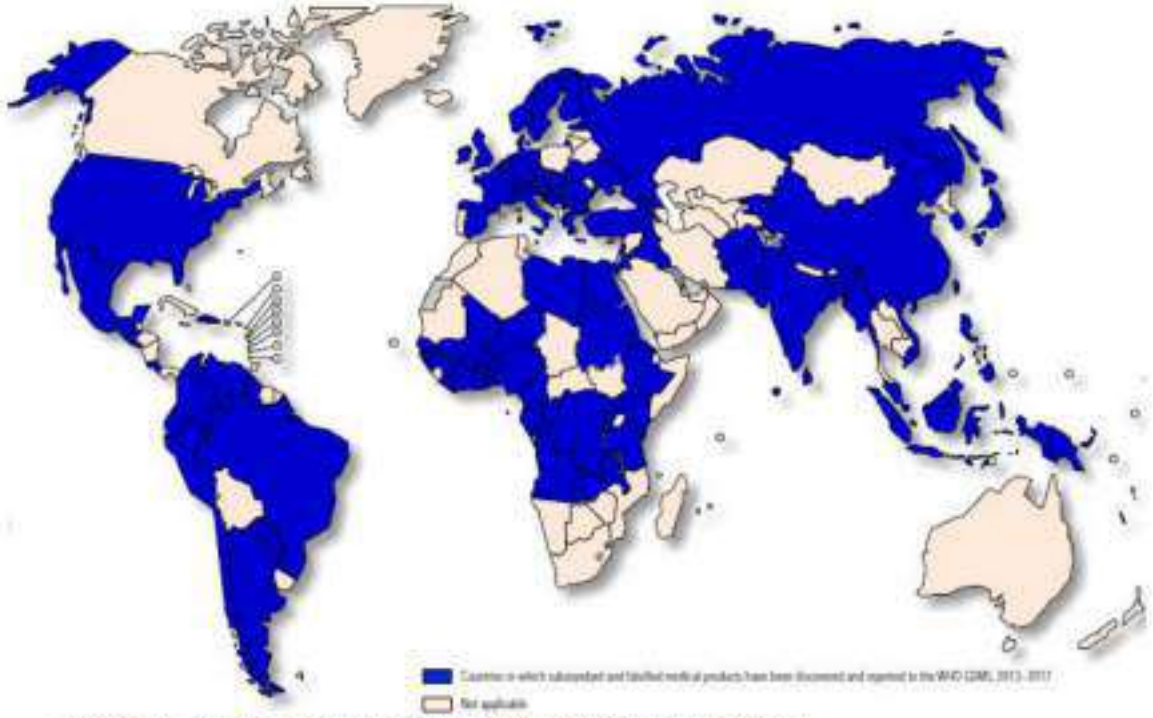
Continuing Professional Development (CPD) Course on

VISUAL IDENTIFICATION OF SUBSTANDARD AND FALSIFIED MEDICAL PRODUCTS

LEARNING OBJECTIVES

COUNTRIES IN WHICH SUBSTANDARD AND FALSIFIED MEDICAL PRODUCTS HAVE BEEN DISCOVERED AND REPORTED TO THE WHO GSMS, 2013–2017



Source: https://www.gphf.org/images/downloads/library/who-es-monitoring.pdf

- Impart basic understanding of Substandard and Falsified (SF) Medical Products
- Introduce the causes and scale of impact of SF medical products
- Describe medical products supply chain quality assurance and ways to conduct visual inspection of medical products
- Establish the role of pharmacists in combating substandard and falsified medicines
- Impart the skill to apply the visual Inspection tool in professional practice

Session	Activity	Facilitator	Slide Number	Time
1.1	Pre-session knowledge test	PQM plus	N/A	30 minutes
1.2	Definitions and case studies	PQM plus	4-16	30 minutes
1.3.a	SF Medical Products: causes and scale of impact	PQM plus	17-22	30 minutes
I.3.b	Scale of SF medical products in Nepal	PQM plus	23-28	20 minutes
1.4	Supply chain quality assurance of medical products	PQM plus	29-33	20 minutes
1.5	Role of pharmacist in combating SF medical products	PQM plus	34-38	20 minutes
	Lunch Break			60 minutes
1.6	Visual Inspection of medical products	Facilitator I	39-56	30 minutes
1.7	Demonstration of visual inspection tool	Facilitator I	57-60	10 minutes
1.8	Group exercises and practical session	Facilitator I	N/A	50 minutes
1.9	Post-Session knowledge Test	PQM plus	N/A	20 minutes
	Module 1, Nine sessions: 240 minutes (4 hours)			

- Substandard medical products

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

- Falsified medical products

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

- Unregistered medical products

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

Source: Appendix 3 to Annex, World Health Assembly document A70/23, 2017

1.2 DEFINITIONS AND CASE STUDIES

SSFMPs endanger public health. What they contain is unknown.

- No API
- Wrong API
- Incorrect dose of API
- Toxic chemicals and Ingredients

Investigators have found these dangerous ingredients in fake medicine.

Heavy metals	Actual poison	Common household items	Drugs you didn't ask for	No drugs at all
				
mercury aluminum lead cadmium arsenic chrome uranium strontium selenium	PCBs benzopyrenes rat poison boric acid antifreeze	road paint wall paint brick dust floor wax sheet rock paint thinner	aminotadalafil homosildenafil xanthoanthrafil pseudovardenafil hongdenafil sibutramine haloperidol	dextrose dextrin lactose starch saline salt

Source: FIP. Launch of the Regulatory Self-Assessment Tool for Substandard or Falsified Medical Products. https://www.youtube.com/watch?v=TTTnMDb0j-Q , Accessed on December 20 2023

Manufactured under conditions like this:

1. Falsified Diazepam –Democratic Republic of Congo

Fig: The medical center set up by ***Médecins Sans Frontières*** where patients affected by the falsified diazepam were treated

- In December 2014, cases of shivering (60%-children), followed by fits and other symptoms of dystonia was observed.
- Urine samples tested positive for *haloperidol*; a schizophrenia medicine.
- **930** people hospitalized with dystonia, and **11** fatalities.
- The tablets were labelled as– diazepam, medicine used to treat anxiety.
- The falsifier used the genuine diazepam bottles, with correct batch number, expiry date and trademark of the product's manufacturer.
- But the API used was haloperidol.

Source: WHO Global Surveillance and Monitoring System for substandard and falsified medical products ISBN 978-92-4-151342-5

2. Isosorbide-5-mononitrate (ISOTAB)- Pakistan

- Almost 1000 serious adverse reactions.
- Over 200 fatalities.
- Medicines supplies by a cardiac hospital was contaminated with high level of *anti malarial medicine (Pyrimethamine).*
- Investigation suggested manufacturing error.

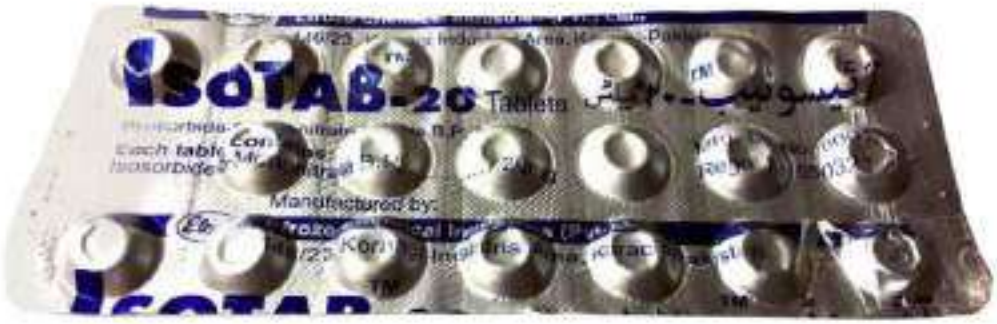


Fig: Contaminated medicines that caused hundreds of deaths in Pakistan in 2011-2012

Source: WHO Global Surveillance and Monitoring System for substandard and falsified medical products ISBN 978-92-4-151342-5

3. Avastin (Bevacizumab- USA)

- Avastin, a cancer medicine, bevacizumab, was widely used in the United States to treat different cancer types, including advanced breast cancer.
- Product did not include any ***API.***
- Two incidents of similar product reported in February and April 2012.
- Product reached patients through clinics and hospitals in the US.
- Supply chain stretches across 3 continents so far, passing through the web of wholesalers, brokers and dealers.

