Substandard and Falsified (SF) Medical Products

World Health Organization

6th Cycle Regional Training Seminar for OIE Focal Points for Veterinary Products (Africa)

Addis Ababa, Ethiopia, 10 July 2019 (Remote Presentation)

Definitions

World Health Organization

SUBSTANDARD

Also called ‘out of specification’, these are authorized medical products that fail to meet either their quality standards or their specifications, or both. e.g. Manufacturing error, expired or degraded

FALSIFIED

Medical products that deliberately/fraudulently misrepresent their identity, composition or source.

UNREGISTERED / UNLICENSED

Medical products that have not undergone evaluation and/or approval by the NRRA for the market in which they are marketed/distributed or used, subject to conditions under national or regional regulation and legislation.

Source: https://www.who.int/medicines/regulation/ssffc/definitions/en/

African Customs Seizure

Customs agents conducting a routine search of a cargo shipping container found this inside…

Coartem – Anti malarial

1.383,528 packs

Postinor 2 – Emergency Contraceptive

4930 packs

Vermox – Worming treatment

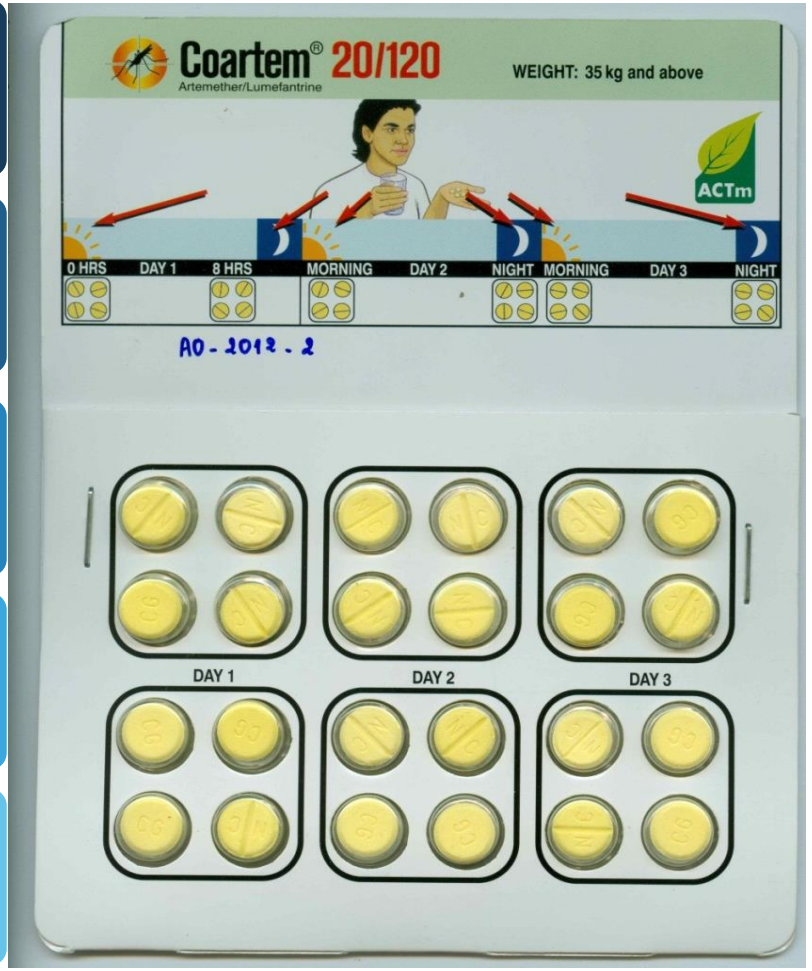
1534 packs

Clomid – Fertility treatment

36,550 packs

Clamoxyl - Antibiotic

744 packs

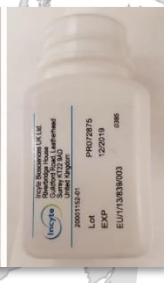


European Customs Seizure

Customs agents intercepted these shipments of separated packaging components at the airport…

WHO Global Alerts 2019

World Health Organization



- *31 Jan:* rabies vaccines
- *31 Jan, 21 Feb:* leukemia treatment traded globally
- *21 Mar:* oral cholera vaccines
- *28 Mar:* meningitis vaccines
- *16 Apr:* contaminated antihypertensive
- *24 Apr:* leishmaniosis treatment

