditions required by the drug.

Inspection of Dosage Forms

Solid oral dosage forms are normally presented as uncoated tablets and capsules. Sometimes they are specially coated and should then be labelled as such—for example, as enteric-coated capsules. Tablets might be dispersible or effervescent for dissolving in water before swallowing.

Tablets and capsules should show no signs of blemishes such as dirty marks or spots, abrasion or erosion, cracks or chips, or any other defects such as fusion or swelling. In

addition, hard gelatin capsules should show no signs of softening, and the capsule shells should be properly sealed and free of cracks and dents. The inside of a broken tablet or the contents of an opened capsule must be white with no signs of any mottling or discolouration. Allowances must be made for products where the drug substance or any excipient itself consists of coloured powder or crystals.

Disintegration Test

Tablets should be sufficiently hard to withstand handling without crumbling or breaking, but they should also be sufficiently soft for easy disintegration in the stomach or intestine so that the drug is available to the body. Poor drug processing or wrong storage may cause tablets and capsules to harden and fail the disintegration test. The test determines whether tablets and capsules disintegrate in water within 30 minutes.

All uncoated tablets and capsules and all soluble, dispersible, effervescent, and film-coated tablets (i.e., all quick-release formulations) must comply with this time of complete disintegration. Sugar-coated tablets may meet this specification, but it is not a requirement. Only modified-release and enteric-coated tablets and capsules are allowed to deviate from this time of complete disintegration. These tablets and capsules should be labelled as such and not be subjected to this test. These products require a more sophisticated disintegration test.

Simple counterfeit preparations such as capsules containing just sand or ground ceramics, or tablets made only of meat flour, are easily spotted by their disintegration behaviour. Ground ceramics or sand settles straight to the bottom of the vial, while the supernatant liquid stays clear or almost clear. Tablets and capsules containing only meat flour never really disintegrate. They just soak up water and form a sticky mass or disintegrate into a couple of sticky lumps that slowly settle to the bottom of the container. State-of-the-art tablets and capsules containing modern disintegrants behave completely differently. For example, uncoated tablets of good quality will normally completely disintegrate in water at 37ºC within 15 minutes.

Disintegration is defined as that state in which no residue of the tablet or capsule, except fragments of undissolved coating, remains in the test solution. It is a major defect if a drug product doesn’t pass this test. The product can be rejected at this stage already. No further TLC assay or any other tests are required. Stopping after this test will save organic solvent and reference samples for later use.

Beginner’s Summary

Place one tablet or capsule into a 100 mL wide-neck bottle containing 100 mL of water. The temperature of the water should be close to body temperature (37ºC). Stir or shake the liquid every few minutes, continuing for 30 minutes. You may stop earlier if the tablet or capsule has already disintegrated. The tablet or capsule passes the test if no residue remains in the liquid, or if any remaining residue consists of fragments of coating or is a soft mass with no palpable core.

Repeat the test on five more tablets or capsules. The batch passes the test if all six tablets or capsules disintegrate. Repeat the entire test cycle if one tablet or capsule fails to disintegrate. Test the batch a third time if another tablet or capsule fails in the second run.

Colour Reactions

Introduction

We have already covered a general overview of the Minilab concept; visual inspection of labels, packaging materials, tablets, and capsules; and a simplified disintegration test.

Both visual and disintegration tests will allow the identification of rough counterfeits for timely rejection prior to employing colour reactions for further examination. Therefore, colour reaction will be our third weapon to use if a product passes the previous tests. We have discussed a number of colour reactions in the previous sections. If you have done colour reactions by using the monographs described above, you will know that most of the colour reactions involved are not only tedious but also time consuming, and you need some special training to be able to do them precisely. In contrast, the colour reactions discussed next are not only cheap but also require little training.

The Minilab colour reaction is easy to use and is the perfect tool for primary screening of spurious drug products. Many national and international pharmacopoeias have been consulted for the selection of colour reactions for pharmaceutical preparations.

All methods selected have been tested and are sufficiently rugged, accurate, and sensitive to verify the identity of drug products on a routine basis. A time-consuming extraction of the drug will not necessarily be required. All the tests are well described in the manual that is provided with the Minilab kits. The tests described in the manual are only intended to verify the identity of pharmaceutical preparations. They should not be used to replace pharmacopoeia monographs.