Source: WHO Global Surveillance and Monitoring System for substandard and falsified medical products ISBN 978-92-4-151342-5

- Which of the previous case do you consider more frightening?

1. Diazepam case, Democratic Republic of Congo
2. Isosorbide case, Pakistan
3. Avastin case, US

- Among the previous cases, which is related to falsification?

Comments….

Representative cases of SF vaccines

Fig: Falsified Covid 19 vaccines seized by South African Authorities.

- During a meningitis epidemic 1995, approximately 60,000 Nigerians were provided with water disguised as meningitis vaccine, resulting approximately 2,500 to 3,000 excess deaths.[1]
- Substandard hepatitis B and rabies vaccines killed or sickened approximately 100 infants in China.[2]
- South African authorities seized hundreds of falsified COVID-19 vaccines. (400 ampoules - equivalent to around 2,400 doses).[3]
- Chinese police identified a network selling counterfeit COVID-19 vaccines, raided the manufacturing premises, seized more than 3,000 falsified vaccines.[3]

References:
1.Cockburn R. Death by dilution. The American Prospect. November 20, 2005. https://prospect.org/features/death- dilution/
2. Jia H, Carey K. Chinese vaccine developers gain WHO imprimatur. Nature Biotechnol. 2011;29(6):471-472
3. Interpol, https://www.interpol.int/en/News-and-Events/News/2021/Fake-COVID-vaccine-distribution-network-dismantled-after-INTERPOL-alert (Accessed on Dec 18 2023)

Global Incidents of DEG/EG contamination

1937	1990-1998	1996	2006	2008-2009	2019
USA	**Argentina, Bangladesh, India, and Nigeria**	**Haiti**	**Panama**	**Nigeria**	**India**
DEG-contaminated Elixir of sulfanilamide. **>100** deaths	DEG poisoning occurred, **hundreds** of deaths recorded.	> 68 cases of AKI in children. > **30** deaths. DEG contaminated paracetamol syrups in local products.	> 82 cases of AKI. > **38** deaths reported due to syrup and topical creams with DEG.	**>84** children died. DEG contaminated paracetamol syrup in local products	>17 suspect AKI cases seen in children. >**12** deaths reported due to DEG contaminated paracetamol syrup.

References: Substandard and falsified medical products, WHO ,Technical briefing seminar 11 May 2023

1. What was the major contaminant present in the previous case series ?

Comments

2. What are adverse effects produced by the abovementioned contaminant in children?

Answer

1.2 DEFINITIONS AND CASE STUDIES

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 on 5 October 2022

Aug.–Oct. 2022

Indonesia:

- Around 325 cases of suspect AKI in children
- About **203** deaths
- Thirteen products contaminated with EG
- Products manufactured by 7 local Pharma
- Medical Product Alert on 6 November 2023

Dec. 2022

Uzbekistan

- Unverified reports of approx. **18** deaths of children
- Cases suspected to be related to contaminated paracetamol syrup.
- Products imported from India
- Medical Product Alert on 11 January 2023

April 2023

Marshall Islands & Micronesia

- Contaminated cough syrup spotted
- No reports of deaths
- Products manufactured in India
- Medical Product Alert on 25 April 2023

References: Substandard and falsified medical products, WHO , Technical Briefing Seminar, ISF team 11 May 2023

Recent incident related to DEG/EG Contamination

- WHO medical product alert referring to five different syrup and suspension medicines initially detected in the Maldives and Pakistan and notified to WHO on 8 November 2023.
- Some has been detected in Belize, Fiji and Lao People's Democratic Republic.
- Five batches were contaminated with ethylene glycol.
- Drug Regulatory Authority of Pakistan (DRAP) ordered the manufacturer to stop production of all oral liquid dosage medicines, and on 16 November 2023.
- DRAP issued a recall alert all syrup medicines.

Source: WHO, Accessed on Dec 29, 2023

1.2 DEFINITIONS AND CASE STUDIES

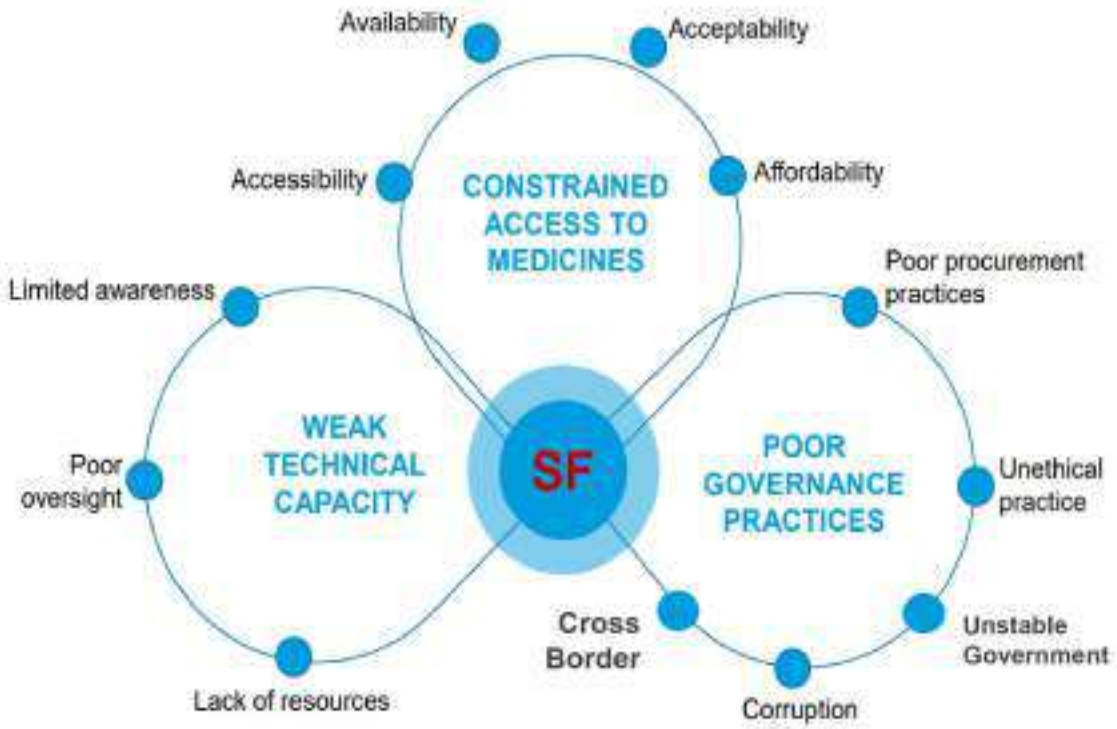
- Falsified remdesivir identified in Biratnagar, Nepal at the patient level.
- *Ceftriaxone vials labelled as Remdesivir*

What were other substandard, falsified and unregistered medical products sold during covid-19 pandemic in Nepal?

Comments….

Source: https://www.eadarsha.com/eng/two-arrested-for-selling-medicines-with-fake-sticker-of-remdesivir-vials/

1.3 SF MEDICAL PRODUCTS: CAUSES AND SCALE OF IMPACT



1.3 SF MEDICAL PRODUCTS: CAUSES AND SCALE OF IMPACT

Drivers of SF Medical Products

Profitability | Low risk of detection | Low risk of prosecution | Weak Penalties

- Global illegal drug sales remains the most lucrative component of global illegal trade surpassing arms dealing and human trafficking.[1]
- The profit margin of SF falsification is reportedly greater than illegal drug trafficking.[3]
- Producing a kilogram of fake sildenafil citrate(viagra) is considered to be more profitable than producing a heroine of the same volume.[2]
- Selling falsified medicine online is 20,000 times more profitable than selling narcotics on the streets.[1]

Table: Maximum incarceration for trademark infringement and narcotics trafficking

	Brazil	Canada	France	United Kingdom	United States	Average
Trademark infringement	1	5	4	10	10	6
Narcotics trafficking	15	10	10 (or life sentence in certain cases)	Up to life sentence	Up to life sentence	25[1]

Source: OECD/EUIPO (2020), Trade in Counterfeit Pharmaceutical Products, Illicit Trade, OECD Publishing, Paris. https://doi.org/10.1787/a7c7e054-en

References

1. International Pharmaceutical Federation. Trusted for health: Pharmacy and Counterfeit Medicines worldwide- problems and solutions, streamed live on September 22, 2021, https://www.youtube.com/watch?v=TL40nbucZ2Q (Accessed on December 22, 2023)
2. J Am Pharm Assoc. 2012;52(2):195-199
3. German Foundation for International Development (DSE); 2021. Jun 11. [2021 Jul 27;]

1.3 SF MEDICAL PRODUCTS: CAUSES AND SCALE OF IMPACT

No country or product is immune to the threat of falsification and substandard manufacturing.