Source: https://www.who.int/medicines/publications/drugalerts/en/

WHO Global Alerts

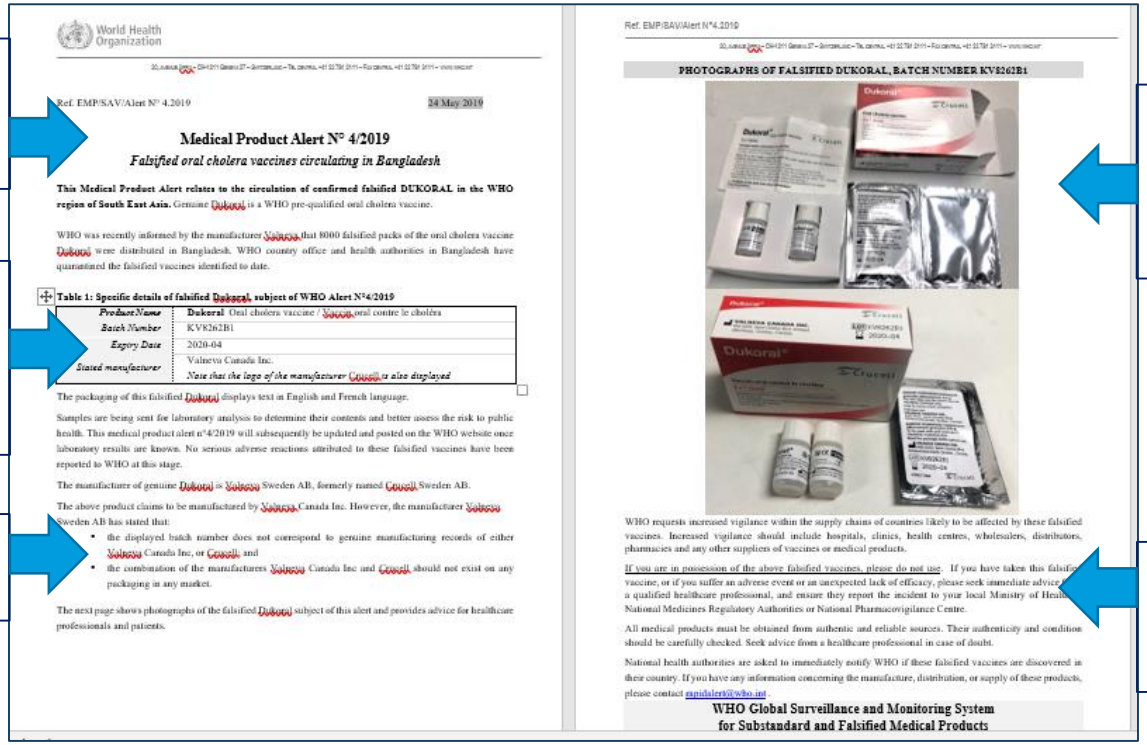
World Health Organization

Risk Communication

- Therapeutic use
- Where and when discovered

- Product specific
- Batch Specific
- Manf and exp dates

- Clarify if falsified or substandard



World Health Organization

Ref. EMP/SAV/Alert N° 4.2019 — 24 May 2019

Medical Product Alert N° 4/2019

Falsified oral cholera vaccines circulating in Bangladesh

This Medical Product Alert relates to the circulation of confirmed falsified DUKORAL in the WHO region of South East Asia. Genuine Dukoral is a WHO pre-qualified oral cholera vaccine.

WHO was recently informed by the manufacturer Valneva that 8000 falsified packs of the oral cholera vaccine Dukoral were distributed in Bangladesh. WHO country office and health authorities in Bangladesh have quarantined the falsified vaccines identified to date.

Table 1: Specific details of falsified Dukoral, subject of WHO Alert N°4/2019

Product Name	**Dukoral** Oral cholera vaccine / Valneva oral contre le choléra
Batch Number	KVE262B1
Expiry Date	2020-04
Stated manufacturer	Valneva Canada Inc. *Note that the logo of the manufacturer Crucell is also displayed*

The packaging of this falsified Dukoral displays text in English and French language.

Samples are being sent for laboratory analysis to determine their contents and better assess the risk to public health. This medical product alert n°4/2019 will subsequently be updated and posted on the WHO website once laboratory results are known. No serious adverse reactions attributed to these falsified vaccines have been reported to WHO at this stage.

The manufacturer of genuine Dukoral is Valneva Sweden AB, formerly named Crucell Sweden AB.

The above product claims to be manufactured by Valneva Canada Inc. However, the manufacturer Valneva Sweden AB has stated that:

- the displayed batch number does not correspond to genuine manufacturing records of either Valneva Canada Inc, or Crucell; and
- the combination of the manufacturers Valneva Canada Inc and Crucell should not exist on any packaging in any market.

The next page shows photographs of the falsified Dukoral subject of this alert and provides advice for healthcare professionals and patients.

Ref. EMP/SAV/Alert N°4.2019

PHOTOGRAPHS OF FALSIFIED DUKORAL, BATCH NUMBER KVE262B1

WHO requests increased vigilance within the supply chains of countries likely to be affected by these falsified vaccines. Increased vigilance should include hospitals, clinics, health centres, wholesalers, distributors, pharmacies and any other suppliers of vaccines or medical products.

If you are in possession of the above falsified vaccines, please do not use. If you have taken this falsified vaccine, or if you suffer an adverse event or an unexpected lack of efficacy, please seek immediate advice from a qualified healthcare professional, and ensure they report the incident to your local Ministry of Health, National Medicines Regulatory Authorities or National Pharmacovigilance Centre.

All medical products must be obtained from authentic and reliable sources. Their authenticity and condition should be carefully checked. Seek advice from a healthcare professional in case of doubt.