All potentially counterfeit samples should be subjected to a TLC assay as described in the GPHF Minilab or referred to a fully equipped laboratory for further investigations prior to taking legal action. For good and reliable analytical results, only reagents and solvents of high purity should be used. The concentrations, which are commonly expressed in normalities or molarities, have been converted into percentages for easier understanding.

Reagents and test solutions are dispensed by volume. Tablets or capsules containing a fixed amount of drug substance are dispensed by just dividing them into equal parts as directed in the individual monograph. A balance (scale) will not be required.

Deionised or distilled water is the most commonly used solvent. In places where deionised or distilled water is not easily accessible, clear tap water or rainwater might be used. Reagents and apparatus required are indicated on the individual monograph concerned.

Heath and Safety

It is recommended to put on protective clothing—for example, an apron and safety spectacles—before starting work on a colour reaction. Spectacles must be worn at all times to avoid accidental contact with potentially hazardous test solutions and subsequent eye injuries.

Preparation of Test Solutions

A measuring cylinder, a funnel, graduated transfer pipettes, and wide-neck bottles are supplied for the preparation of test solutions.

1. The measuring cylinder should have a 5 to 50 mL capacity.

2. The transfer pipettes should have a volume of 0.5 to 3 mL. These and the graduated test tubes are the only dosing aids supplied.

3. A funnel is used for transferring liquid and solid reagents into polyethylene dispensing bottles for mixing and finally for dispensing.

4. The wide-neck bottles are designed for the preparation and mixing of test solutions requiring frequent shaking—for example, dissolution of NaOH pellets in water. The bottles come with a Teflon-lined closure.

5. More information on how to prepare your reagent and test solutions can be found on pages 70–72 of the GPHF Minilab colour reaction manual.

A label tape and marker pen should be used for the permanent identification of test solutions. Test solutions should be kept in polyethylene dispensing bottles or brown glass bottles with an attached transfer pipette.

Note the following:

- Remember to write down the date the test solution was prepared.

- All test solutions have been shown to be stable for at least three months under tropical climate conditions.

- Protective clothes and safety spectacles must be worn to prevent accidental contact with strong acids and alkaline solutions or any other potentially hazardous chemicals.

Sample Preparations

A pestle and circular filter paper (instead of a mortar) is needed for grinding tablets or granules to fine powder. Using filter paper avoids the risk of cross-contamination between different batches during routine work because each sample will need a fresh filter paper.

Note the following:

- If no filter paper is available, it may be replaced with any other sort of paper, such as newsprint.

- Grinding should be done away from strong fans, as a fan will blow the sample off the work surface. This may be of potential hazard to you if the substance is inhaled or comes in contact with eyes or skin, and may trigger an allergic reaction to penicillin or other related compounds.

For sachets, hard gelatin capsules are opened and their contents poured straight onto the filter paper. Division of the powder should be done according to the instructions given in an individual monograph, using a spatula. Soft gelatin capsules are opened by cutting them into an appropriate number of pieces using a pair of scissors, a blade, or a scalpel. Then the appropriate amount of powdered sample or the appropriate number of pieces is transferred into a graduated test tube using either the spatula or a micro-spoon as directed in the individual monographs.

Test Performance

The test tube should be held using a wooden clamp. Add the required volume of the test sample and then shake the tube: a characteristic colour for identification purposes is produced. Polyethylene dropping bottles or brown glass bottles with an attached transfer pipette are used to accommodate the test solutions for easy dispensing. The graduated test tube will indicate how much of that solution has been applied already. Dispense the required volume as directed in the individual monograph.

Note the following:

- Vigorous shaking of the test tube is often required to achieve the necessary colour reaction.

- Shake, do not swing, the test tube; swinging may lead to anomalous test results.

You might want to place the test tube for a moment into the tube rack . Sometimes a hot water bath is required to get the colour reaction started. Fill a 100 mL wide-neck bottle with about 50 mL of water, and heat it on a hotplate. Then insert the test tube containing the test sample into the water, making sure that the reaction mix in the test tube is just below the water surface. A colour that didn't appear in the cold will now be gradually produced in the heat.

Note the following:

- A travel iron can serve as a hotplate when placed upside down.

- Avoid direct contact with any hotplate.

Sometimes even a hot water bath doesn't produce enough heat to get a colour reaction started; then an alcohol lamp containing methylated spirits is used to produce a flame sufficiently hot to cause the colour reaction. Just hold the test tube containing the test sample

in the flame using a clamp and frequently shake the tube. Gradually, a colour is produced that would not emerge in the cold.