Antibiotics and antimalarials are amongst the most reported SF medical products.

SF medicine targets differ between developed and developing countries:

- Life-style medicines (slimming pills, hormones, or steroids) are often the target in developed, whereas life-saving medicines (antibiotics) are targeted in developing countries

However, major targets includes but not limited to:

- Antibiotics and anti-malarials
- Vaccines
- CNS medicines
- Cardiovascular medicines
- Antidiabetics

Reference: Kalliroi S. Ziavrou et al, Trends in counterfeit drugs and pharmaceuticals before and during COVID-19 pandemic: Forensic Science International 338 (2022) 111382. https://doi.org/10.1016/j.forsciint.2022.111382

1.3 SF MEDICAL PRODUCTS: CAUSES AND SCALE OF IMPACT

Evidence of prevalence and impact

WHO estimates that 1 in 10 medicines circulating in low-income and middle-income countries (LMICs) is either substandard or falsified [1].

Overall prevalence of poor-quality medicines is reported to be 13.7% in Asia [2].

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: https://iris.who.int/bitstream/handle/10665/332635/WHO-MVP-EMP-SAV-2019.04-eng.pdf?sequence=1

References
1. https://www.who.int/news-room/fact-sheets/detail/substandard-and-falsified-medical-products
2. *JAMA Netw Open [Internet]*. 2018 Aug 10;1(4):e181662

1.3 SF MEDICAL PRODUCTS: CAUSES AND SCALE OF IMPACT

Evidence of prevalence and impact

- Approximately 1 million people die globally per year from SFMPs due to poor efficacy or adverse effects caused by contamination [1].
- SF Medicines for tuberculosis and malaria is estimated to cause 700,000 fatalities per year globally [2].
- As per the estimates, in just one year, 122,000 children under the age of five from 39 sub-Saharan African countries died due to poor-quality antimalarials [2].
- 12.4% of antibiotics and 19.1% of antimalarials in LMICs were found substandard or falsified [2].
- A study evaluating quality of cardiovascular drugs (e.g., anticoagulants, antihypertensives, and statins) in sub-Saharan Africa found that 16.3% of more than 1,500 samples randomly tested of cardiovascular failed the content analysis for APIs [3].
- 13.6% of essential medicines tested in LMICs failed quality criteria.
- The highest SF prevalence was in Africa, where 18.7% of samples were unsatisfactory [4].

References
1.Nature reviews (2022) 8:55
2.United States Pharmacopoeia, USP Global Public Policy Position: Combatting Substandard and Falsified Medicine, Accessed on December 18 2023
3. Int J Cardiol. 2017;243:523-528. doi:10.1016/j.ijcard.2017.04.099
4. A systematic review and meta-analysis. JAMA Netw Open. 2018;1(4):e181662.

1.3 SF MEDICAL PRODUCTS: CAUSES AND SCALE OF IMPACT

Impact of SF Medical Products

References :
1.WHO Public health and socioeconomic impact study 2017 https://apps.who.int/iris/handle/10665/331690

What might be the actual prevalence percentage of substandard and falsified products in Nepal?

Comments....

Why do you think the extent of SFMPs is poorly understood in countries like Nepal?

Comments....

Scale of SF Medical Products In Nepal

"Nepal stands in a vulnerable position as two of its major trade partners countries are leading producers of falsified healthcare products." [1]

- A study reported 32.5% of the tested samples to be of substandard quality in Nepal.[2]
- Out of 244 batches (20 different generics) of essential medicines, 37 batches failed to meet the required pharmacopeial standards.[3]
- In 2018, INTERPOL-led "Operation Rainfall" Nepalese police seized 5,399 doses of opioid analgesics.[4]

Source: https://kathmandupost.com/national/2020/01/04/nepal-may-be-becoming-the-new-transit-point-for-the-drug-smugglers

References
1. JNMA J Nepal Med Assoc. 2022 Dec; 60(256): 1070–1072
2. J Nepal Health Res Council 2015 Sep-Dec;13(31):233-40
3. NHRC Drug Report 2019
4. Lyon (FR): International Criminal Police Organization; 2018. [2022 Mar 28;]. https://www.interpol.int/fr/Actualites-et-evenements/Actualites/2018/Fake-goods-arrests-and-seizures-in-worldwide-operations

1.3 SF MEDICAL PRODUCTS: CAUSES AND SCALE OF IMPACT

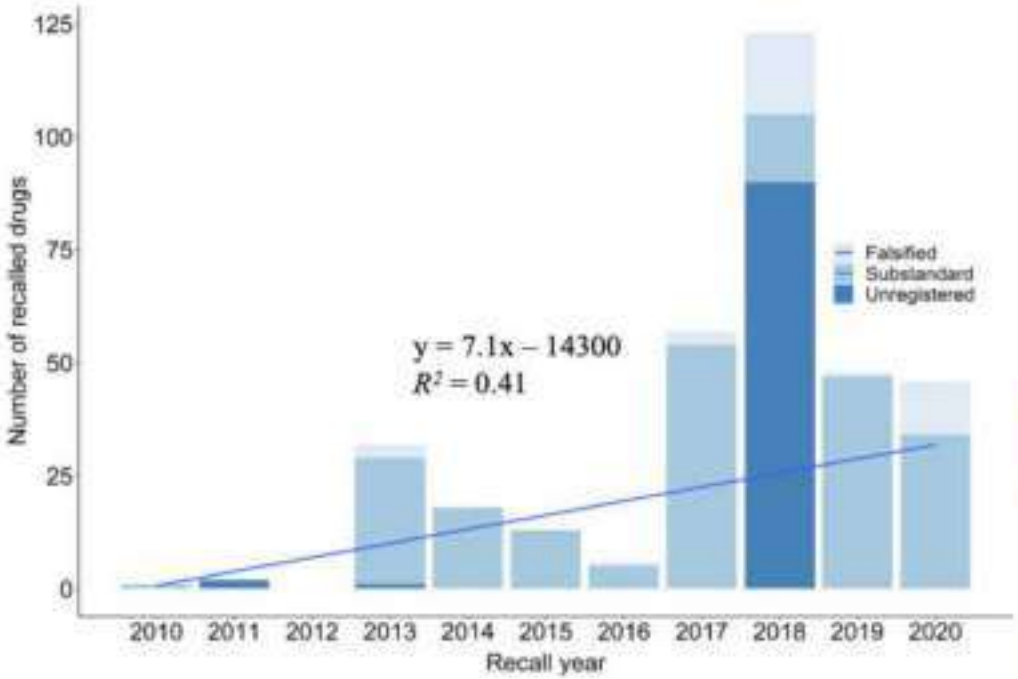


Figure :Temporal trend of recalled products (2010-2020)

346 pharmaceutical products were recalled by DDA between January 2010 – December 2020 in Nepal.

