Substandard and falsified medical products

Technical briefing seminar

11 May 2023

World Health Organization

Presentation overview

- Substandard and Falsified (SF) medical products – What are they?
- What are the consequences of SF medical products?
- Case study & WHO's role
- What is your role?

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What is the first word that comes to mind when you hear of Substandard and Falsified medical products?

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What is a Substandard medical product?

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SUBSTANDARD

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

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What is a Falsified medical product?

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FALSIFIED

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

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What is an unregistered/unlicensed product?

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UNREGISTERED/ UNLICENSED

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

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There are three main causes and drivers of Substandard and Falsified medical products, would you be able to mention one?

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Causes and drivers of SF medical products

Constrained access

- Availability
- Affordability
- Acceptability

Poor governance

- Unethical practices & corruption
- Inefficient administrative structure
- Poor procurement

Weak technical capacity

- Lack of resources in overburdened agencies
- Limited awareness
- Poor oversight

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Let's guess... What is the failure rate for the quality of medicines in LMIC?

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How big is the global problem?

Estimates	Impact models
10.5%  Observed failure rate on medicines samples in LMIC	 **72,430-169,271 deaths** Caused by SF antibiotics in children under 5 suffering from *Pneumonia*
USD 30.5 billon  Estimated spending on SF medicines in LMIC, based on wholesale level sales	**31,000-116,00 deaths** Caused by SF antimalarials in sub-Saharan Africa*  **USD 38.5 million** Estimated spending on SF antimalarials in sub-Saharan Africa**

* University of Edinburgh
** London School of Hygiene and Tropical Medicine

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Mention one consequence related to the use of Substandard and Falsified medical products?

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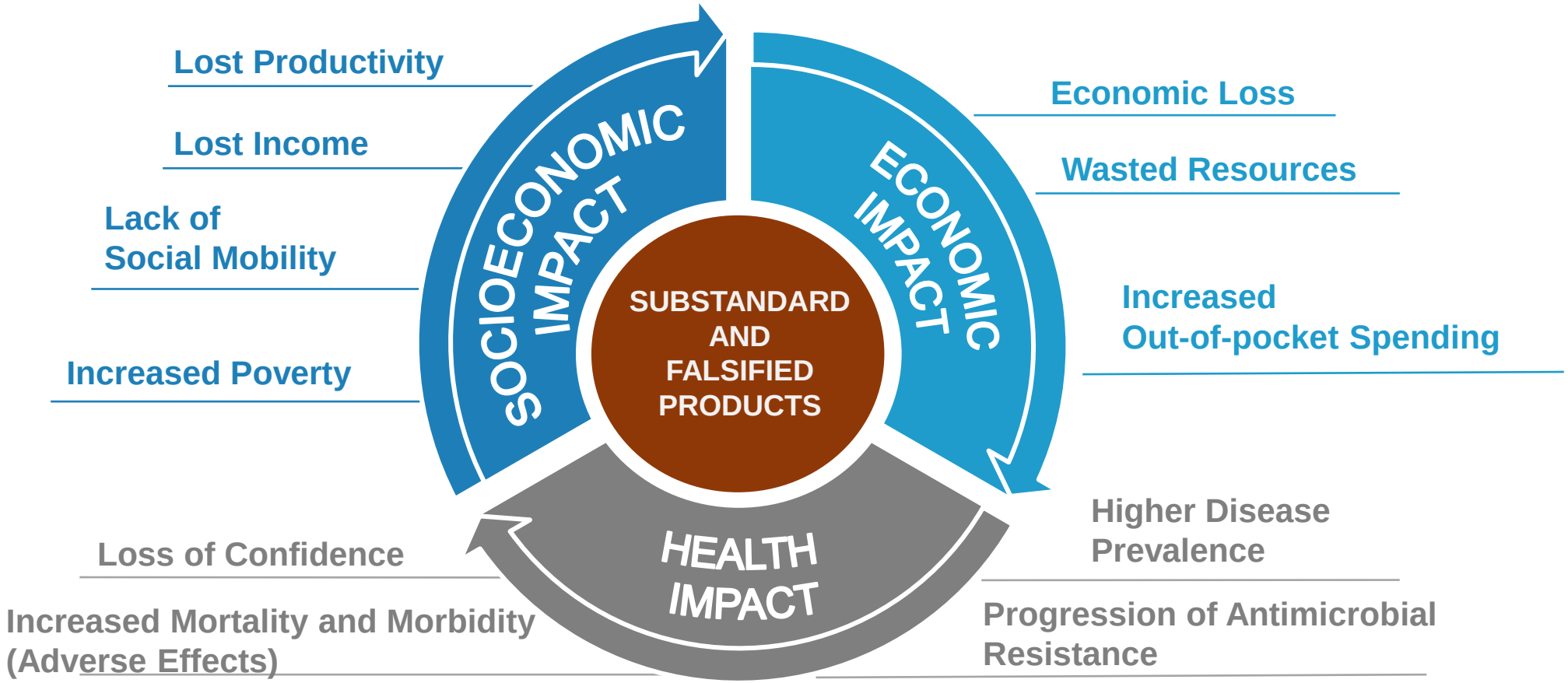
What are the consequences of SF medical products