Cleaning and Storing the Minilab After Use

The test tubes should be thoroughly cleaned after use, and the reagents and test solutions properly stored or disposed of.

- Disposal of used reagents and test solutions should be done in a special dedicated waste liquid container, preferably made of polypropylene. Follow the rules of your local area.
- After disposal of test mixtures, rinse the empty test tubes with tap water.
- Use the test tube brush for test tube cleaning.
- If stains persist, soak the tubes in a mixture of water and detergent overnight.
- Do not use a spatula or anything similar to scrape off resistant stains. This will destroy the test tube.
- Finally, rinse all test tubes with deionised water, if available, before drying to avoid leaving a residue. Return the tubes upside down to the test tube rack.

All items should be put back into the protective case after being properly cleaned and dried.

ANNEXES

THE UNITED REPUBLIC OF TANZANIA
MINISTRY OF HEALTH

Web site: http//www.tfda.or.tz
Telephone: 255 22 2450512, 2450751
Direct line: 255 22 2450979
Fax: 255 22 2450793

TANZANIA FOOD AND DRUGS AUTHORITY
P.O. BOX 77150
DAR ES SALAAM

REJECTION/DETENTION FORM

Exporter/Manufacturer.....
Importer/Consignee.....
The inspected consignment(s) as per Pro Forma Invoice Number .....
and Airway Bill/Import Declaration Form Number.....dated.....
and Single Bill of Entry Number.....dated.....
has been rejected/retained for the following reasons: (tick all that apply)

1. Pro Forma Invoice is not approved by the TFDA ☐
2. 2% FOB is not paid to the TFDA ☐
3. The product(s) is/are not registered by the TFDA ☐
4. Consignee is unauthorized dealer of pharmaceuticals ☐
5. Manufacturer of the product is not indicated ☐
6. Description of the item is not clear ☐
7. Manufacturing and/or expiry date of product(s) not indicated ☐
8. The product(s) shelf life is too short/expired ☐
9. Physical quality of the product is poor ☐
10. Other(s).....
    .....
    .....

....
Name of Drug Inspector Signature Date

....
Name of Consignee/Clearing Agent Signature Date

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P.O. BOX 77150
DAR ES SALAAM

CONFISCATION/QUARANTINE FORM

DRUGS FOUND AT THE PREMISES CONTRARY TO THE LAW AND CONFISCATED/SEIZED/QUARANTINED AS EXHIBIT/SAMPLE ACCORDING TO TANZANIA FOOD, DRUGS AND COSMETICS ACT 2003, SECTION 106

Date: .....

Name of the Premises: .....

DRUGS CONFISCATED/SEIZED/QUARANTINED BY INSPECTORS

1.	**17.**
2.	**18.**
3.	**19.**
4.	**20.**
5.	**21.**
6.	**22.**
7.	**23.**
8.	**24.**
9.	**25.**
10.	**26.**
11.	**27.**
12.	**28.**
13.	**29.**
14.	**30.**
15.	**31.**
16.	**32.**

PARTICULARS

I, ..., the owner/in-charge of the above-named premises, confirm that the drugs listed above have been confiscated/seized by inspectors after being found at the premises illegally.

Signature of the Owner/In-charge.....

Name of Inspector.....
Signature of Inspector.....

Name of Inspector.....
Signature of Inspector.....

Name of Inspector.....
Signature of Inspector.....

Name of Inspector.....
Signature of Inspector.....

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SAMPLE RECEIPT FORM

Name of Institution/Company under Inspection.....

Address.....

Date of Inspection/Sample Collection.....

Reason for Collection (indicate analysis needed where possible) .....
.....

Product Name and Description/Identification (e.g., colour, dosage form).....
.....

Size of Lot Sample Taken From.....

Name and Address of Manufacturer.....
.....

Batch No. .....Manufacturing Date.....Expiry Date.....

Place Sampled (e.g., Port of Entry, Manufacturing Plant, Wholesale/Retail Pharmacy)
.....

No. of Samples Taken (indicate tins, packets, etc.).....

Collectors Identification on Seal.....

Name of Representative(s) of the Inspected Establishment	Signature	Date
.....	.....	.....
.....	.....	.....

Name of Drug Inspector(s) (Sampling Officer[s])	Signature	Date
.....	.....	.....
.....	.....	.....