Table: Recalls initiated by Department of Drug Administration

Fiscal Year	Number of Recalled Products
2078-79(16 July 2021-15 July 2022)	13
2079-80 (16 July 2022-15 July 2023)	24

Source: https://www.dda.gov.np/information/CIRCULAR

Ref: Neupane A, et al. BMJ Open 2022;12:e053479. doi:10.1136/bmjopen-2021-053479

1.3 SF MEDICAL PRODUCTS: CAUSES AND SCALE OF IMPACT

Categories of recalled products (2010-2020)

- 62 % substandard, 11 % counterfeit, and 27 % unregistered products
- 60% allopathic, 35% traditional or ayurvedic, 5 % others

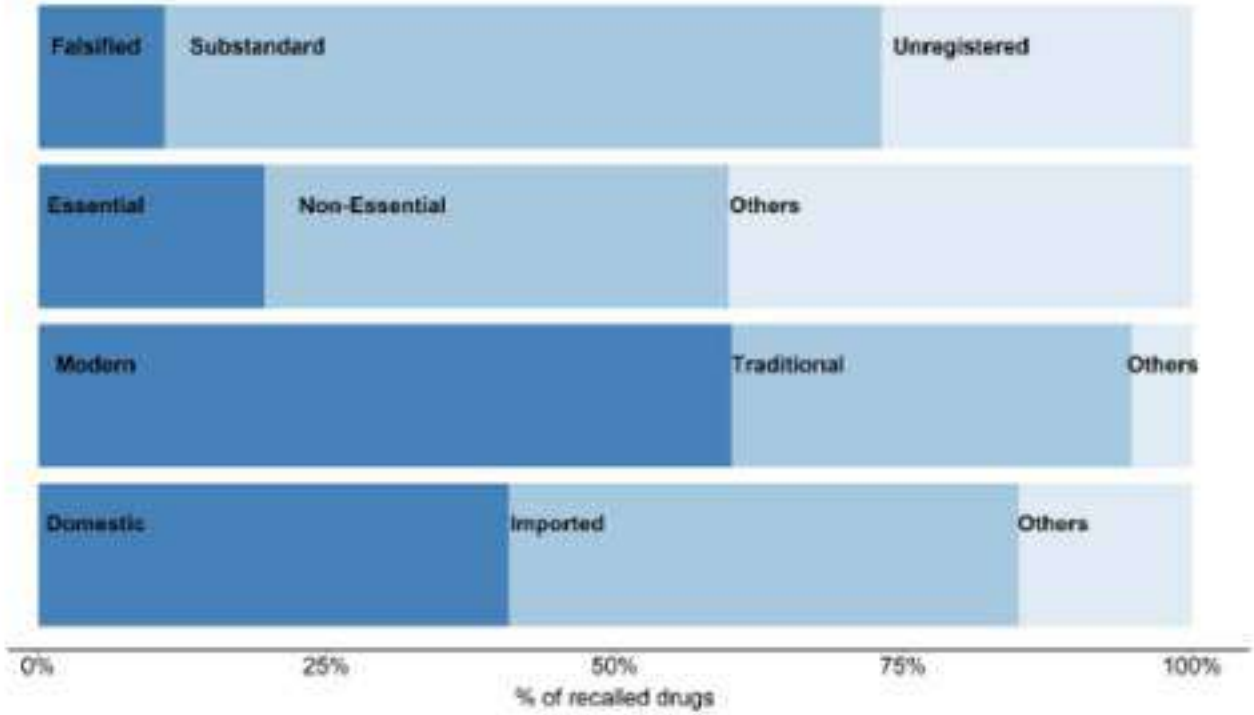
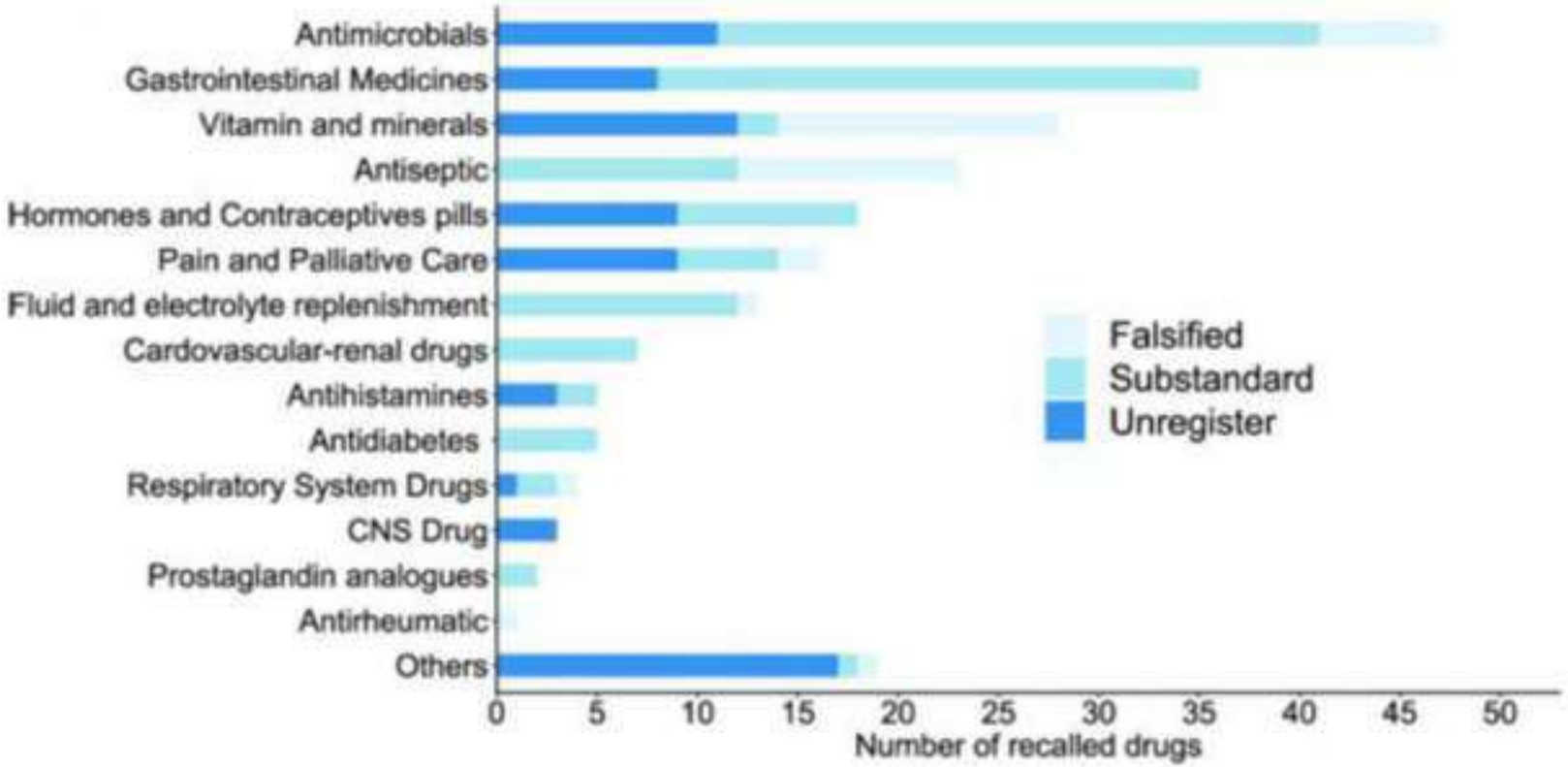


Figure : Contribution of different categories of recalled products

Ref: Noupane A, et al. BMJ Open 2022;12:e053479. doi:10.1136/bmjopen-2021-053479

1.3 SF MEDICAL PRODUCTS: CAUSES AND SCALE OF IMPACT

Therapeutic category of recalled products



Ref: Neupane A, et al. BMJ Open 2022;12:e053479. doi:10.1136/bmjopen-2021-053479

PARTICIPANT REFLECTION AND FEEDBACK

- Which therapeutic category do you think is the most vulnerable to falsification in developing countries like Nepal?

- ❑ Antibiotics and anti-malarials
- ❑ Lifestyle medicines
- ❑ Vaccines
- ❑ Others

Reason

1.4 SUPPLY CHAIN QUALITY ASSURANCE OF MEDICAL PRODUCTS

Our challenges

- Unique and extent of SF medical product infiltration may not be adequately known.
- Nepal shares open border with India, presumed to be among leading producer of sub-standard and falsified medicines.[1]
- Lack of financial and technical resources to effectively conduct oversight and monitoring functions.
- Limited access to quality control testing laboratories, currently only one government owned central medicine testing laboratory exists.
- All three levels of government are involved in procurement and supply of medicines. Local governments lack technical capacity for safe and scientific procurement of quality assured medical products.
- Medicines management and dispensing functions are often carried out by allied health care professionals who lack appropriate qualification and training.

References
1.OECD/EUIPO (2020), Trade in Counterfeit Pharmaceutical Products, Illicit Trade, OECD Publishing, Paris, https://doi.org/10.1787/a7c7e054-en

1.4 SUPPLY CHAIN QUALITY ASSURANCE OF MEDICAL PRODUCTS

Quality testing is an essential part of comprehensive QA program- but it is not the only one component.

