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Ecumenical Pharmaceutical Network
Réseau Pharmaceutique Œcuménique

The Minilab Project

ASSURING QUALITY MEDICINES AT THE HEALTH FACILITY

A training manual for the health worker

DIFAEM
German Institute for Medical Mission

FOREWARD

- The manual is intended for training the health workers to equip them with the requisite knowledge and skills for assuring quality medicines at the health; facilities
- The course is divided in four interrelated units, each presented in a simplified and easy to understand manner
- This manual was developed by the Ecumenical Pharmaceutical Network (EPN) with the kind support of DIFAEM

About EPN

EPN

- **A Christian, not for profit, independent organization** committed to the provision of **quality pharmaceutical services** as a means to achieving global goals and targets on **health and access to medicines**

Vision

- A valued global partner for just compassionate **quality pharmaceutical services for all**

Mission

- To support churches and church health systems **provide** just and **compassionate quality pharmaceutical services**

DIFAEM

- The German Institute for Medical Mission (DIFAEM) is a Christian Non-Governmental Organization (NGO) offering technical expertise and financial support for health services in resource-limited settings;
- Its special focus is on Primary Health Care and access to good health services especially for poor and marginalized communities.

Course units

Unit 1

Importance of quality medicines

Unit 2

The global menace of Falsified/Counterfeit /substandard Medicines

Unit 3

The role of MINILAB in the Fight Against Falsified/Counterfeit /substandard Medicines

Unit 4

Facilities' roles in the Fight Against Falsified/Counterfeit /substandard Medicines

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Unit 1:The Importance of Medicine Quality

http://www.bochealthcare.co.uk/en/Quality-and-safety/Regulations-and-classifications/Pharmaceutical-quality/Pharmaceutical-Quality.html

Session Objectives

At the end of this session, the trainee should be able to:

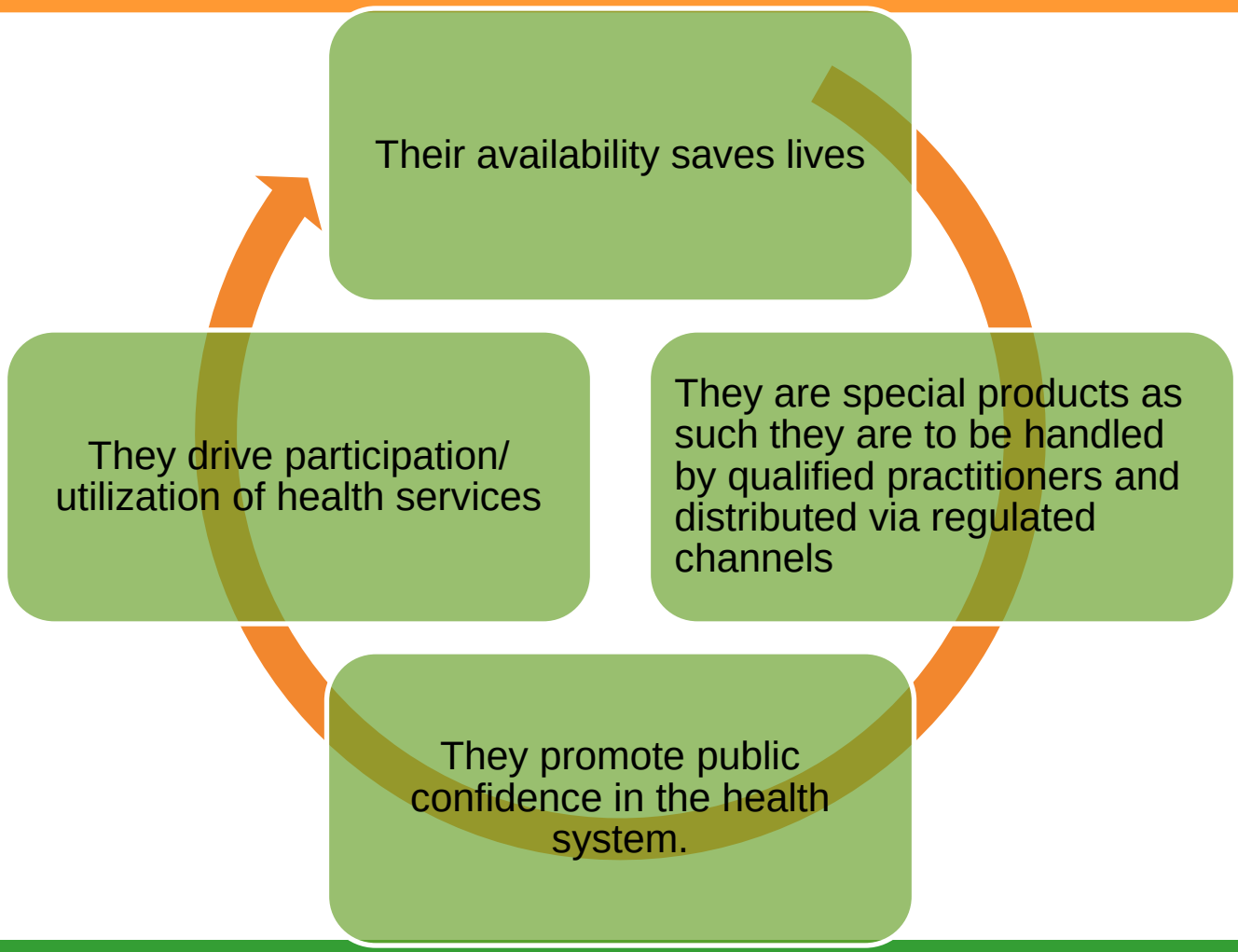
01 Explain the role of medicines in a health system.

02 Describe and explain the characteristics of high quality medicines.

03 Describe the factors that affect the quality of medicines

04 Understand and explain the differences between generic, substandard and falsified/counterfeit medicines

The role of medicines in Health System



What is Quality?