National health authorities are asked to immediately notify WHO if these falsified vaccines are discovered in their country. If you have any information concerning the manufacture, distribution, or supply of these products, please contact rapidalert@who.int .

WHO Global Surveillance and Monitoring System for Substandard and Falsified Medical Products

- Clear photos
- secondary packaging
- WHO guide on taking good photos

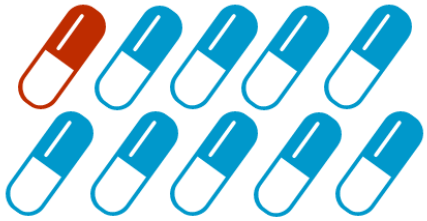
- Advice to patients and health care workers

Accurate Information, Advice and Reassurance

WHO Estimates 2017*

**Limited to medical products for human use*

10.5%



Observed failure rate of analysed medical product samples from low and middle-income countries

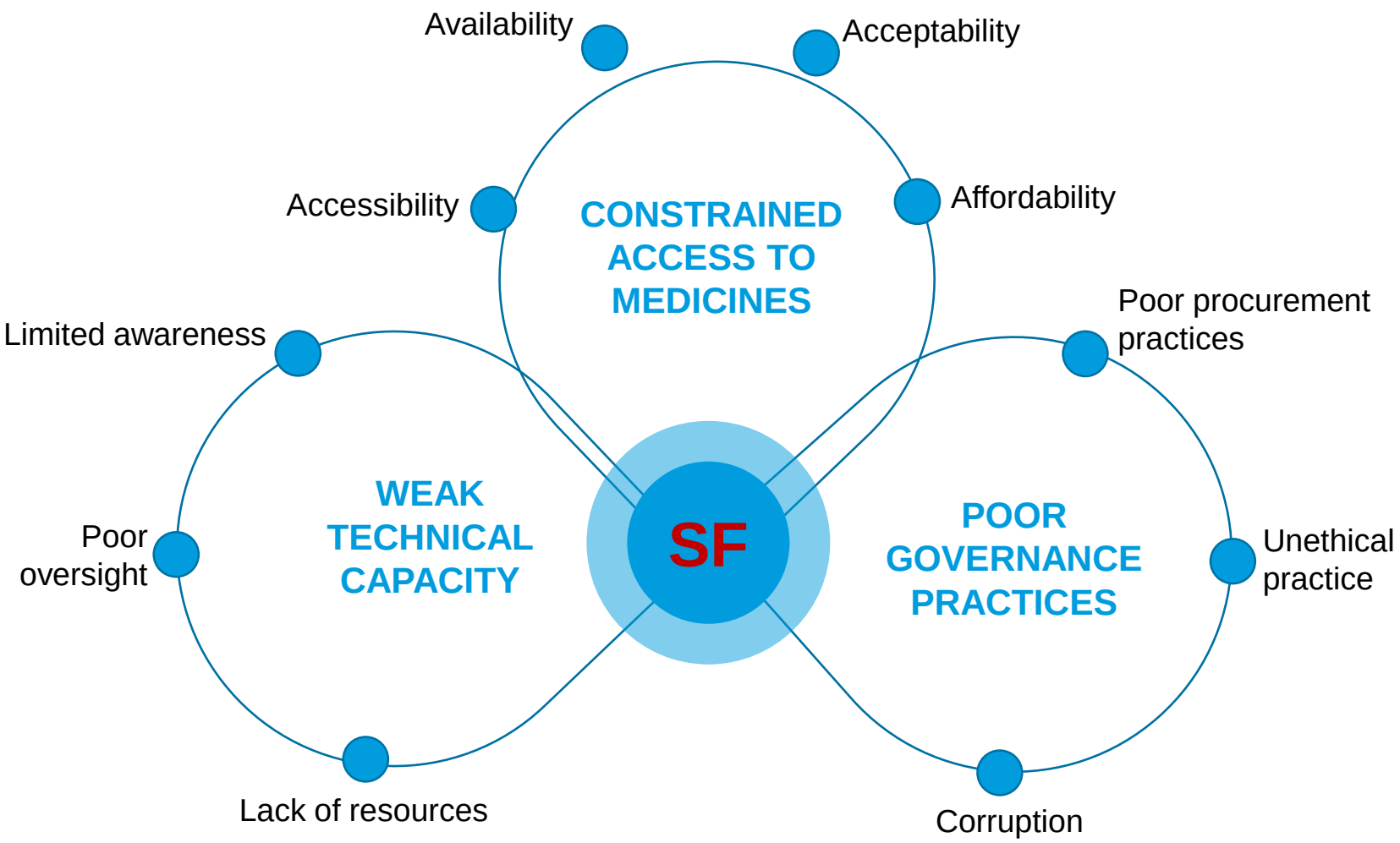
---

US$ 30.5 Billion

Estimated spending on SF medical products in low and middle-income countries based on un-weighted estimates of pharmaceutical sales