Cost Realities from Product QA procedures in PSM

Procedures	Cost	Effectiveness
Verify documents	$ 1	30%
Visual inspection	$ 2	40%
Screening test	$ 20	80%
Basic lab test	$ 1,000	98%
Full assay pharmacopeial	$ 10,000	99%

Note : These figures provide the general estimates and are not absolute as the costs varies depending upon the type and nature of the product and tests to be performed.

Reference: Expert session on managing product quality assurance in public sector procurement and supply chains, Empower school of health, accessed on Dec 8, 2023 : https://www.youtube.com/watch?v=ax-s1QPV5gI

- What might be the most cost-effective approach to assure the quality of medical products in countries resource constrained lower and middle income come countries like Nepal?

Comments….

1.4 SUPPLY CHAIN QUALITY ASSURANCE OF MEDICAL PRODUCTS

The Three-Level Approach: A Framework for Ensuring Medicines Quality in Limited-Resource Countries

Level 1

Visual and physical inspection

Initial check of registration status, expiration date, labeling, packaging, appearance, physical and organoleptic properties, use of track and trace technologies

Level 2

Field-based screening

Use of field-based screening technologies which may test for identity, content and other quality attributes

Level 3

Compendial testing

The prioritization and use of pharmacopeial methods or other validated methods approved by the NMRA

Reference: United States Pharmacopoeia, *Risk-based post-marketing surveillance of medicines: Implementation resources for low- and middle income countries*, 2021

Arrange the tests approach in sequential order.	
1. Compendial tests	
2. Field based screening	
3. Visual and physical Inspection	

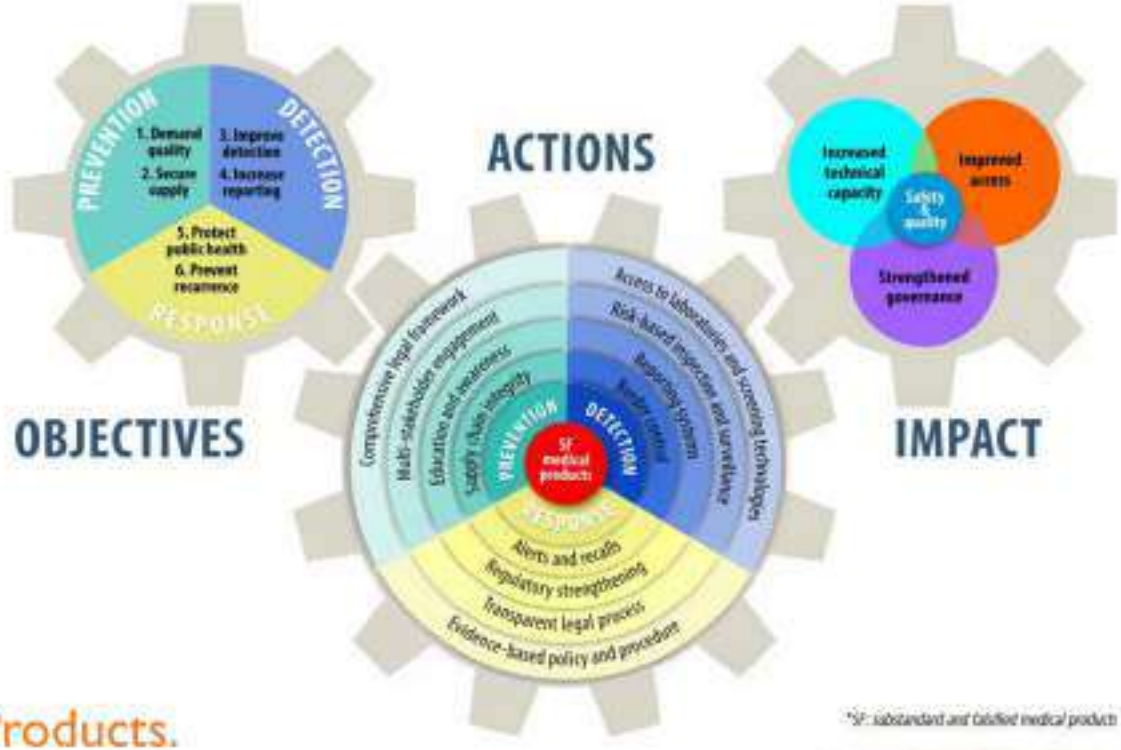
1.5 ROLE OF PHARMACISTS IN COMBATING SF MEDICAL PRODUCTS

B	**Be observant. If anything about medicines is unusual or different, consider substandard/ falsified (SF) medicines.**
E	**E**valuate your patient's response to the medicine use. If treatment fails, or has an unexpected effect, consider SF medicines as possible suspects.
A	**A**cquire as much information as possible about the product, its packaging, pharmaceutical properties and usage.
W	**W**here was the product procured? Find out whether it was purchased from a known and reliable source.
A	**A**ctively inform your health professional colleagues if medicines have been confirmed as SF medicines, as well as other patients who might also have received the medicines.
R	**R**emove any suspect medicines from the pharmacy, clinic, hospital or consulting room. Report the suspected SF medicines to the relevant health authorities.
E	**E**ducate your colleagues, patients and the public to identify and avoid SF medicines by purchasing their medicines from known and reliable sources.

Source: The World Health Professions Alliance (WHPA), https://www.whpa.org/sites/default/files/2018-12/Toolkit_BeAware_Background.pdf (Accessed on December 22, 2023)

Sources of Information

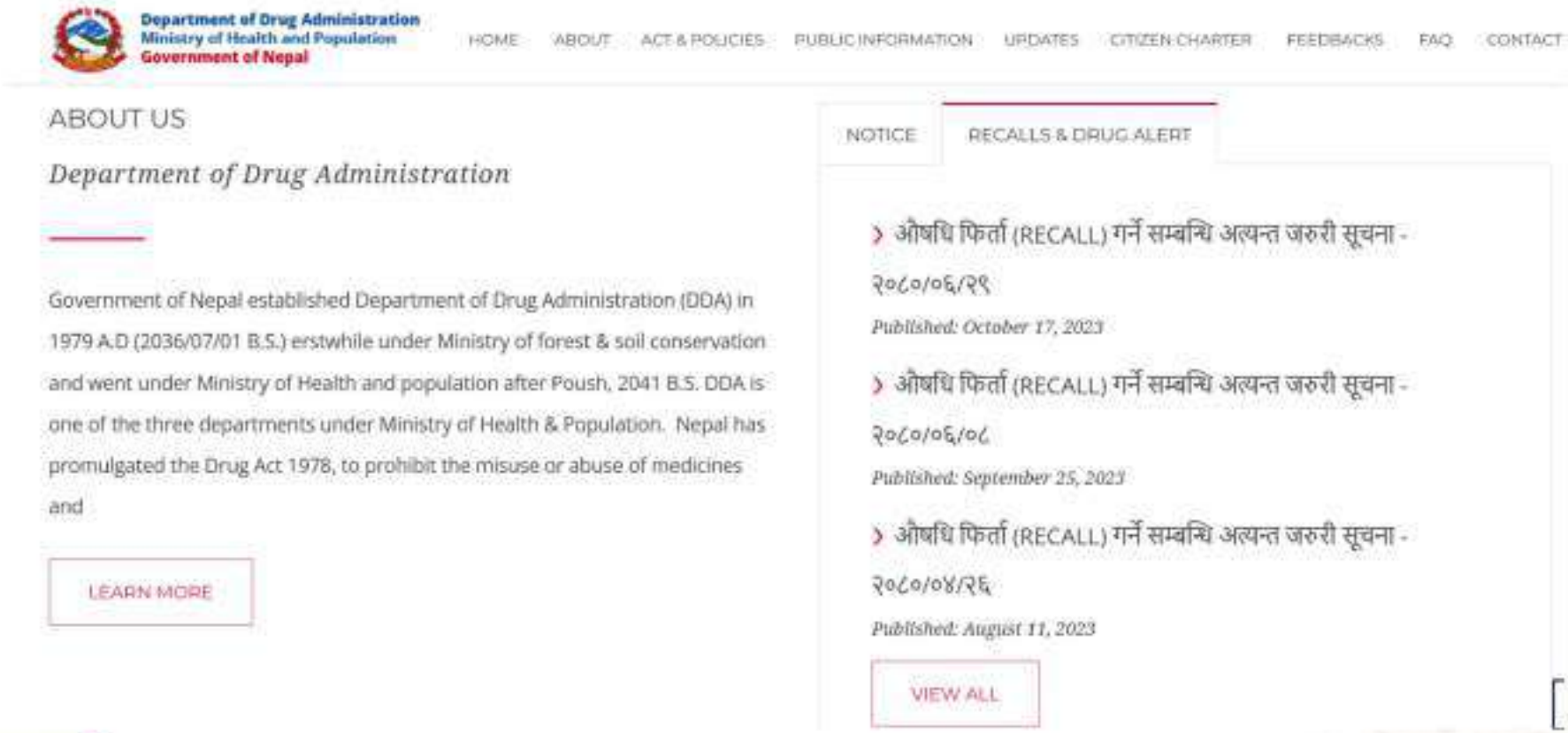
- WHO Drug Alerts
- DDA Recalls and Drug Alerts / Drug Bulletin
- NPC, MoHP, DDA websites
- Scholarly Research articles
- EMA, FDA and other RAs
- News papers



Always be vigilant of suspect SF Products.