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Case study: Global Incidents of DEG/EG contamination

1937

USA

DEG-contaminated Elixir Sulfanilamide. >100 deaths. Led to enactment of the Federal Food, Drug, and Cosmetic Act

1990-1998

Argentina, Bangladesh, India, and Nigeria

DEG poisoning reportedly occurred, hundreds of deaths.

1996

Haiti

> 68 cases of AKI in children. > 30 deaths. DEG contaminated Paracetamol syrups. Local Products.

2006

Panama

> 82 cases of AKI. > 38 deaths. Syrup preparations & topical creams contaminated with DEG

2008-2009

Nigeria

>84 children died. DEG contaminated Paracetamol syrup. Local products

2019

India

>17 suspect AKI cases in children. >12 deaths reported. DEG contaminated Paracetamol syrup

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Press coverage then…

The New York Times

F.D.A. Tracked Poisoned Drugs, but Trail Went Cold in China

Give this article

By Walt Bogdanich
June 17, 2007

After a drug ingredient from China killed dozens of Haitian children a decade ago, a senior American health official sent a cable to her investigators: find out who made the poisonous ingredient and why a state-owned company in China exported it as safe, pharmaceutical-grade glycerin.

The Chinese were of little help. Requests to find the manufacturer were ignored. Business records were withheld or destroyed.

The Americans had reason for alarm. "The U.S. imports a lot of Chinese glycerin and it is used in ingested products such as toothpaste," Mary K. Pendergast, then deputy commissioner for the Food and Drug Administration, wrote on Oct. 27, 1997. Learning how diethylene glycol, a syrupy poison used in some antifreeze, ended up in Haitian fever medicine might "prevent this tragedy from happening again," she wrote.

The F.D.A.'s mission ultimately failed. By the time an F.D.A. agent visited the suspected manufacturer, the plant was shut down and Chinese companies said they bore no responsibility for the mass poisoning.

Ten years later it happened again, this time in Panama. Chinese-made diethylene glycol, masquerading as its more expensive chemical cousin glycerin, was mixed into medicine, killing at least 100 people there last year. And recently, Chinese toothpaste containing diethylene glycol was found in the United States and seven other countries, prompting tens of thousands of tubes to be recalled.

Five jailed in Panama over toxic cough syrup scandal that killed hundreds

Five jailed in Panama over toxic cough syrup scandal that killed hundreds

Posted Sat 30 Jul 2016 at 4:09am

The medicine had been mixed and distributed by the national health agency. *(ABC)*

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abc.net.au/news/five-jailed-in-panam...

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Five people were sentenced to prison in Panama on Friday over a 2006 poison cough syrup scandal in which hundreds of people died after unwittingly ingesting a toxic compound found in antifreeze.