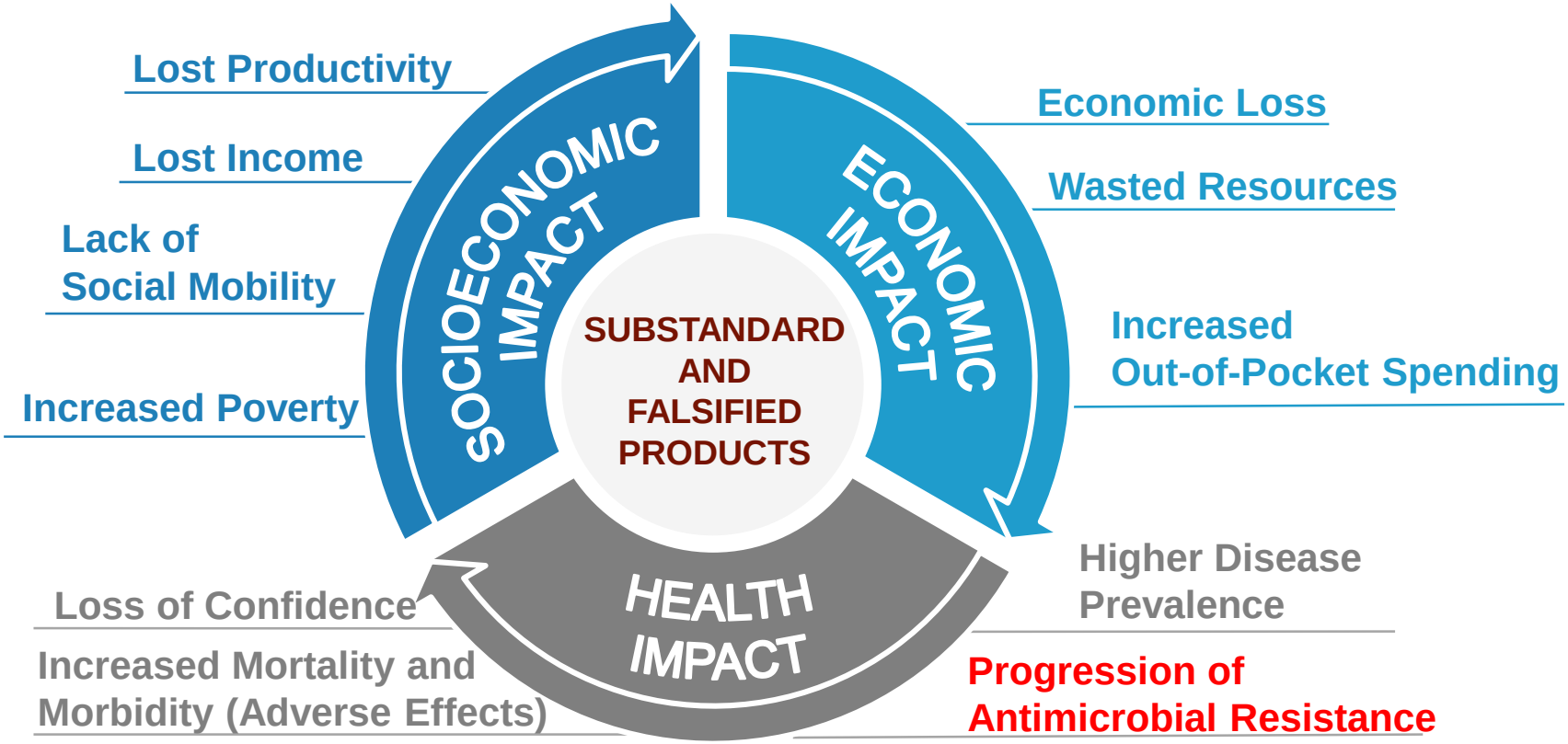
Source: : http://www.who.int/medicines/regulation/ssffc/publications/se-study-sf/en/

Causes


Availability
Acceptability
Accessibility
Affordability
CONSTRAINED ACCESS TO MEDICINES
Limited awareness
Poor procurement practices
Poor oversight
WEAK TECHNICAL CAPACITY
SF
POOR GOVERNANCE PRACTICES
Unethical practice
Lack of resources
Corruption

Consequences

World Health Organization



WHO Response

World Health Organization

POLITICAL RESPONSE

Member State Mechanism

- Political support
- Promote access to affordable, safe, efficacious, and quality medical products
- Effective Member States' collaboration and coordination

OPERATIONAL RESPONSE

Global Surveillance and Monitoring System

- Immediate technical and operational support
- Regulatory capacity building and policy guidance
- Improve current knowledge for in depth analyses. landscape, etc.