- Brainstorm!
  - Each participant names one aspect he can think of.

http://www.quinncreative.com/time-alone-improves-your-life/

Characteristics of a Good Quality Medicine

- A medicine is of good quality if it meets internationally accepted pharmacopeia standard used in its manufacture, {*For example International Pharmacopoeia (IP), British Pharmacopoeia (BP), or United States Pharmacopeia (USP)*}, with respect to :
  - **Identity:**
  - **Purity:**
  - **Potency:**.
  - **Uniformity:**.
  - **Stability:**
  - **Packaging**

Characteristics of a Good Quality Medicine (2)

- **Identity:**
  - This relates to the Active ingredient contained in the medicine. High quality medicines always contain the correct type of ingredient, in the correct quantity, as stated on the label:
  - Note: Medicines always also contain excipients, tablets e.g. contain lactose powder, syrups contain water etc.
- **Purity:**
  - This relates to the absence of any form of contaminants. High quality medicines should not be impure.

Characteristics of a Good Quality Medicine (3)

Potency:

- This refers to the medicine containing the right amount of active ingredients as stated on the label. e.g. Each tablet contains 500mg of Paracetamol

Uniformity:

- This implies that the shape, colour, size and texture of the medicine should have similar consistency for each dosage form.

Characteristics of a Good Quality Medicine (4)

- **Stability:**
  - If stored correctly, the medicine is guaranteed to be secure and safe for consumption and maintain its physical and chemical properties until the date of expiry.

Factors that Affect the Quality of Medicines

- **Direct Input Materials**
  - Active ingredients, Excipients.

- **Processes**
  - Formulation, Production/ Manufacturing processing, Quality Control and Packaging.

Factors that Affect the Quality of Medicines (2)

- **Indirect Input Materials**
  - Skills level of personnel, production environment, equipment, packaging materials.
- **Handling & Storage conditions**
  - Until its use, each medicine should be stored in the correct storage condition that ensures it maintains its physical and chemical properties with its shelf-life.

Generic medicines are bad??

- Discuss what are generic medicines in comparison to branded/original medicines ?
- Do you think there is a difference in quality
- What is a brand name?
- What is a generic name?

Source: http://www.paulonpaul.org/discussion.htm

Substandard & Falsified Medicines

- The global community has not agreed on the unified definition of substandard and falsified medicines.
- WHO however defines it as:
  - *Those medicines that are deliberately or fraudulently mislabelled with respect to identity and source.*
- In other words falsified medicines:

Have fake Identity, mislabelled, are impure, not potent, non-uniform and highly unstable.

Example of Mislabelled Counterfeit

What Constitutes Falsified/Counterfeit Medicines

- Both branded and generic products can be affected
- All kinds of medicines can be counterfeit, both expensive and inexpensive, originator and generics, including medicines for the treatment of life-threatening conditions to generic versions of painkillers and antihistamines.

Categories of Falsified Medicines

- Medicines without active ingredients.
  - E.g. containing just lactose or starch.

- Medicines with incorrect amount of active ingredients
  - E.g. 50mg of Amoxicillin instead of 500mg

Categories of Falsified Medicines

- Medicines with active ingredients different from label claim
  - E.g. Paracetamol labelled as Sulphadoxine – Pyrimethamine.
- Clones of fast moving products.

Impact of Poor Quality Medicines

Impact on Patients

- Lack of therapeutic effect may lead to prolonged illness or death.
- Cause financial waste on the patient through extended treatment costs
- Degraded product may cause toxic or adverse reactions.
- Under dosing because of too little active ingredient can cause resistance.

Impact of Poor Quality Medicines

Impact on Facility

- Monetary waste as a result of procurement of useless products.
- Loss of confidence can discourage patients from using the health service leading to decline in revenue.
- Continued low patronage can lead to low morale and loss of job among employees and eventual closure of the facility.

Impact of Poor Quality Medicines

Impact on Public Health

- Decline in public confidence in health systems.

- Increase in anti microbial resistance, a problem that can occur when a medicine is under dosed.

Key factors driving the supply of counterfeit medicine

- Poverty
- Weak regulatory enforcement
- Chaotic distribution channel of medicines
- Stock out syndrome/intermittent stock shortage
- Weak or absence of stiff legislative policies /laws against counterfeiters in many countries.
- Low awareness by the public about counterfeit medicines and its dangers

Key factors driving the supply of counterfeit medicine

- Poor governance and lack of political will
- Porosity of borders
- Conflicting interests
- Increased disease burden and added pressure on health systems

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Unit 2: The Global Menace of Counterfeit/ Substandard Medicines

Main Unit Objective

Increase the participants' appreciation of the menace caused by Falsified/Counterfeit or Substandard medicines to the patients and society.

Specific Objectives

At the end of this session, the participants should be able to

01 Appreciate the historical background of counterfeit medicines.

02 Understand the global burden and geographical spread of the menace of counterfeit medicines.

03 List factors enabling counterfeit medicines industry to thrive

04 List the dangers/consequences posed by counterfeits to patients and the society at large.

Fake or Genuine?

- *Counterfeiting* – literally ***copying*** or ***imitating***.

One of these medicines is fake.

Can you tell which?

History of Counterfeit Medicines

Herbal Medical

- **1600s**, discovery of fake herbs such as **cinchona**
- **1800s** incidence of fake **quinine**

Early Medicine

- **1948** fake **penicillin** was found in post-war Vienna
- **10years** later, WHO addressed the issue for the first time.