The verdict capped years of investigation and a convulsion of shock at the many deaths in this small Central American nation.

Officials say 400 people died when they drank the adulterated cough syrup, which had been mixed and distributed by the national health agency using an ingredient supplied by a private company, Medicom.

Some Panamanian organisations believe

Key points:

- Officials say 400 people died as result of syrup
- Same organisations in Panama say toll could actually be up to 10,000
- Toxic ingredient is used as a solvent, in brake fluid, heating fuel and antifreeze

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My Pikin deaths: Nigerians jailed over poisoned baby drug

17 May 2013

Two Nigerians have been sentenced to seven years in prison over the deaths of at least 80 children who took adulterated teething medicine.

The officials from the company which made the My Pikin syrup were found guilty by a court in Lagos.

After children started dying in 2008, the mixture was found to contain engine coolant.

The judge also ordered that the company be closed and its assets forfeited to the state.

The paracetamol-based syrup, used for treating sore gums, was found to have been contaminated with diethylene glycol, used as an engine coolant.

It caused the babies' kidneys to fail.

My Pikin means "my baby" in Nigerian pidgin, the language widely used in Lagos.

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Maiden Pharmaceuticals: Gambia panel says India firm culpable for cough syrup deaths

21 December 2022

The WHO had advised regulators to stop the sale of the four Indian-made cough syrups

A parliamentary committee in The Gambia has recommended prosecution of the Indian manufacturer of cough syrups suspected of causing the deaths of at least 70 children in the country.

It said Maiden Pharmaceuticals should be held accountable for exporting what it called contaminated medicine.

The WHO had issued an alert in October advising regulators to stop the sale of the syrups.

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Indonesia bans all syrup medicines after death of 99 children

20 October 2022

Indonesia says it's banning the sale and use of all syrup and liquid medicines temporarily

By Frances Mao
BBC News

Cough Syrup Linked to 20 Kids' Deaths Was Circulating for Months

- Export records show tainted medicine made as early as May 2021
- Indian drug maker defends quality of exports to Uzbekistan

By Zachary Mider and Chris Kay
January 12, 2023, 10:00 PM GMT+1

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An Indian drug maker blamed for the deaths of 20 children in Uzbekistan produced multiple batches of tainted cough syrup over more than a year, according to data from export records and the World Health Organization.

The WHO said this week that 21 batches of cough syrup made by India's Marion Biotech Ltd. were tested by Uzbek authorities and found to contain unsafe levels of two toxic chemicals. Bloomberg News identified some of these batches in separate Indian export records as having been manufactured as early as May 2021 and exported to the Central Asian nation that June. Other batches appear to have been made on more than half a dozen dates and as recently as August 2022.

Asia / Australasia

WHO: contaminated cough syrup made in India found in Western Pacific

- Samples from a batch of imported cough syrup in the Marshall Islands and Micronesia were contaminated with unacceptable amounts of ingredients toxic to humans
- The new alert follows three similar warnings issued last year; the manufacturer of the medicines in the latest alert was India's QP Pharmachem, based in Punjab

Reuters +FOLLOW
Published: 9:36pm, 26 Apr, 2023

Why you can trust SCMP

Samples from a batch of cough syrup, with the product name Guaifenesin syrup TG syrup, were contaminated with unacceptable amounts of diethylene glycol and ethylene glycol. Photo: Shutterstock

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Case study: Key Events and Alerts on DEG/EG Contamination

Aug.–Oct. 2022

The Gambia:

- Approx 92 suspect AKI cases in children
- More than 70 deaths reported
- Four different cough/cold syrups preparations
- All imported products manufactured in India
- Medical Product Alert N°6/2022 on 5 October 2022

Aug.–Oct. 2022

Indonesia:

- Approx 325 cases of suspect AKI in children
- Approx 203 deaths
- At least thirteen products contaminated with EG
- All products manufactured by 7 different local manufacturers.
- Medical Product Alert N°7/2022 issued on 6 November 2022