1.5 ROLE OF PHARMACISTS IN COMBATING SF MEDICAL PRODUCTS

Look for DDA drug recalls, alerts and notices.



Source : https://www.dda.gov.np/information/CIRCULAR

1.5 ROLE OF PHARMACISTS IN COMBATING SF MEDICAL PRODUCTS

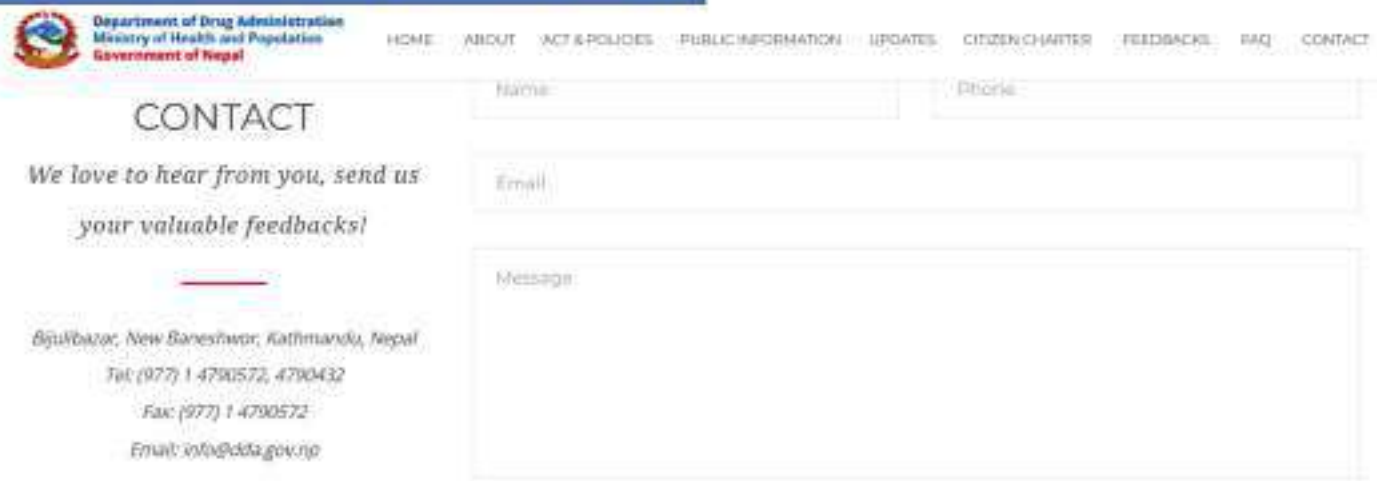
WHO launched its **Global Surveillance and Monitoring System for substandard and falsified medicines, vaccines and in-vitro diagnostic tests** in July 2013.

Source: https://www.who.int/health-topics/substandard-and-falsified-medical-products

1.5 ROLE OF PHARMACISTS IN COMBATING SF MEDICAL PRODUCTS

In case you contact a suspect SF Medical Product, you should report immediately to DDA.

Department of Drug Administration



World Health Organization

Email: rapidalert@who.int

REPRESENTATIVE EXAMPLE OF SF PRODUCTS

Fig: Vials of meningitis vaccine found in Nigeria in 2015 with the expiry date manually extended by two years.

Source: WHO Global Surveillance and Monitoring System for substandard and falsified medical products ISBN 978-92-4-151342-5

REPRESENTATIVE EXAMPLE OF SF PRODUCTS

Sulphadoxine-pyrimethamine

Genuine Counterfeit

Sulfametopyrazine-pyrimethamine

Genuine Counterfeit

Duo-cotecxin

Genuine Counterfeit

Fig: Samples of genuine and counterfeit drugs confiscated in Tanzania.

Source: P. Karungamye Forensic Science International: Reports 7 (2023) 100302

REPRESENTATIVE EXAMPLE OF SF PRODUCTS

One of the four falsified "furosemide 40 mg BP" samples with a manipulated expiry date-November 2018, instead of the genuine expiry date November 2015.

Reference: Am. J. Trop. Med. Hyg., 104(5), 2021, pp. 1936–1945

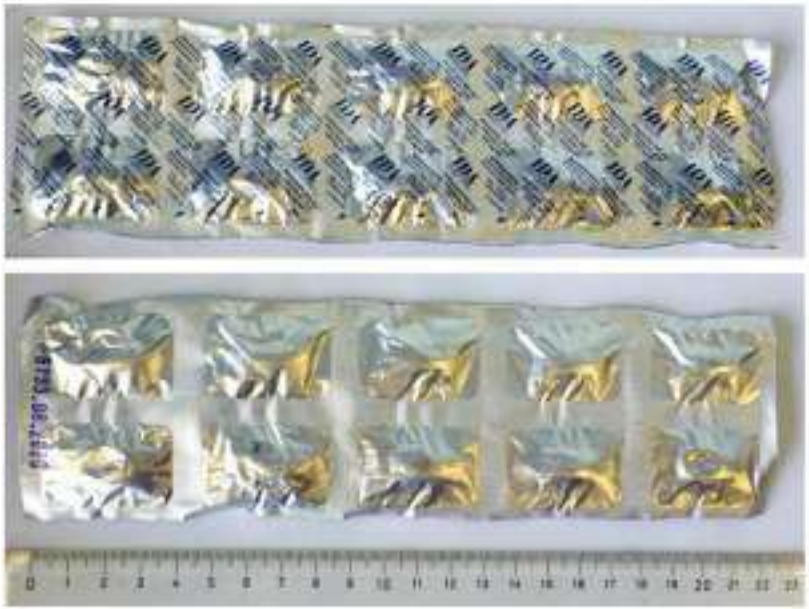
REPRESENTATIVE EXAMPLE OF SF PRODUCTS

Falsified penicillin V tablets (sample no. QMCA035), containing 50 mg paracetamol. Note that the API is misspelled on the label

Source: Am. J. Trop. Med. Hyg., 103(2), 2020, pp. 894–908

REPRESENTATIVE EXAMPLE OF SF PRODUCTS

Falsified "amoxicillin 500 mg + clavulanic acid 125 mg BP" tablets. Batch number, shelf life, blister length and further labeling details do not match those of the genuine product.



Blister pack with a length of 220 mm, not matching the length of the blister pack of the genuine product which was 195 mm according distributor

Source: Am. J. Trop. Med. Hyg., 104(5), 2021, pp. 1936–1945

REPRESENTATIVE EXAMPLE OF SF PRODUCTS

I. Falsified

II. Genuine

Falsified (I) and genuine (II) "co-trimoxazole (sulfamethoxazole and trimethoprim)" tablets.