PROTECT PUBLIC HEALTH

WHO Member State Mechanism

World Health Organization

MANDATE

World Health Assembly 65.19 ; 2012

Recognised as an unacceptable threat to public health

PURPOSE

International collaboration from a public health perspective on substandard and falsified medical products

GOVERNANCE

- **Steering Committee**
- **1 Chair (India)**
- **11 Vice Chairs**
- **Regional Rotation**

2018-19 Prioritized Activities

World Health Organization

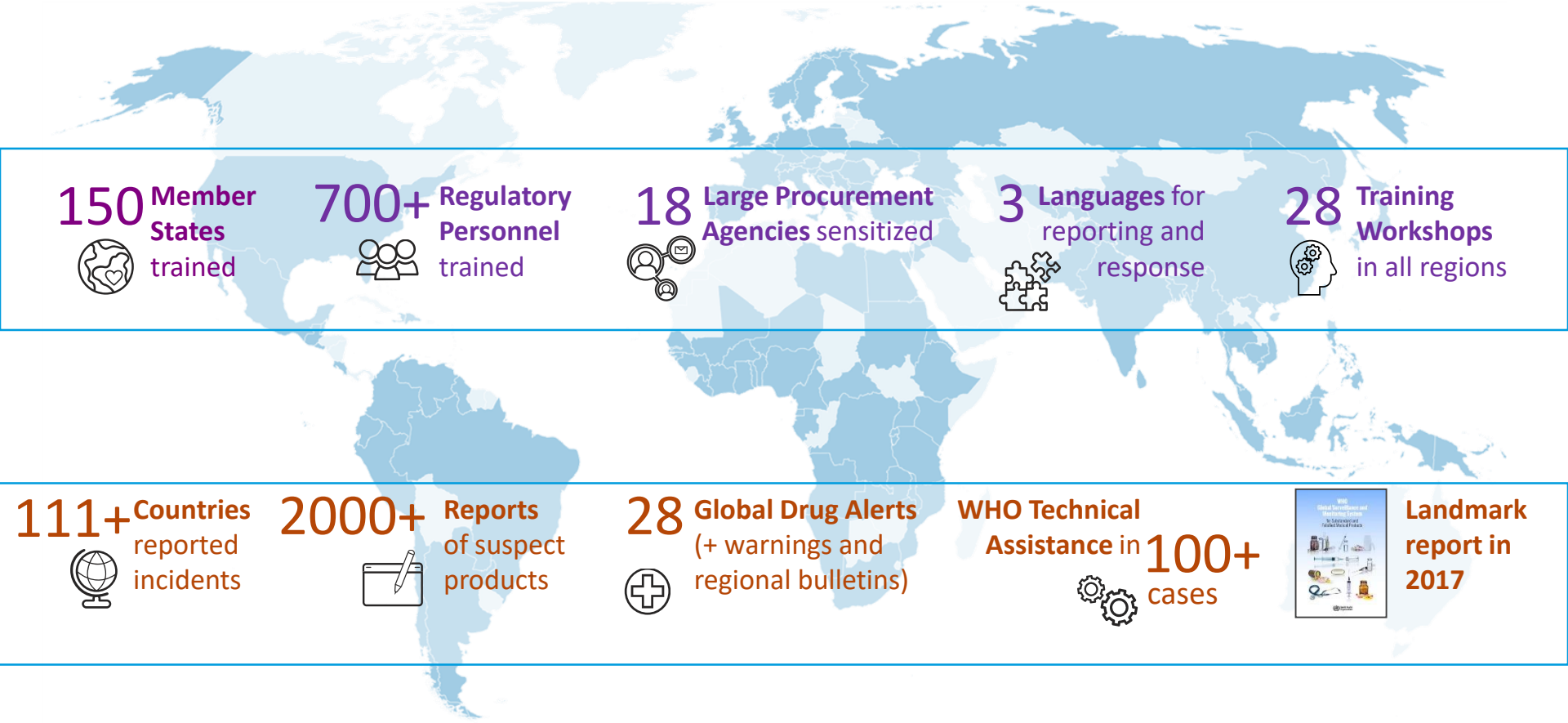
As agreed by the Member State Mechanism

- Develop and promote training material and guidance documents for the prevention, detection and response to SF medical products
- Expand and maintain the global focal point network among national medicines regulatory authorities
- Improve understanding of detection technologies, methodologies, and “track and trace” models
- Increase knowledge of links between SF medical products and access to quality, safe, efficacious and affordable medical products
- Develop and leverage risk communication and awareness campaigns
- Expand awareness, effectiveness, impact and outreach
- Promote understanding from a public health perspective regarding medical products in transit
- Identify strategies for the distribution or supply of SF medical products via the Internet

WHO GLOBAL SURVEILLANCE and MONITORING SYSTEM

World Health Organization

Available in **English, French** and **Spanish**



150 **Member States** trained

700+ **Regulatory Personnel** trained

18 **Large Procurement Agencies** sensitized

3 **Languages** for reporting and response

28 **Training Workshops** in all regions

111+ **Countries** reported incidents

2000+ **Reports** of suspect products

28 **Global Drug Alerts** (+ warnings and regional bulletins)

WHO Technical Assistance in **100+** cases

Landmark report in 2017

What to Report

World Health Organization

Medical products stolen from public aid or humanitarian programmes

Unexpected adverse reactions, particularly a lack of efficacy

Falsified or seriously substandard products (suspected or confirmed)

When to Report

World Health Organization

The product and batch may have already been reported by another Country

The risk to public health may have already been assessed

Report suspicion early and search the WHO Portal

The suspicious product may have already undergone laboratory analysis which can be shared

Another country may be investigating the origin of the product and have helpful information