Dec. 2022

Uzbekistan

- Unconfirmed reports of approx. 18 deaths of children
- Cases suspected to be linked to contaminated paracetamol syrup.
- Imported product manufactured in India
- Medical Product Alert No1/2023 on 11 January 2023

April 2023

Marshall Islands & Micronesia

- Contaminated cough syrup detected
- No reports of deaths
- Imported product manufactured in India
- Medical Product Alert No4/2023 issued 25 April 2023

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General observations

Delays in associating Acute Kidney Injury (AKI) cases with potentially contaminated medicines
Reported AKI involve mostly children
Products for treatment of symptoms of cough, cold or fever
Cases involve liquid dosage medicines (mainly paediatric formulations)
Common excipients – (propylene glycol, polyethylene glycol, glycerin/glycerol or sorbitol solution)
Products locally produced and/or imported
Market withdrawal of the suspected liquid dosage medicines leads to decline in number of reported AKI cases
Challenges in accessing medical interventions e.g. haemodialyis or antidotes - fomepizole or ethanol

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Overall lessons learnt

Public awareness and risk communication is critical

More countries reporting presence of DEG/EG in products on their market at levels below or just above the set minimum limits

Limited access to laboratories for confirmation of poisoning and contamination

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If you were to receive this alert from WHO, what would you do?

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WHO call to action 23 January 2023

Regulators

- **Detect and remove** any SF medical product identified in any of the WHO medical product alerts
- Ensure that all medicines are **approved for sale** by competent authorities and obtainable from authorized/licensed suppliers;
- Improve and increase **risk-based inspections** of manufacturing sites;
- Increase market surveillance including **risk-based targeted testing** for medicines; and
- Enact and **enforce legal provisions** that help to combat the manufacture, distribution and/or use of substandard and falsified medicines

Manufacturers

- Only purchase **pharmaceutical grade excipients** from qualified suppliers;
- Conduct **testing upon receipt of supplies and before use** in manufacture of finished products;
- Provide assurance of product quality including through **certificates of analyses**; and
- Keep **accurate, complete and proper records** of purchase of materials, testing, manufacture, and distribution to facilitate traceability during investigations in case of incidents.

Suppliers and distributors

- Always **check for signs** of falsification and physical condition of medicines and other health products they distribute and/or sell;
- Only distribute and/or sell medicines **authorized** by, and from sources approved by, **competent authorities**;
- Keep accurate, complete and proper **records** relating to the medicines and their distribution and/or sale; and
- Engage **competent personnel** to handle medicines and provide advice to the public on appropriate use of the medicines