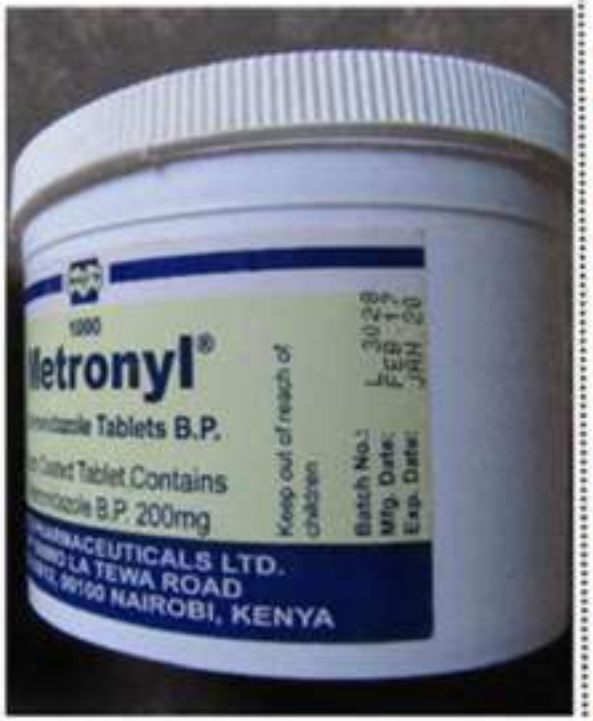
The falsified sample shows an incorrect batch number. Batch number and expiry date are printed rather than being embossed onto the blister; blister length, artwork, and color of the blister, as well as the embossing of the tablets, do not match those of the genuine product.

The falsified product had been sold without secondary packaging

Source: Am. J. Trop. Med. Hyg., 104(5), 2021, pp. 1936–1945

REPRESENTATIVE EXAMPLE OF SF PRODUCTS

QMC266



Falsified

QMC036

Genuine

Sample no. QMC036, manufactured date: March 2016, batch no: K2343, complying with U.S. Pharmacopeia 41 specifications for metronidazole tablets.

QMC 266 does not comply compendial tests.

Source: Am. J. Trop. Med. Hyg., 103(2), 2020, pp. 894–908

REPRESENTATIVE EXAMPLE OF SF PRODUCTS

Falsified Augmentin (sample no. QMCA241), containing no detectable active pharmaceutical ingredient (API).

Source: Am. J. Trop. Med. Hyg., 103(2), 2020, pp. 894–908

List out any 5 issues identified on representative images of substandard and falsified products.

1. .....
2. .....
3. .....
4. .....
5. .....

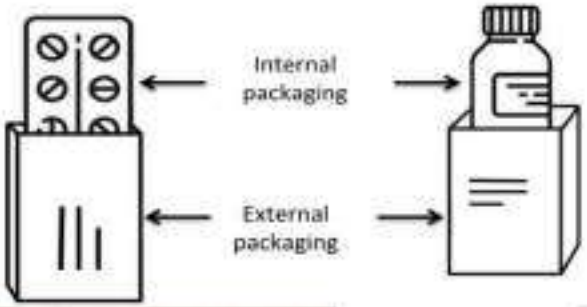
1.6 Visual and Physical Inspection

- Visual inspection focuses on labeling, packaging integrity, and package information, and physical inspection centers on its appearance.

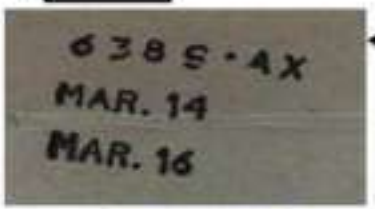
- Both ensure that product comply with the appropriate quality standards, regulatory requirements, and registration specifications.

Source: https://www.paho.org/en

1.6 VISUAL AND PHYSICAL INSPECTION



Unreadable packaging information



Non-explicit

Packaging information

Explicit

Batch no. 638SAX

Exp. Date 04/2022

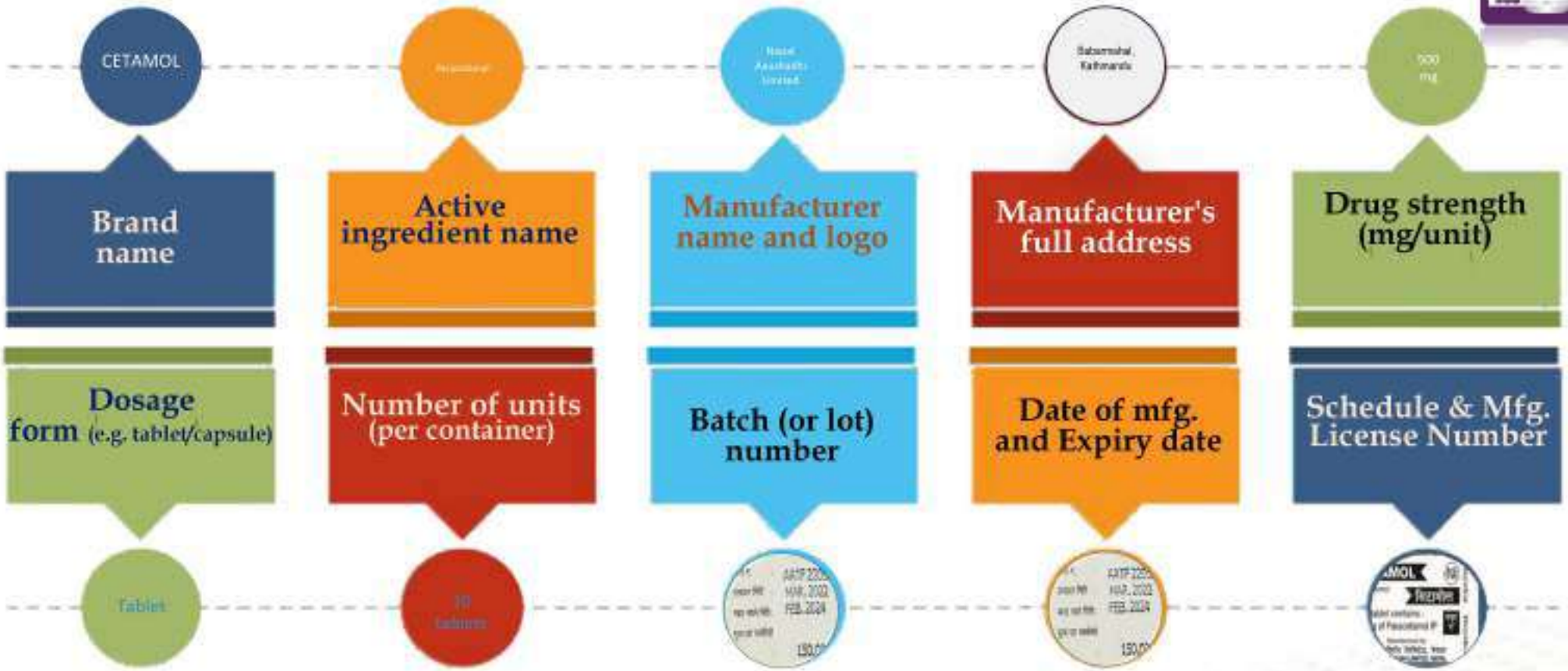
Manufactured by: Alpha Tech Industry, Portobello avenue 54, 1076 Infinite Village, NOWHERE

Example of sticky powder

Examples of child-resistant safety cap

Ref: Schiavetti et al. Journal of Pharmaceutical Policy and Practice (2020) 13:9 https://doi.org/10.1186/s40545-020-00211-9

Packaging and Labelling Information



Inspection of container and closures

- Check for material, spelling, logo, hologram, trademark and information that is supposed to be on the label.
- Check the type of packaging and compare it to known containers for the same drug from the same manufacturer
- Check the closures and all the details on the label
- Check whether the number of tablets/capsules listed on the label matches the number of tablets stated on the container
- If there is a carton for container, check if the information on the label of carton matches label on container