Who Reports

Terms of Reference for Global Focal Point Network

- Situated within the National Medicine Regulatory Authority
- Empowered to closely cooperate with relevant government entities
- Trained on the use of the WHO GSMS
- Empowered to receive and respond appropriately to all alerts

[1] *Global Focal Point Network Terms of Reference: http://www.who.int/medicines/regulation/ssffc/mechanism/A69_41-en6-8.pdf?ua=1*

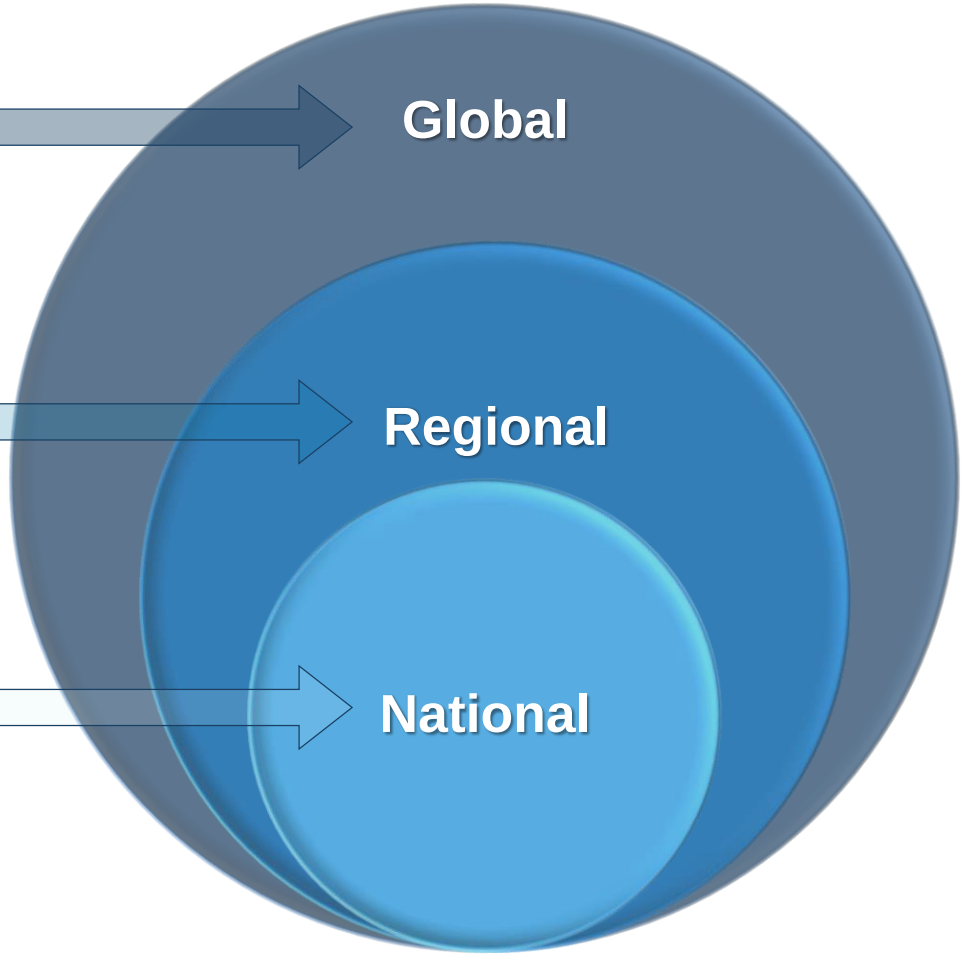
Coordination and Collaboration

World Health Organization

WHO Global Surveillance and Monitoring System for substandard and falsified medical products

Regional Rapid Alert Network

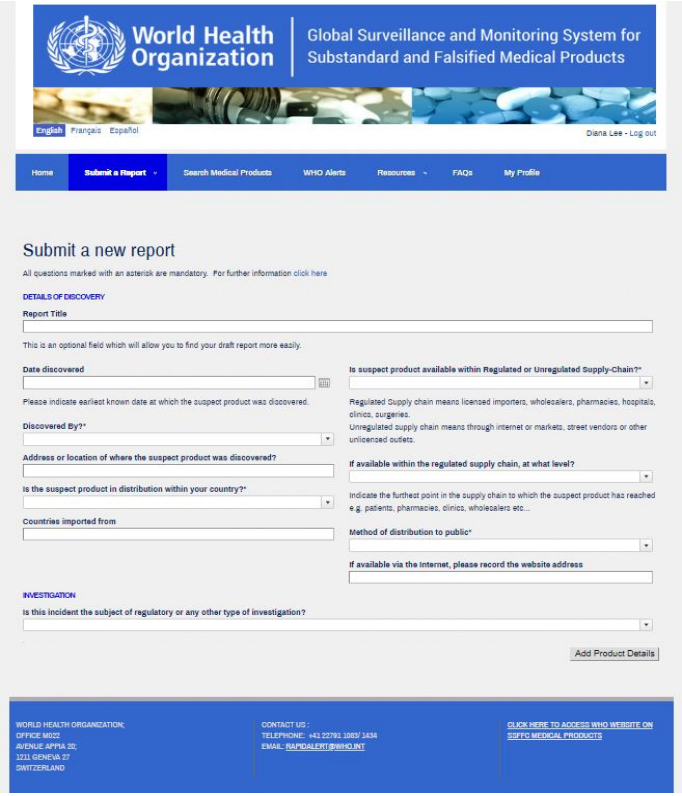
National risk based post market surveillance and reporting systems