Illustration of Inspectors' Activities and Actions during Inspections at Port of Entry

Section B of POE Consignment Inspection Form: Documentation

DOCUMENTATION CHECKS #1a and #1b

1a. Inspector shall check if the consignee has Pro Forma Invoice (PI) with the original endorsement by the TFDA.

1b. Inspector shall check if the consignee has Import Certificate (IC) with the original endorsement by the TFDA.

⇩

If yes

Inspector shall proceed to verify Item 1c.

⇨

If no

Inspector shall:

1. Stop the inspection
2. Complete the Detention/Rejection Form
3. Inform the TRA/C&E of the detention/rejection and give a copy of the form to the TRA
4. Give a copy of the form to the consignee

* Upon resolution of detention issues, by written instructions from the TFDA, the inspector will continue with the inspection from where it had been stopped.

DOCUMENTATION CHECK #1c

1c. Inspector shall check if the specific products are imported from sources indicated in the PI/IC.

⇒ **If no**

Inspector shall:
1. Stop the inspection
2. Complete the Detention/Rejection Form
3. Inform the TRA/C&E of the detention/rejection and give a copy of the form to the TRA
4. Give a copy of the form to the consignee

* Upon resolution of detention issues, by written instructions from the TFDA, the inspector will continue with the inspection from where it had been stopped.

⇓ **If yes**

Inspector shall proceed to verify Item 1d.

DOCUMENTATION CHECK #1d

1d. Inspector shall verify if the consignment is imported through the declared POE.

⇒ **If no**

Inspector shall:
1. Stop the inspection
2. Complete the Detention/Rejection Form
3. Inform the TRA/C&E of the detention/rejection and give a copy of the form to the TRA
4. Give a copy of the form to the consignee

* Upon resolution of detention issues, by written instructions from the TFDA, the inspector will continue with the inspection from where it had been stopped.

⇓ **If yes**

Inspector shall note the PI number and date and proceed to verify Item 2.

DOCUMENTATION CHECK #2

2. Inspector shall verify whether the CRF/FCVR of the consignment receipt date is within the expiry of the PI/IC.

⇒ **If no**

Inspector shall:
1. Stop the inspection
2. Complete the Detention/Rejection Form
3. Inform the TRA/C&E of the detention/rejection and give a copy of the form to the TRA
4. Give a copy of the form to the consignee

* Upon resolution of detention issues, by written instructions from the TFDA, the inspector will continue with the inspection from where it had been stopped.

⇓ **If yes**

Inspector shall proceed to verify Item 3.

DOCUMENTATION CHECK #3

3. Inspector shall verify whether the exporter and the importer named in the CRF/FCVR are the same as those indicted in the PI.

⇒ **If no**

Inspector shall:
1. Stop the inspection
2. Complete the Detention/Rejection Form
3. Inform the TRA/C&E of the detention/rejection and give a copy of the form to the TRA
4. Give a copy of the form to the consignee

* Upon resolution of detention issues, by written instructions from the TFDA, the inspector will continue with the inspection from where it had been stopped.

⇓ **If yes**

Inspector shall proceed to verify Item 4.

DOCUMENTATION CHECK #4a

4a. Inspector shall verify whether the FOB value indicated in the CRF/FCVR is the same as that of the approved PI.

⇒ **If no**

Inspector shall:
1. Stop the inspection
2. Complete the Detention/Rejection Form
3. Inform the TRA/C&E of the detention/rejection and give a copy of the form to the TRA
4. Give a copy of the form to the consignee

* Upon resolution of detention issues, by written instructions from the TFDA, the inspector will continue with the inspection from where it had been stopped.

⇓ **If yes**

Inspector shall proceed to verify Item 4b.

DOCUMENTATION CHECKS #4b, #4c, and #4d

4b. Inspector shall verify whether item's description and quantity for each of the products indicated in the CRF/FCVR match the quantities authorised in the PI.

If yes

Inspector shall proceed to verify Item 5.

If no

4d. Inspector shall verify whether the item's description and quantity indicted in the CRF/FCVR are LESS THAN those authorised in the PI.

If yes

Inspector shall mark the quantities of short-landed items on the PI, label it with the words "Partial Shipment," and proceed to verify Item 5.

If no

4c. Inspector shall verify whether the item's description and quantity indicated in the CRF are GREATER THAN authorised in the PI.