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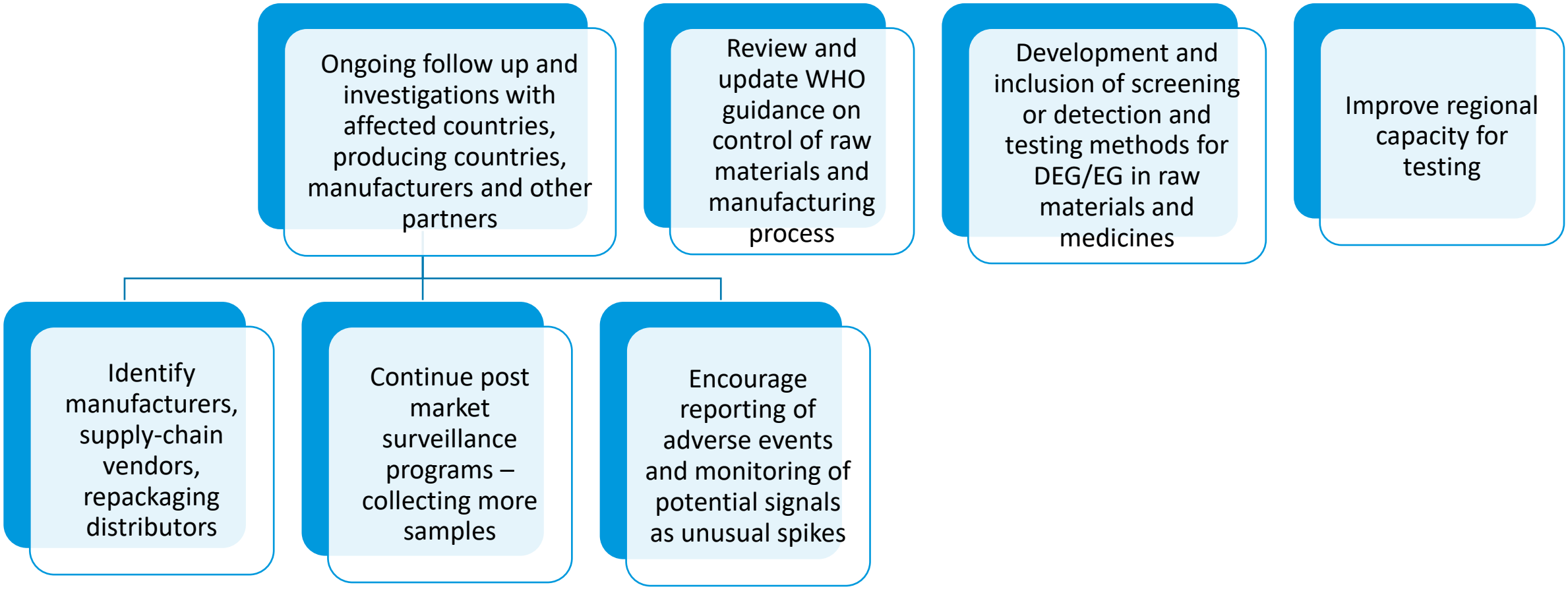
What is the WHO doing? : Current activities



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What is ISF team doing?

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OPERATIONAL RESPONSE

Global Surveillance and Monitoring System

- Improve reporting of SF medical products
- Assess the scale and harm caused
- Provide immediate technical / operational support to Member States reporting SF medical products
- Issue Global Medical Product Alerts
- Strengthen regulatory capacities to prevent, detect and respond to SF medical products

POLITICAL RESPONSE

Member State Mechanism

- Facilitate international coordination and collaboration amongst Member States
- Implement workplan on key prioritized activities to prevent, detect and respond to SF medical products
- Governed by Steering Committee; Chaired by - Australia, Deputy Chair - China.

Understand the global landscape through **VALIDATED EVIDENCE**

INFLUENCE CHANGE in health and governance systems

WHO's prevent-detect-response strategy

- WHO supports NRAs
  - Conduct investigations
  - Conduct sampling and testing for market surveillance
- WHO issues risk communications
  - Global Medical Product Alerts
  - Targeted Market Surveillance
  - WHO information notices for IVD users
- WHO develops normative guidance
  - National action plans for SF
  - Selecting technologies to screen/detect SF
  - Handbook for introducing SF into pharmacy school curriculum