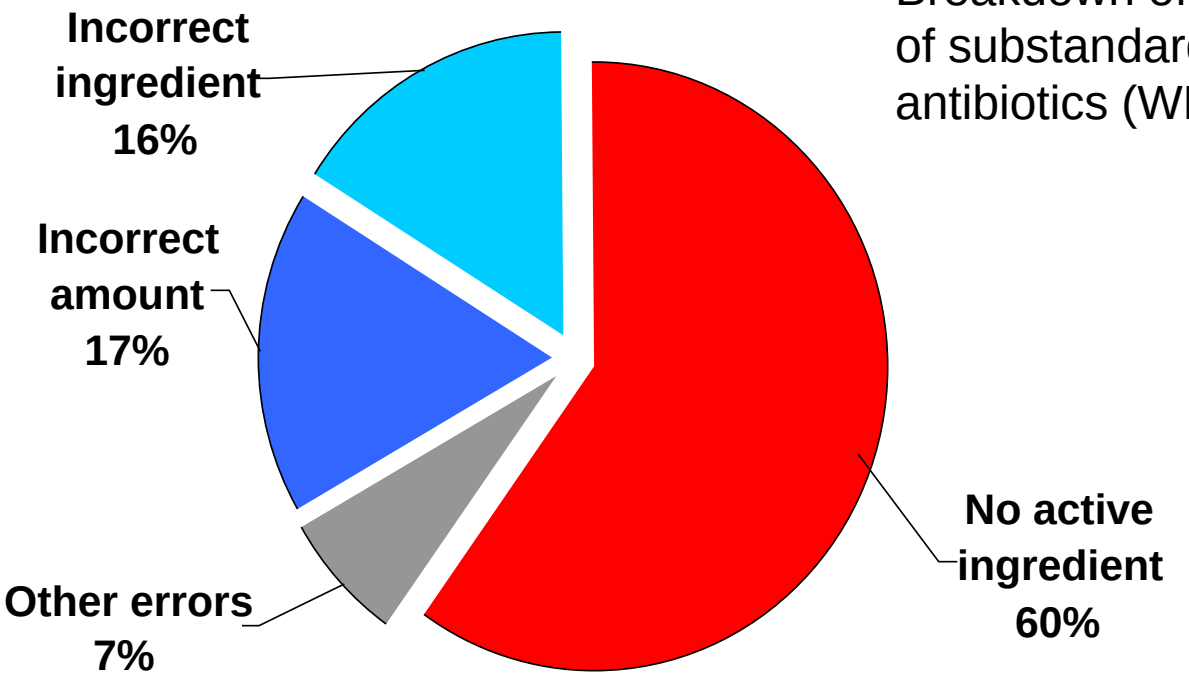
High Tech Medicines

- **1980** WHO officially initiated an offence against counterfeit medicine
- **2006** the International Medical Products Anti-Counterfeiting Taskforce (IMPACT) was launched

Global Prevalence of Counterfeit Medicines

- Spurious Falsely labeled Falsified Counterfeit (SFFC) medicines are found everywhere in the world;
- The statistics on the exact prevalence is nonexistent.
- Prevalence is greatest in regions where regulatory and enforcement systems for medicines are weakest – World Health Organisation (WHO).
- The source of a SFFC medicine is usually unknown and its content unreliable.
- Global sales of counterfeit medicines to be in excess of $75 billion annually – WHO estimates.

Global Incidences of Falsified/Counterfeit Medicines



Breakdown of data on 325 cases of substandard drugs - including antibiotics (WHO database)

Sampled Incidences of Counterfeit Medicines

SFFC Medicine	Country/ Year	Report
Avastin (for cancer treatment)	United States of America, 2012	Affected 19 medical practices. The drug lacked active ingredient
Zidolam-N (for HIV/AIDS)	Kenya, 2011	Nearly 3 000 patients got their prescription re-fill from this counterfeit batch
Metakelfin (antimalarial)	United Republic of Tanzania, 2009	Discovered in 40 pharmacies. The medicine lacked sufficient active ingredient
Truvada and Viread (for HIV/AIDS)	United Kingdom, 2011	Seized before reaching patients. Diverted authentic product in falsified packaging

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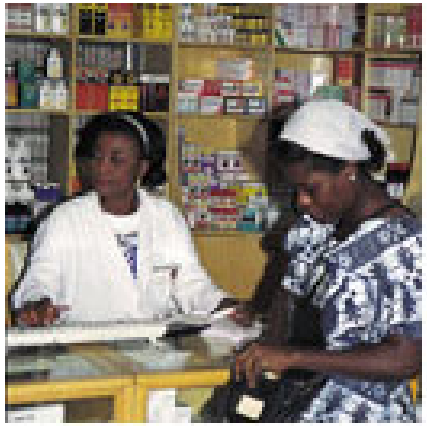
Unit 3: Role of GPHF- Minilab® in the fight against Counterfeit/ Substandard Medicines



Session Objectives

At the end of this session, the participants should be able:

01 *To understand the role of GPHF-Minilab® in the fight against counterfeit medicines;*

02 *To conduct Visual Inspection test and refer suspect products to the nearest GPHF-Minilab® for further tests;*

03 *Take remedial steps to prevent counterfeit medicines in their respective facilities*

04 *Know how to contact their nearest GPHF-Minilab facility and send samples incase of a suspect product*

What is GPHF*-Minilab® ?

The Minilab ® had been developed by GPHF in Germany as a simple, low tech and less expensive method for first quality screening of medicines. About 700 sets have been distributed to about 90 countries since 1997 by GPHF.