If yes

Inspector shall:

1. Stop the inspection
2. Complete the Detention/Rejection Form
3. Inform the TRA/C&E of the detention/rejection and give a copy of the form to the TRA
4. Give a copy of the form to the consignee

* Upon resolution of detention issues, by written instructions from the TFDA, the inspector will continue with the inspection from where it had been stopped.

DOCUMENTATION CHECK #5a

5a. Inspector shall verify to see if the consignment requires a Certificate of Analysis (COA).

⇒ **If no** ⇒ Go to Section C (Physical Examination and Testing).

⇓ **If yes**

Inspector shall proceed to verify Item 5b.

DOCUMENTATION CHECK #5b

5b. Inspector shall determine whether the COA is present with the consignment.

⇒ **If no** ⇒ Inspector shall:
1. Stop the inspection
2. Complete the Detention/Rejection Form
3. Inform the TRA/C&E of the detention/rejection and give a copy of the form to the TRA
4. Give a copy of the form to the consignee

* Upon resolution of detention issues, by written instructions from the TFDA, the inspector will continue with the inspection from where it had been stopped.

⇓ **If yes**

Inspector shall proceed to verify Item 5c.

DOCUMENTATION CHECK #5c

5c. Inspector shall determine whether there is a COA for each pharmaceutical batch.

⇒ **If no**

Inspector shall:
1. Stop the inspection
2. Complete the Detention/Rejection Form
3. Inform the TRA/C&E of the detention/rejection and give a copy of the form to the TRA
4. Give a copy of the form to the consignee

* Upon resolution of detention issues, by written instructions from the TFDA, the inspector will continue with the inspection from where it had been stopped.

⇓ **If yes**

Inspector shall proceed to verify Item 5d.

DOCUMENTATION CHECK #5d

5d. If the consignment contains vaccines, inspector shall ensure that there is a COA from the manufacturer and an approval from the regulatory authority of the country of origin.

⇒ **If no**

Inspector shall:
1. Stop the inspection
2. Complete the Detention/Rejection Form
3. Inform the TRA/C&E of the detention/rejection and give a copy of the form to the TRA
4. Give a copy of the form to the consignee

* Upon resolution of detention issues, by written instructions from the TFDA, the inspector will continue with the inspection from where it had been stopped.

⇓ **If yes**

Inspector shall proceed to verify Item 5e.

DOCUMENTATION CHECK #5e

5e. Inspector shall review the COA to determine if the COA has been signed and stamped by an authorised person.

If no

Inspector shall:
1. Stop the inspection
2. Complete the Detention/Rejection Form
3. Inform the TRA/C&E of the detention/rejection and give a copy of the form to the TRA
4. Give a copy of the form to the consignee

* Upon resolution of detention issues, by written instructions from the TFDA, the inspector will continue with the inspection from where it had been stopped.

If yes

Inspector shall proceed to verify Item 5f.

DOCUMENTATION CHECK #5f

5f. Inspector shall review the COA to determine if the reported test results are within specification limits.

All COA must bear parameters being measured, specifications limits, and test results.

If no

Inspector shall:
1. Stop the inspection
2. Complete the Detention/Rejection Form
3. Inform the TRA/C&E of the detention/rejection and give a copy of the form to the TRA
4. Give a copy of the form to the consignee

* Upon resolution of detention issues, by written instructions from the TFDA, the inspector will continue with the inspection from where it had been stopped.

If yes

Inspector shall proceed to verify Items 5g and 5h.

DOCUMENTATION CHECK #5g and 5h

Inspector shall review the COA to ascertain:

5g. Whether products with a shelf life of more than 24 months have 60% of their remaining shelf life at time of arrival

5h. Whether products with less than 24 months shelf life have 80% of their shelf life remaining at time of arrival

⇒ **If no**

Inspector shall:
1. Stop the inspection
2. Complete the Detention/Rejection Form
3. Inform the TRA/C&E of the detention/rejection and give a copy of the form to the TRA
4. Give a copy of the form to the consignee

* Upon resolution of detention issues, by written instructions from the TFDA, the inspector will continue with the inspection from where it had been stopped.

⇓ **If yes**

Inspector shall proceed to verify Item 5i.

DOCUMENTATION CHECK #5i

5i. Inspector shall determine if the batch numbers on the unit samples and the COAs match.

⇒ **If no**

Inspector shall:
1. Stop the inspection
2. Complete the Detention/Rejection Form
3. Inform the TRA/C&E of the detention/rejection and give a copy of the form to the TRA
4. Give a copy of the form to the consignee

* Upon resolution of detention issues, by written instructions from the TFDA, the inspector will continue with the inspection from where it had been stopped.