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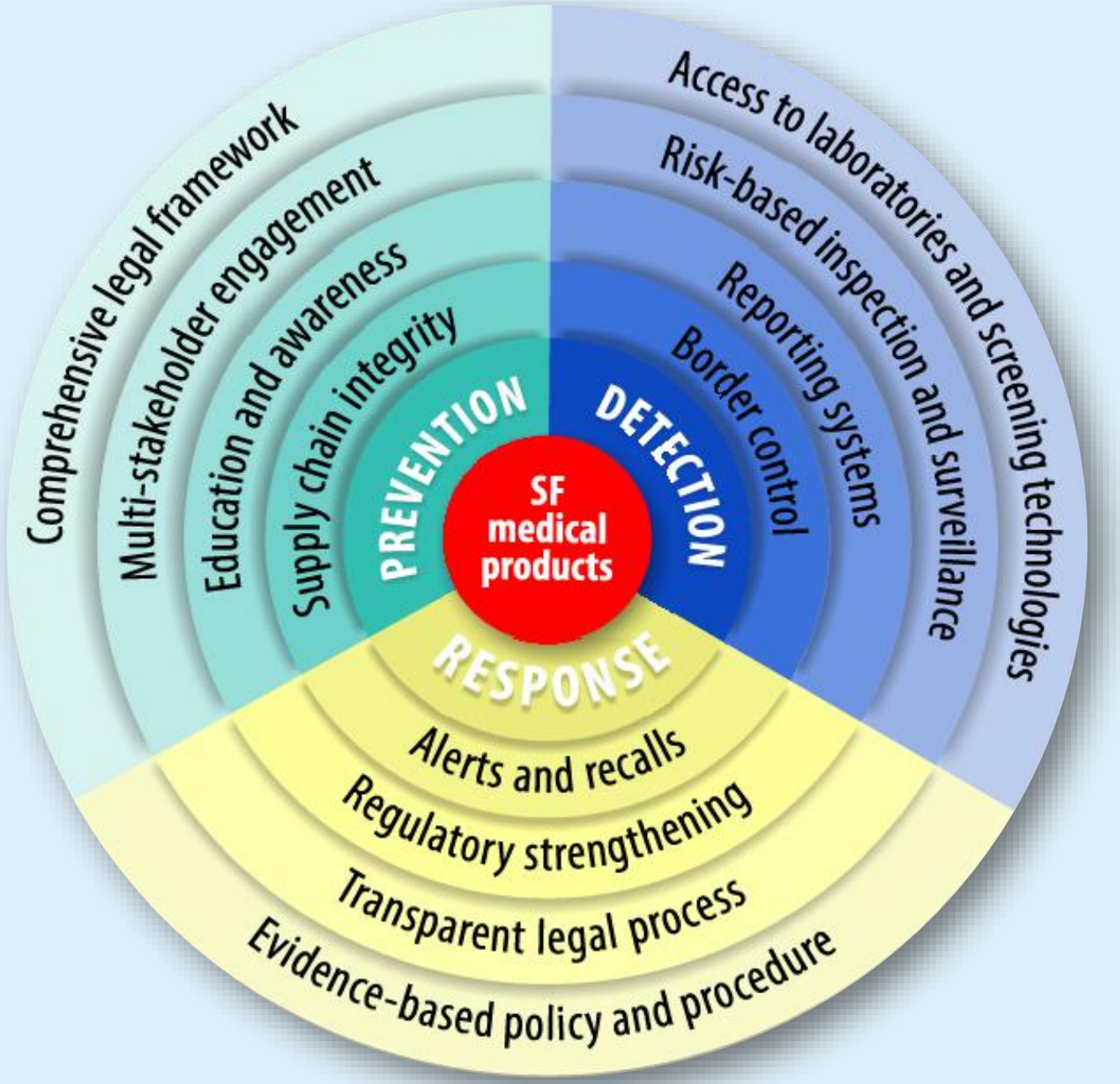
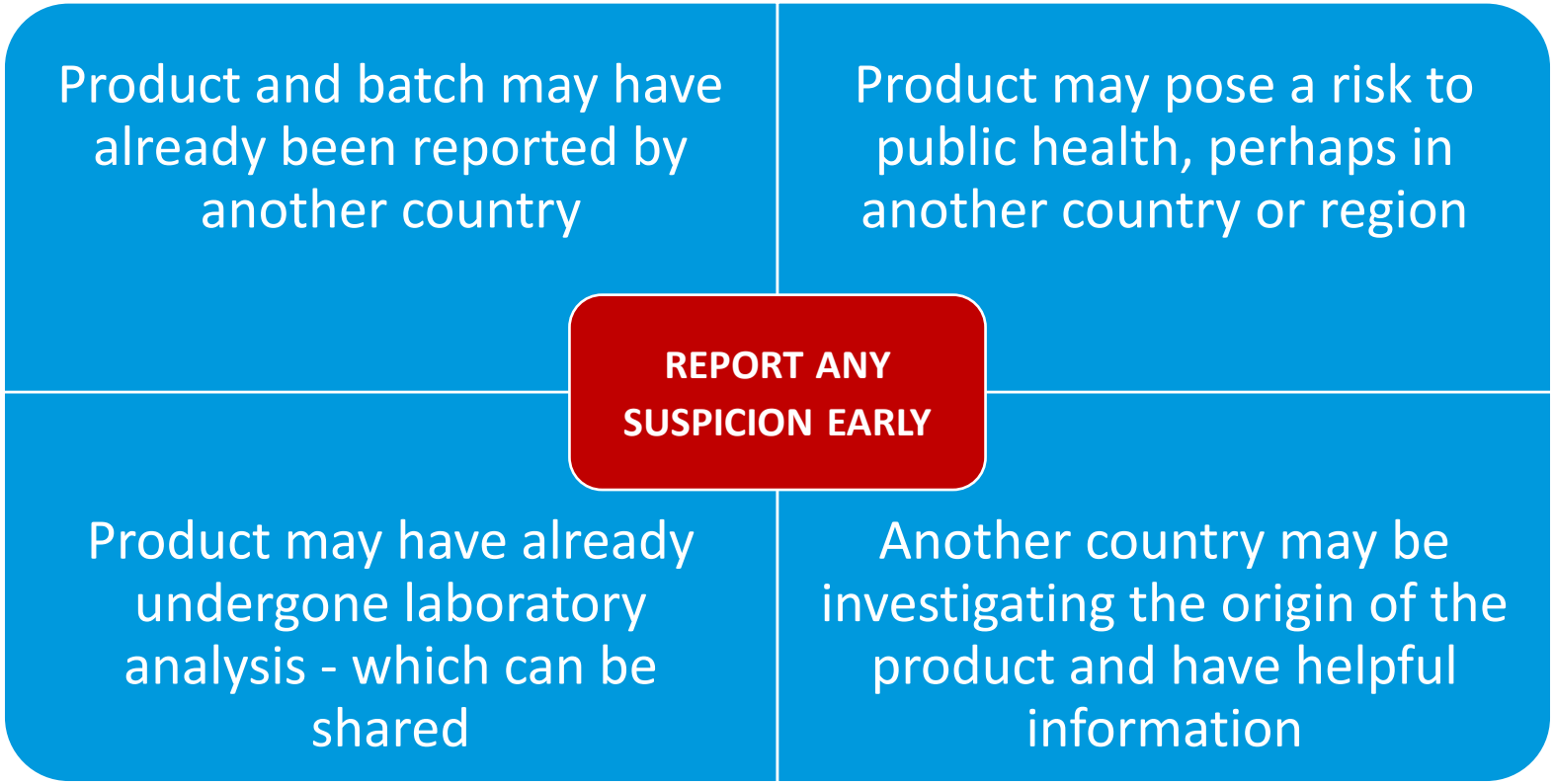


WHO Global Surveillance and Monitoring System



The WHO GSMS is

- A global database of SF medical products; AND
- A network of national regulatory focal points, plus others (private sector, implementing partners, etc.)
- **REPORT ANY SUSPICIONS TO rapidalert@who.int**

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What is your role?

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What is your role?

Regulators

- Establish the facts (reporter, ADRs, photos…)
- Check GSMS portal
- Contact genuine manufacturer
- Secure samples
- Testing (reliance)
- Conduct Regulatory actions (suspensions, recalls, notices for users, alerts…
- Report to WHO GSMS
- Risk communication activities

Health care professionals

- Awareness of potential SF medical products
- Report to the NRA
- Secure sample and take good pictures
- Follow regulatory actions

WHO staff – implementing partners

- Advocate HCP to report to NRAs
- Advocate NRAs to report to WHO GSMS
- Technical support
- Liaise with ISF team
- Coordinated message on risk communication

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Thank you

For more information, please contact:
Incidents and Substandard/Falsified Medical Products (ISF)

Regulation and Prequalification
rapidalert@who.int

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