Difaem, an EPN member in Germany started a project in 2010 to support and network FBO-Drug Supply Organisations in using the Minilab ®

*Global Pharma Health Fund

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GPHF-MINILAB Boxes

GPHF-Minilab®: Range of Test Methods

Physical and Visual Inspection	Disintegration	Colour Reaction	Thin Layer Chromatography
			
1. Physical inspection to verify batch and licence number, address, product specifications and authentic features	2. Simplified disinte-gration test to verify health risks associated with improper drug release due to poor tablet/capsule formulations	3. A kit for specific colour reactions can be added as second independent test on drug identity (WHO Basic Tests etc.)	4. TLC assay to verify label claims on drug identity and content thus detecting health risks associated with wrong, high, low and zero drug content

Majority of all fake medicines already detected here

This is to detect more counterfeit medicines sitting in perfectly copied packaging and to identify associated health risks when being of extremely poor quality

DISINTEGRATION TEST

Disintegration Testing

Testing in Water of 37ºC

An Initiative of Merck Darmstadt · Germany

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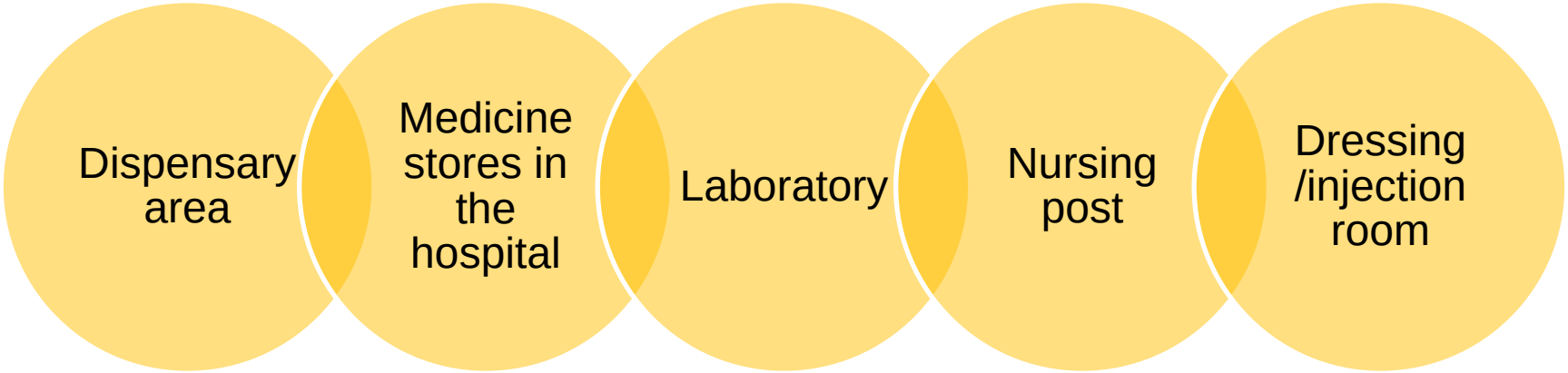
COLOUR REACTION TEST

Fake Products Identified with THIN LAYER CHROMATOGRAPHY

COARTEM BATCH F1909

Conducting Visual Inspection (VI) at SERVICE DELIVERY POINT(SDP)

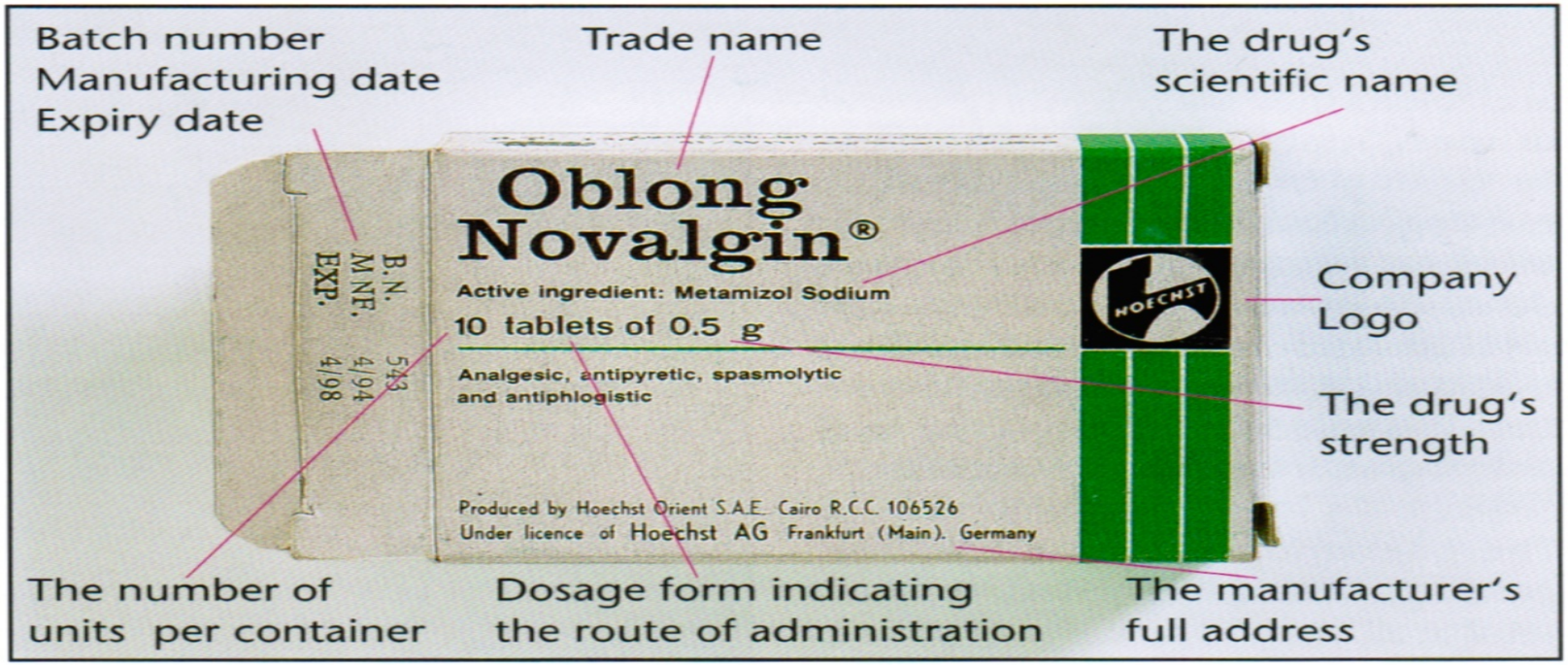
All areas in the hospital where medicines are handled are considered SDPs and will include:



Parameters to look out for when conducting Visual Inspection

- ✓ Expiration date (should be legibly printed)
- ✓ Manufacturing date (also be legibly printed)
- ✓ Shelf life (should be consistent for all batches)
- ✓ Label on the outer package (carton) must match with the label inside package (container)
- ✓ Batch number (have a regular pattern consistent with same manufacturer)
- ✓ Look out for spelling errors on the package
- ✓ Manufacturers' details and logos
- ✓ Strength and dosage form

How to Conduct Visual Inspection (VI)



Visual inspection of labels: prints must be legible and indelible and deliver a minimum of information. Claims on batch number, expiry date, product licence number etc. can be verified when contacting the originator company and the appropriate drug authorities responsible for product registration. Claims on drug identity and content can be verified using the GPHF-Minilab® and confirmatory compendial testing.