How to Report

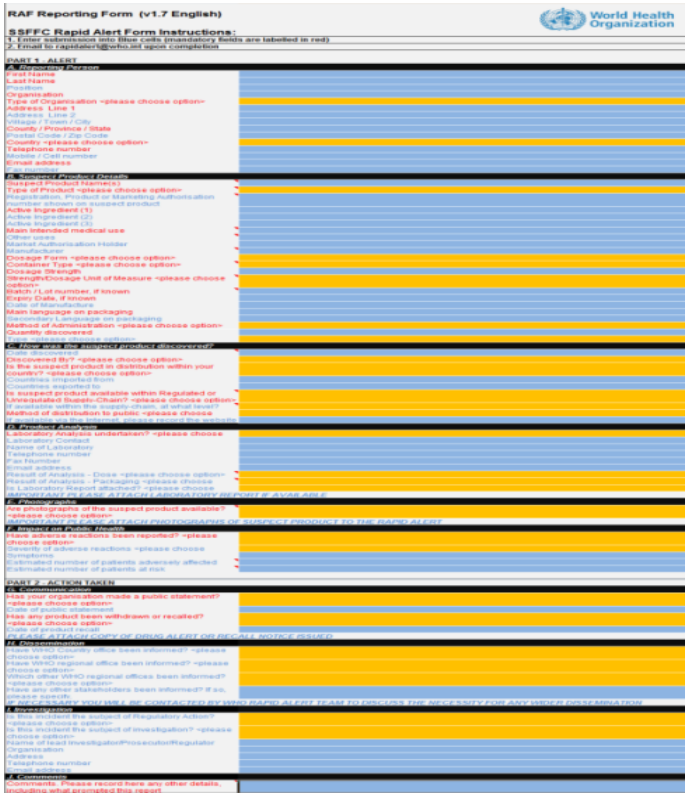
Online Portal

1. Via secure online portal, which is also used to search the database and access training material



Excel Form

2. Offline reporting form in Excel and email to WHO



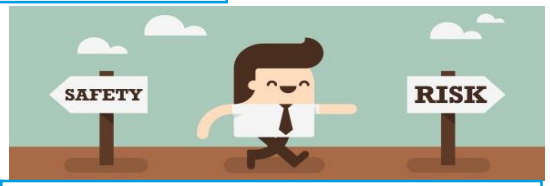
WHO GLOBAL SURVEILLANCE and MONITORING SYSTEM