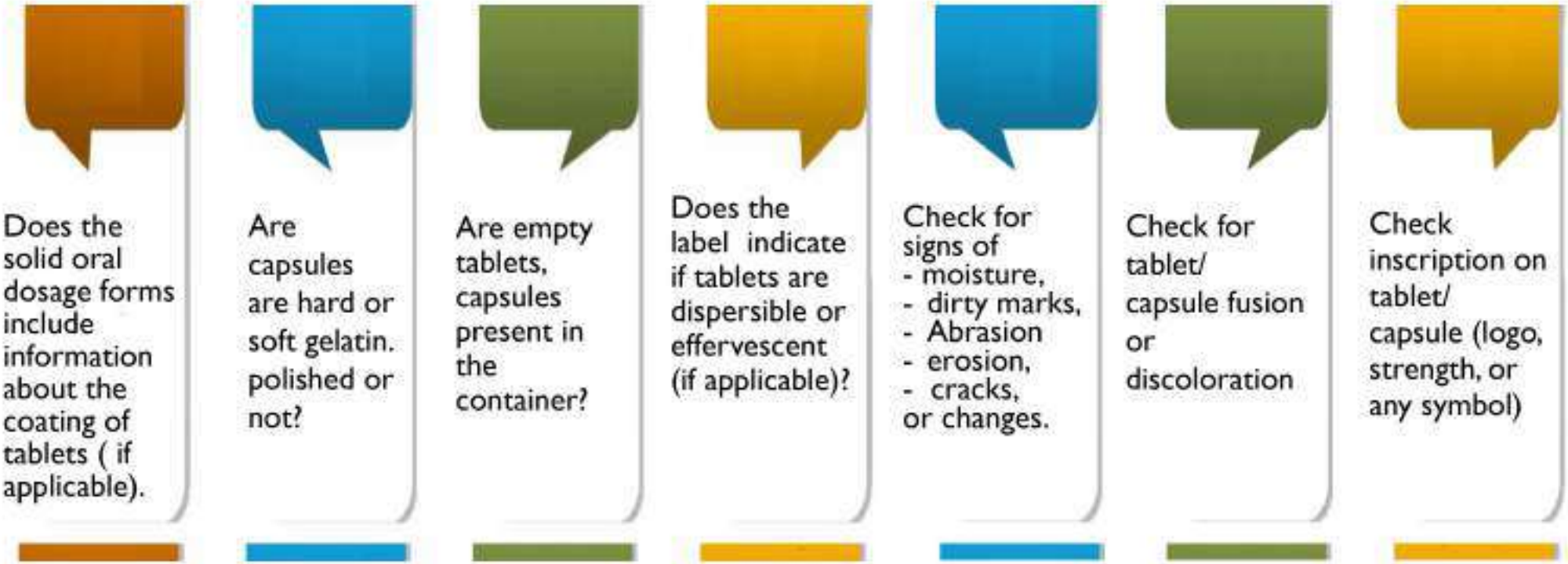
Storage Information

Storage conditions must be indicated on the label and must be checked to assure that drug is stored properly.

a. Are the product storage conditions indicated on the label?

b. Is the storage area indicated on the label?

Physical inspection of solid dosage forms:



1.6 VISUAL AND PHYSICAL INSPECTION

Inspect the following details based on the type of dosage forms:

Are markings uniform (shape, size and markings) and identical?

Are tablets free of breaks, cracks, splits and pinhole free capsule?

Are the tablets/capsules free of embedded surface spots and foreign particle? contamination?

Is the base of the tablets fully covered?

Is the sample examined free of empty tablets and capsules?

What are different issues observed in the following images?

1.6 Visual and Physical Inspection

Suspect if liquid dosage forms do not meet the following criteria:

Syrup

- Clear, Transparent, Free from foreign body
- Uniform color and volume in original color
- Sealed and no leakage

Suspension

- Easily dissolved, delay in sedimentation
- No cake formation.
- Sealed and no leakage

Emulsion

- No Phase separation
- Sealed and no leakage

Semisolid

- Easy in discharge.
- Sealed and no leakage

Injectable

- Not broken and no leakage
- Clear, free from foreign body or particles
- Uniform color and volume in
- Original color

1.7 Visual Inspection Tool

1. Packaging

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

	Yes	No	Other observations
1.1 Container and closure			
Do the container and closure protect the drug from the outside environment e.g. properly sealed?			
Do they assure that the drug will meet the proper specifications throughout its shelf life?			
Are the container and the closure appropriate for the drug inside?			
Is the container safely sealed?			
1.2 Label The information written on the label is very important. The information can be printed on a label adhered to the container, or printed directly onto the container itself, but all information must be legible and indelible.			
If there is a carton protecting the container, does the label on the carton match the label on the container?			
Is all information on the label legible and indelible?			
1.2.1 The trade name			
Is the trade name spelled correctly?			
Is the drug (trade name) registered in the country by the DRA (drug regulatory authority)?			
Is the drug legally sold in the country?			
Does the symbol ® follow the trade name?			
1.2.2 The active ingredient name (scientific name)			
Is the active ingredient name spelled correctly?			
Do the trade name and the active ingredient name correspond to the registered drug?			
1.2.3 The manufacturer's name and logo			
Are the manufacturer's name and logo legible and correct?			
Does the logo or hologram (if applicable) look authentic? Does it change colour when viewed from different angles?			

This document has been produced by World Health Professionals Alliance (WHPA), which was originally developed by the International Council of Nurses in partnership with the United States Pharmacopoeia (USP) and modified by the Military and Emergency Pharmacists Section of FIP. The tool is designed to help health professionals carry out a visual inspection of medicines for signs of counterfeiting such as improper packaging, labelling or description of dosage. All suspicious products with incorrect labels, missing information about the strength, dosage, or expiration date should be reported to the appropriate national authority or to the WHO or FIP.

1.7 Visual Inspection Tool

	Yes	No	Other observations
1.2.4 The manufacturer's full address All manufacturers are required by international law to print their complete address on the label. Many companies making substandard or counterfeit drugs do not have a traceable address on the label.			
Is the manufacturer's full address legible and correct?			
Has the company or its agent registered the drug in the country?			
1.2.5 The drug strength (mg/unit)			
Is the strength - the amount of active ingredient per unit - clearly stated on the label?			
1.2.6 The dosage form (e.g., tablet/capsule)			
Is the dosage clearly indicated?			
Is the indicated drug under this dosage form is registered and authorized for sale in the country?			
1.2.7 The number of units per container			
Does the number of tablets listed on the label match the number of tablets stated on the container?			
1.2.8 The batch (or lot) number Drugs under the same batch/lot number are expected to be equivalent. In a continuous process, a batch corresponds to a defined portion of the production, based on time or quantity. Drugs from the same batch number should have the same history of manufacturing, processing, packing, and coding. All drug quality control testing should be based on batch/lot numbers.			
Does the numbering system on the package correspond to that of the producing company?			
1.2.9 The date of manufacture and the expiry date An expired drug should not be sold under any circumstances.			
Are the manufacture and expiry dates clearly indicated on the label?			
1.3 Leaflet or package insert All drug packages should contain a leaflet explaining dosage, the drug content, the adverse affects, the drug actions, and how the drug should be taken. The only exceptions are where the packaging includes all the information that would otherwise be in the leaflet.			
Is the package insert printed on the same coloured or same quality paper as the original?			
Is the ink on the package insert or packaging smudge-proof?			

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2. Physical characteristics of tablets/capsules

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

	Yes	No	Other observations
2.1 Uniformity of shape			
Are the tablets/capsules uniform in shape?			
2.2 Uniformity of size			
Are the tablets/capsules uniform in size?			
2.3 Uniformity of colour			
Are the tablets/capsules uniform in colour?			
2.4 Uniformity of texture Tablets can be film-coated, sugar-coated or enteric-coated.			
Do the tablets have a uniform coating?			
Is the base of the tablets fully covered?			
Are the tablets uniformly polished, free of powder, and non-sticking?			
2.5 Markings (scoring, letters, etc)			
Are markings uniform and identical?			
2.6 Breaks, Cracks and Splits			
Are the tablets/capsules free of breaks, cracks, splits or pinholes?			
2.7 Embedded surface spots or contamination			
Are the tablets/capsules free of embedded surface spots and foreign particle contamination?			
2.8 Presence of empty capsules in the case of a sample of capsules			
Is the sample examined free of empty capsules?			
2.9 Smell			
Does the medicine smell the same as the original?			

Source: The World Health Professions Alliance (WHPA), https://www.whpa.org/sites/default/files/2018-12/Toolkit_BeAware_Background.pdf (Accessed on December 22, 2023)

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"There is no universal health coverage, no health security without access to quality medicines".

Dr. Tedros Adhanom Ghebreyesus
Director General
World Health Organization (WHO)

Q/A Session

EXERCISES AND EVALUATION SESSION

- General Overview of SF Medicine
- Scenario of SF Medicine
- Impact of SF to the human kind
- Method of Visual inspection of SF