VI in DISPENSING AREA

- ✓ Check discoloration or black spots on tablets and caps when open
- ✓ Tablets should not turn to powders in the course of dispensing them
- ✓ Look for growth and particles in liquid preparation
- ✓ Powders to be reconstituted with water should not cake. They should be free flowing in the bottles

VI in INJECTION/DRESSING ROOM

- ✓ Reconstituted injections should not be cloudy and should dissolve completely (common with fake benzathine penicillin and ceftriaxone)
- ✓ Look out for growth and particles especially in Infusions

How to Identify and Prevent Counterfeits

The first and most important step
is the visual inspection of the medicine!

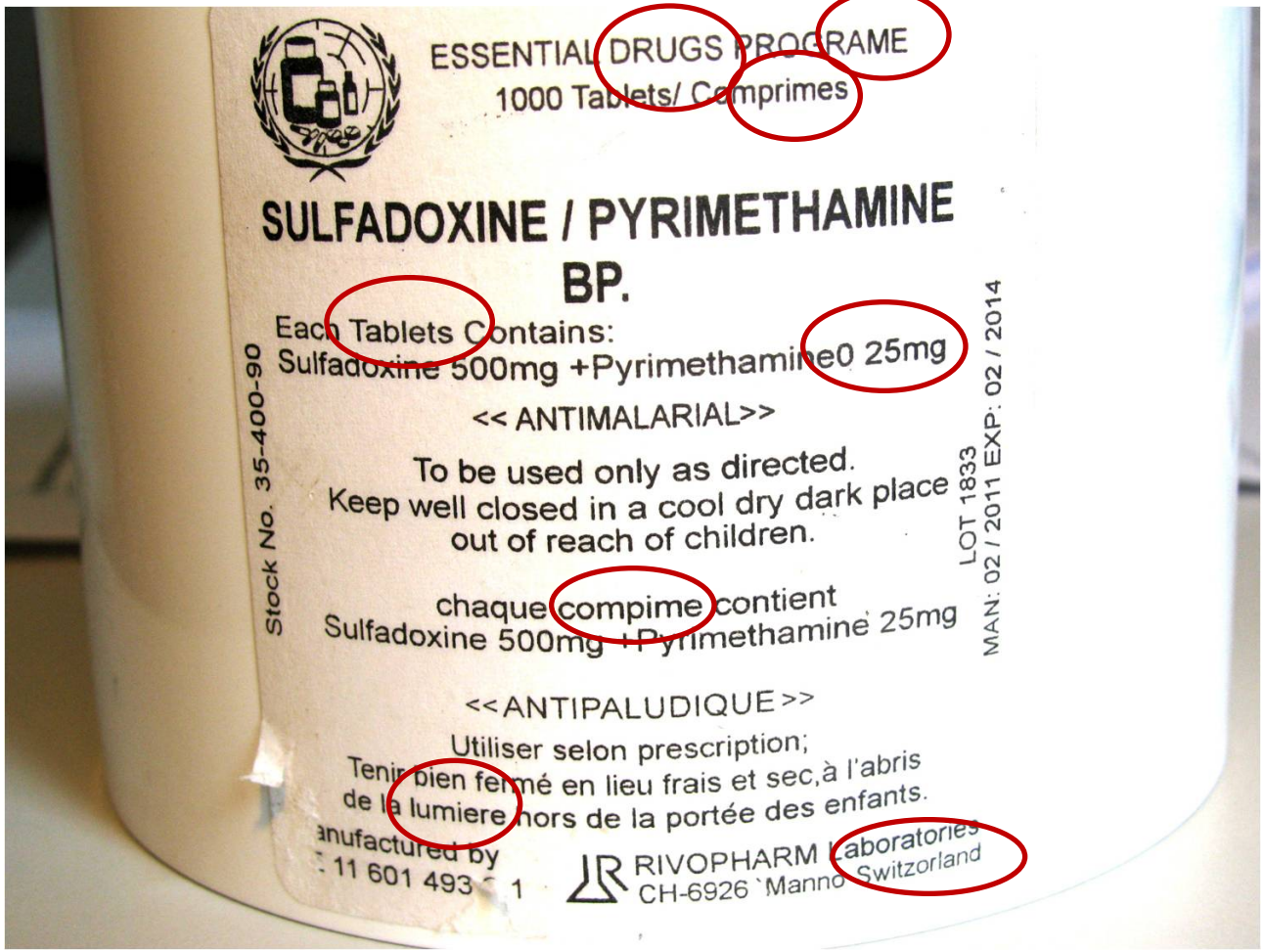
Train your eyes to look out for signs!

What do you look for during Visual Inspection?

Visual Test!

What signs indicate that this medicine is counterfeit?

Hints that Indicate a Counterfeit



Why is the Minilab such an important tool?