World Health Organization

1 Focal Point sends Report
Auto receipt sent from WHO

2 Automatic email notification to WHO

3 Report uploaded and translated in database

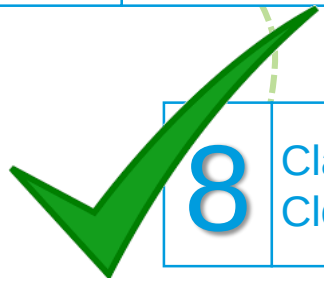


4 Internal risk assessment for prioritization

5 Immediate link to similar reports

6 Validate Data and Technical support

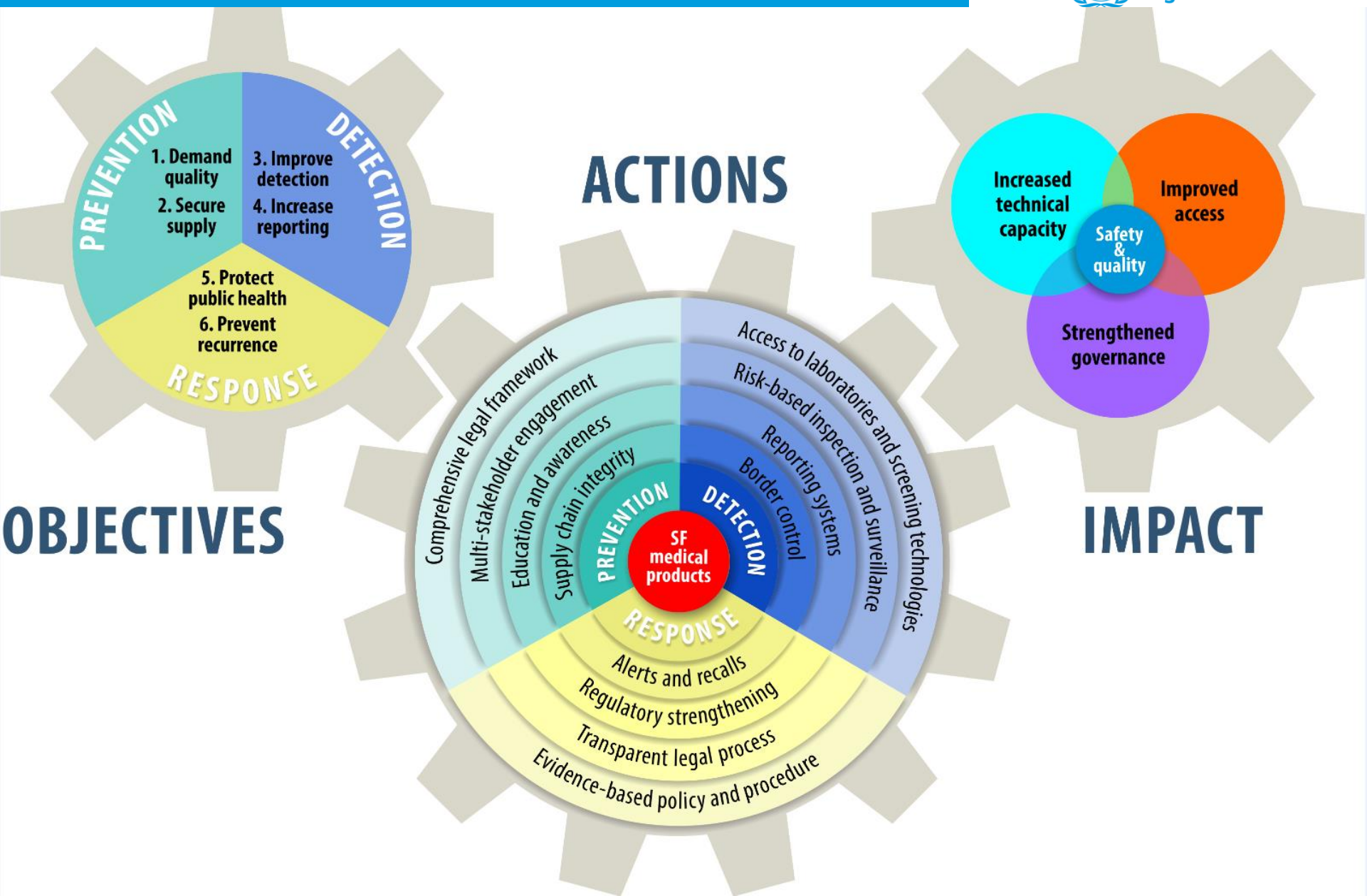
7 WHO medical product alert and other necessary action



8 Classification & Closure

Prevent, Detect, Respond Strategy

World Health Organization



One Health: Veterinary Meds

World Health Organization

Year	Overview of SF Veterinary Product Reports Received
2017	1. Substandard Canigen LR rabies vaccines in France 2. Falsified Trisulfon powder in Ukraine 3. Falsified Neostomosan concentrate in Hungary 4. Substandard Tylosin 20 H in Germany 5. Substandard Cefshot DC in the UK 6. Substandard Rabies Vaccines in Thailand 7. Substandard Deparvax/Deparmune in Hungary, Poland and France 8. Substandard Avinew Neo vaccines in France 9. Substandard Colistina Solfato in Czech Republic 10. Substandard Amoxinject in Germany 11. Falsified Biocan R rabies vaccines in Poland 12. Substandard Aivlosin in the UK 13. Unregistered Nifuramycin Powder in Germany 14. Substandard Narcostop in Hungary
2018	1. Substandard Oxytoxin in Germany, EU countries, Serbia, Egypt, UAE, Cuba and Sri Lanka 2. Contaminated Overvac EC in Spain 3. Substandard Lactaclox Intrammary Infusion in the UK 4. Substandard Willcain in the UK 5. Substandard Bovigam Lactacion in Spain 6. Suspension of Diethanolamine in the Netherlands 7. Substandard Vectormune ND vaccines in Hungary 8. Substandard Norocarp in Spain 9. Substandard Oxyvet 100 LP in Barbados and Jamaica
2019	1. Falsified Micotil in the UK 2. Stolen Eravac, Eryseng Parvo PET, Suiseng PET, and Vepured Pet in Denmark 3. Substandard Meloxidolor in Spain 4. Substandard Anaestamine in Czech Republic, France and UK 5. Substandard Media Fill Simulation for Suite 11 Aseptic Manufacturing System 1 in UK, Croatia and France 6. Substandard Norocarp, Enrotril, Noromectin, Alamycin, and Paramectin Injectable in Spain 7. Substandard Pyceze 8. Substandard Carprosan in Spain

Lessons Learned

World Health Organization

From global policy to local impact	**POLITICAL WILL** is required to translate policy agreed at the global level to **SUSTAINABLE ACTIONS** on the ground with **APPROPRIATE FINANCIAL AND HUMAN RESOURCES**
Sound investment strategies	**STRENGTHENING REGULATORY CAPACITY AND SYSTEMS** is a key step and **SOUND INVESTMENT** to safeguard the manufacture, distribution and supply of medical products
Cooperation and coordination	Improved **REPORTING SYSTEMS** and greater **TRANSPARENCY** within and between countries is required, together with wide and **EFFECTIVE MULTI STAKEHOLDER ENGAGEMENT**

Diana Lee
Technical Officer, Substandard and Falsified Medical Products Group
leedi@who.int / rapidalert@who.int