⇓ **If yes**

Inspector shall proceed to verify Item 5j.

DOCUMENTATION CHECK #5j

5j. Inspector shall determine if the expiration dates on the unit samples and the COAs match.

If no

Inspector shall:
1. Stop the inspection
2. Complete the Detention/Rejection Form
3. Inform the TRA/C&E of the detention/rejection and give a copy of the form to the TRA
4. Give a copy of the form to the consignee

* Upon resolution of detention issues, by written instructions from the TFDA, the inspector will continue with the inspection from where it had been stopped.

If yes

Inspector shall proceed to verify Section C.

Section C of POE Consignment Inspection Form: Physical Examination and Testing

PHYSICAL EXAMINATIONS #1, 2, 3, and 4

1. Inspector shall indicate the category of products
2. Inspector shall indicate the total number of products in the consignment
3. Inspector shall indicate the number of pharmaceutical products
4. Inspector shall indicate the number of pharmaceutical batches

PHYSICAL EXAMINATION #5

5. Inspector shall check to see if labels show any evidence of tampering.

⇒ **If yes**

Inspector shall:
1. Stop the inspection
2. Complete the Detention/Rejection Form
3. Inform the TRA/C&E of the detention/rejection and give a copy of the form to the TRA
4. Give a copy of the form to the consignee

* Upon resolution of detention issues, by written instructions from the TFDA, the inspector will continue with the inspection from where it had been stopped.

⇓ **If no**

Inspector shall proceed to verify Item 6.

PHYSICAL EXAMINATION #6

6. Inspector shall verify if the language written on the labels and package inserts is Swahili and/or English.

⇒ **If no**

Inspector shall:
1. Stop the inspection
2. Complete the Detention/Rejection Form
3. Inform the TRA/C&E of the detention/rejection and give a copy of the form to the TRA
4. Give a copy of the form to the consignee

* Upon resolution of detention issues, by written instructions from the TFDA, the inspector will continue with the inspection from where it had been stopped.

⇓ **If yes**

Inspector shall proceed to verify Item 7.

PHYSICAL EXAMINATION #7

7. Inspector shall verify if the samples have tamperproof seals that are intact.

⇒ **If no**

Inspector shall:
1. Stop the inspection
2. Complete the Detention/Rejection Form
3. Inform the TRA/C&E of the detention/rejection and give a copy of the form to the TRA
4. Give a copy of the form to the consignee

* Upon resolution of detention issues, by written instructions from the TFDA, the inspector will continue with the inspection from where it had been stopped.

⇓ **If yes**

Inspector shall proceed to verify Item 8.

PHYSICAL EXAMINATION #8

8. Inspector shall determine whether the consignment contains expired units.

⇒ **If yes**

Inspector shall:
1. Stop the inspection
2. Complete the Detention/Rejection Form
3. Inform the TRA/C&E of the detention/rejection and give a copy of the form to the TRA
4. Give a copy of the form to the consignee

* Upon resolution of detention issues, by written instructions from the TFDA, the inspector will continue with the inspection from where it had been stopped.

⇓

If no

Inspector shall proceed to verify Item 9.

PHYSICAL EXAMINATION #9

9. Inspector shall conduct physical examination according to SOP No. TFDAINS 002. Do the samples pass?

⇒ **If no**

Inspector shall:
1. Stop the inspection
2. Complete the Detention/Rejection Form
3. Inform the TRA/C&E of the detention/rejection and give a copy of the form to the TRA
4. Give a copy of the form to the consignee

* Upon resolution of detention issues, by written instructions from the TFDA, the inspector will continue with the inspection from where it had been stopped.

⇓

If yes

Inspector shall proceed to verify Item 10.

PHYSICAL EXAMINATION #10

10. Inspector shall determine whether the consignment includes products under the surveillance program.

⇒ **If no** ⇒ Proceed to Section D (Conclusion).

⇓

If yes

Inspector shall proceed to verify Item 11.

PHYSICAL EXAMINATIONS #11, 12, and 13

11. Inspector shall indicate the total number of products included in the surveillance program.

12. Inspector shall indicate the total number of batches included in the surveillance program.

13. Inspector shall take samples for screening according to SOP Nos. SPD 02-00, SPD 02-01, SPD 03-01, and SPD 05-01.