- It's affordable compared to setting up a standard QC laboratory

Affordable

- More than 95% of its results have been confirmed to be the same as using more stringent methods in a standard Laboratory

Comparable

- The minilab is easy to use with little time and investment in training

Easy

- It is mobile and suitable to be adapted even in very remote areas in low income countries

Suitable

- Results are reliable and rapid to get so as to make rapid judgement about medicines quality

Reliable

The DIFAEM-EPN Minilab Network

- Difaem supported EPN members to implement Minilab system
- At present, there are 15 EPN-MINILAB members who currently conduct free screening of products in the minilab compendium
- The members are drawn from 10 countries
  - Incl. Nigeria, Cameroon, Kenya, Tanzania, Ghana, DRC, Burundi, Uganda, Malawi and India

DIFAEM-EPN Minilab Network

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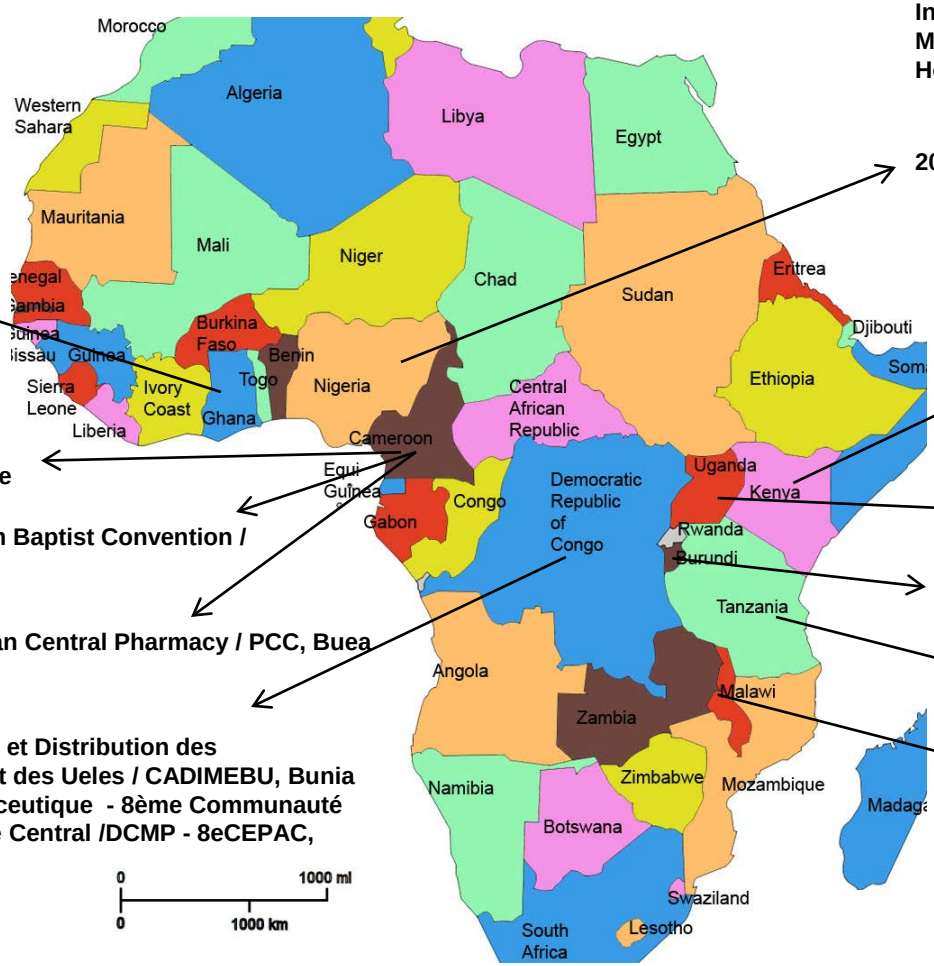

India: 2013: Community Development Medical Unit / CDMU, Odisha / Emmanuel Hospital Association / EHA, Tezpur

2012: CHAN-Medipharm, Jos

2012: National Catholic Health Service / NCHS, Accra

2013: Mission for Essential Drugs and Supplies / MEDS, Nairobi

2014: Organisation Catholique pour la Santé au Cameroun / OCASC, Yaounde

2010: Joint Medical Store / JMS, Kampala

2010: Cameroon Baptist Convention / CBC, Tiko

2014: LifeNet International, Bujumbura

2011: Presbyterian Central Pharmacy / PCC, Buea

2015: Rift Valley Diocese / Kilimatinde Hsp, Manyoni

2013: Nkhoma Hospital, Nkhoma

2013: Centrale D'Approvisionnement et Distribution des Médicaments Essentiels / de Bunia et des Ueles / CADIMEBU, Bunia DRC / Dépôt Central Médico-Pharmaceutique - 8ème Communauté Evangélique / Pentecôte de L'Afrique Central /DCMP - 8eCEPAC, Bukavu

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Training is Essential

A five days training of staff in the use of Minilab is part of the project like here in Cameroon. Each participant gets a Certificate afterwards

Work done by the EPN-DIFAEM Minilab Network

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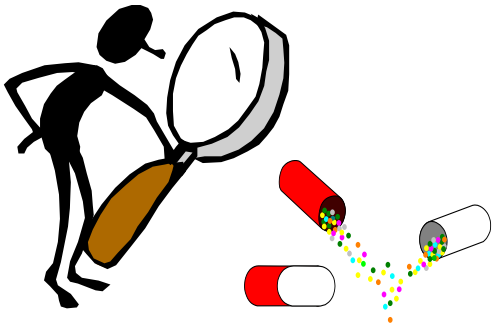
Status up to July 2015

Year	Samples
2011	92
2012	155
2013	288
2014	709
2015_…	499
Together	**1743**



Up to now the Minilab-Network has done a number of preliminary testing for products of its own DSOs, where a few cases of falsified products have so far been detected

Product	Active Pharmaceutical Ingredient	Batch	Company
Coartem	Artemether/Lumefantrine 20/120mg	F2951	Novartis
Cloxzem	Cloxacillin 500 mg	121242	ZMC
Quinine sulfate	Quinine sulfate	SD13-8001	Pharmakina
Coartem	Artemether/Lumefantrine 20mg/120mg	F2261	Novartis
Coartem	Artemether/Lumefantrine 20mg/120mg	F2153	Novartis
Duo-Cotecxin	Dihydroartemesine/ Piperaquin	10906	Zhej. Holley
Sulfadox-Pyrimeth.	Sulfadoxine/ Pyrimethamine 500/25mg	1833	Rivopharm
Zinnat	Cefuroxime Axetil 250 mg	C419061	Glaxo
Amatem Tab	Artemether/Lumefantrine 20mg/120mg	AMMH0013	Micro Labs.
Coartem	Artemether/Lumefantrine 20mg/120mg	N0F2153	Novartis
Coartem	Artemether/Lumefantrine 20mg/120mg	F1901	Novartis
Lumartem	Artemether/Lumefantrine 20/120mg	FD3016	Cipla
Lumartem	Artemether/Lumefantrine 20/120mg	DY1402542	Ipca lab
Duo-Cotecxin	Dihydroartemesine/ Piperaquin	110240	Holley-Cotec

Confirmation Tests

Minilab test: → **if positive (product suspicious)**
2nd test for confirmation
→ **if still positive:**
Repeating the test by 2nd Minilab Network partner
→ **If still positive:**
Confirmation test by WHO prequalified laboratory
(e.g. Mission for Essential Drugs and Supplies/MEDS in Kenya)

<u>If confirmed:</u>

By DIFAEM:

- **Info to Minilab Partner to inform health facilities by warning letters etc.**
- **Detailed info to World Health Organization /WHO Rapid alert system**

By WHO:

- **Warning info by WHO-Alert**
- **Contacting local and regional Medicines Regulatory Authorities of MoH**
- **Contacting manufacturer of product of origin**

Minilab in Bukavu DRC

Your role as a Health Worker in Preventing Counterfeit Medicine

1. Implement **WHO/EPN Guidelines on Good Pharmacy Practices** in our facility

2. Select only **quality assured medicine products** from authorized pre-qualified and reputable manufactures and supplies

3. Put in place a **quality assurance SOP*** for checking all incoming supplies

*Standard Operating Procedure

4. Conduct **Visual Inspection** on all medicines at the store at a predetermined schedule and at all the service delivery points before any administration or dispensing to patients and lastly

5. Contact your local Minilab partner for further instructions on how to send a sample for testing

What to do after a Product Fails Visual Inspection Test

- **After carrying out visual inspection, you suspect a medicine to be counterfeit, contact your local Minilab-Network member immediately to receive instructions about next steps**

How to contact your Nearest GPHF-Minilab® Facility

To know your nearest Minilab facility, please contact EPN on:

Tel: +254 724 301755/ 572 522702
E-mail: info@epnetwork.org

Unit 4: Facilities' Roles in the Fight Against Counterfeit /Substandard Medicines

Food for Thought!

- Are you satisfied with the quality of medicines you receive in your facility?
- Is quality maintained throughout your facility, if yes, how?
- Are there complaints of poor quality by patients/staff?
- Is there a formal mechanism for reporting and investigating complaints?
- Who is the quality focal person in your facility?

Session Objectives (1)

At the end of this session, the participants should be able to:

01 Identify stakeholders of medicine quality within and outside the facility.

02 Explain the goals of instituting a Quality Assurance(QA) system in the facility.

03 Describe the characteristics of a QA system

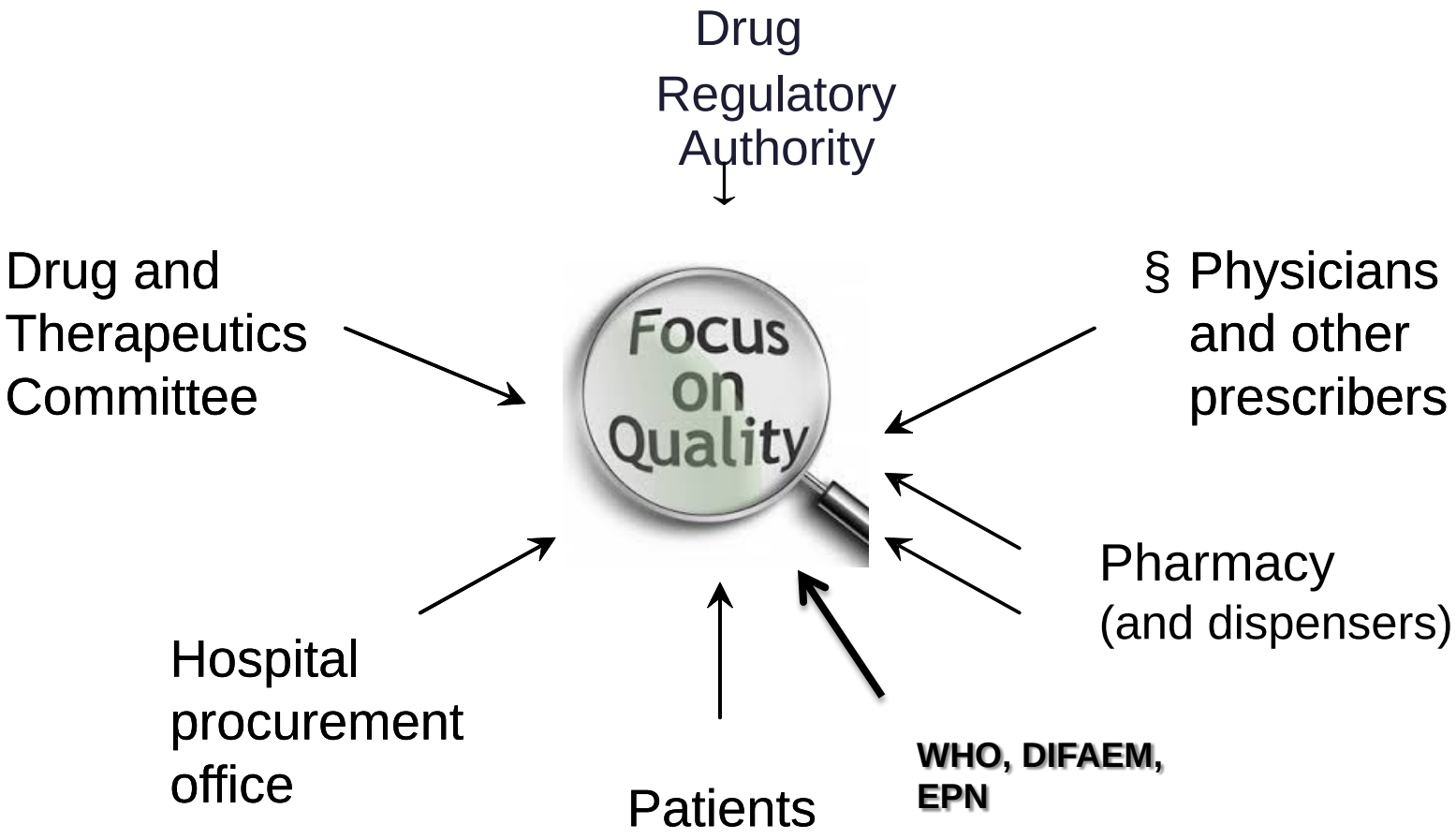
Session Objectives (2)

04 List specific actions that can be taken to ensure selection of suppliers, products.

05 Mention at least 2-3 organizations they can collaborate with locally &Internationally in the global fight against falsified/ medicines.

06 Establish a Product Monitoring System in the facility

Stakeholders of Medicine Quality?



Objectives of Facility Based Medicine QA Program

To make certain that each medicine reaching a patient is safe, effective, and of standard quality

1. Obtaining quality products that are safe and effective through structured selection and procurement methods

2. Maintaining quality products through the appropriate storage, distribution, monitoring, and use by prescribers, dispensers, and consumers

Characteristics of a Comprehensive QA Program

- ✓ Medicines are selected on the basis of safety and efficacy, in an appropriate dosage form with the longest shelf life
- ✓ Suppliers with acceptable quality standards are selected
- ✓ Medicines received from suppliers and donors are monitored to meet quality standards

Characteristics of a Comprehensive QA Progr.(cont)

- ✓ Repackaging activities and dispensing practices maintain quality
- ✓ Adequate storage conditions in all pharmaceutical areas are maintained.
- ✓ Product quality concerns are reported and monitored.

Careful Supplier Selection

- Prequalify and select suppliers competitively

- Select only quality assured medicine products from authorized pre-qualified and reputable manufacturers and suppliers

Actions to Obtain Good-Quality Products

Careful Product Selection should be done by:

- **Selection of medicines** based on safety, efficacy, quality profiles evidenced by clinical trials and reference literatures
- **Selection of dosage forms** that have longer shelf life-tablets instead of liquid preparation.
- **Selection of properly packaged** products

Actions to Obtain Good-Quality Products

- **Issue standard contract** for all procurement.
- **Use generic names** of products.
- **Ensure the strength**, pack size, and quantity are clearly stated
- **State the minimum shelf –life acceptable** to the Local Purchase Order(LPO)
- Any other **additional information required**
- Select the **Drug Supply Organization of your church/country** instead of wholesalers

Action Points for Receiving Products

- ✓ Medicines should always be received by an authorised person at the health facility.
- ✓ There should be clear written guidelines on receiving procedures.
- ✓ If one person receives a consignment, it should be a different person from the one who ordered.

Action for Receiving Medicines

- ✓ Standard checklists should also be provided.
- ✓ All medicines received should be inspected.
- ✓ Any discrepancy should be documented immediately and communicated to the supplier.

Sample Checklist for receiving medicines

	Yes	No
Is the delivery note or invoice for your facility?		
Are the goods delivered the ones ordered?		
Are the quantities delivered those in the delivery note or those invoiced?		
Is the condition of the boxes at the time of delivery acceptable?		
Are the goods delivered in good condition (check liquids for leakages, broken containers, unsealed , unusual odours and colours)?		
Is expiry date of medicines acceptable for your facility?		
Document any discrepancies and follow up with supplier?		

Establishment of Product Monitoring System in Facility

Develop SOP for reporting product quality issues in the facility.

The SOP should:

- **Design or adapt a form** for this purpose
- **Identify who is responsible** for reporting product quality issues
- **Specify how to identify** poor quality products
- **Specify where and whom to direct** the completed forms

Establishment of Product Monitoring System in Facility(2)

The SOP should:

- **Provide information** on additional steps to be taken on receipt of the form. For e.g. where to send samples, what to do with the concerned products.
- **Indicate how to institute** products recall if necessary.
- **Specify feedback** to give the product suppliers

Product Testing & Recall

- Testing of suspicious products can be done by first using:
  - Minilab system for screening purposes

    To be confirmed by:
  - WHO-prequalified laboratory

Products that are confirmed to be of poor quality following laboratory testing should be recalled from circulation.
National Medicines Regulatory Authority will be informed by Minilab-Network member

International Watch-Dog of Medicine Quality

- International
  - WHO- Essential Drug Unit
  - DIFAEM-EPN Minilab Network
  - DIFAEM-Germany
  - Global Fund to fight AIDS, TB and Malaria
  - Interpol
  - IMPACT

Postlude

This training module has been developed under the Difaem* Project “Awareness on Quality of Medicines” by Minilab Network Members in close cooperation and assistance by EPN secretariat in 2015

*German Institute for Medical Mission, Tuebingen / Germany

Thank you!

Ecumenical Pharmaceutical Network
Rosami Court, Muringa road, Kilimani, Nairobi
P. O. Box 749 - 00606 Sarit Centre, Nairobi, Kenya

Tel: +254 724 301755/ 572 522702
E-mail: info@epnetwork.org
Website: www.epnetwork.org