5 Technical resources

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Distribution of antiretrovirals at a social clinic.


5.1 WHO practical guidance materials on SFMPs
5.2 Supplementary training resources
5
5.3 Bibliography

5 Technical resources

This section includes selected technical resources that the trainer can incorporate into their curriculum (Table 33). These include practical guidance material from WHO and case studies linked to relevant modules of the curriculum guide, sample course content and reference resources. A section on frequently asked questions (FAQ) will also be provided as part of the website for the trainer's toolkit in 2025. We recommend routinely reviewing the resources as some of the practical resources may be regularly updated.

Table 33. Practical resources and supplementary training material

Resources	Module
5.1 WHO practical guidance materials on SFMPs	
5.1.1 Identifying suspected SFMPs	B, D
5.1.2 Characteristics of suspect websites likely to distribute SFMPs	B, D
5.1.3 Taking good photographs of suspected SFMP samples	D
5.1.4 SFMP incident management aide-memoire	D
5.1.5 Prioritization and risk parameters	B, D
5.1.6 Questions to consider when assessing risk	B, D
5.2 Supplementary training resources	
5.2.1. Glossary of terms	All
5.2.2. WHO prevent–detect–respond strategy to combat SFMPs	All
5.2.3. Exercises and case studies	All
5.2.4. WHO e-course on SFMPs	All
5.2.5. Assessment questionnaire for learners	All
5.3 References and further reading	All
Bibliography: Selected WHO guidance documents	
Annex 2: WHO GMP for pharmaceutical products: main principles	B
Annex 7: good storage and distribution practices for medical products	B
Global benchmarking tool for evaluation of national regulatory system of medical products	B
Protecting the supply chain: reports on informal markets	B
Policy paper on traceability of medical products	B
Guidance for post-market surveillance and market surveillance of medical devices	C
Identification of reporting barriers by national focal points	D
Rapid risk assessment of acute public health events	D

SFMP: substandard and falsified medical product; WHO: World Health Organization.

5.1 WHO practical guidance materials on SFMPs

The practical guidance material (5.1.1. to 5.2.2) is also available as separate leaflets that are available online.

5.1.1 Identifying suspected SFMPs for healthcare professionals

5.1.2 Characteristics of suspect websites likely to distribute SFMPs

5.1.3 Taking good photographs of suspected SFMP samples

5.1.4 SFMP incident management aide-mémoire

5.1.5 Prioritization and risk parameters

5.1.6 Questions to consider when assessing risk

5.2.1 SFMPs glossary of terms

5.2.2. WHO prevent–detect–respond strategy to combat SFMPs

5.1.1 Identifying suspected SFMPs for healthcare professionals

Fig. 5 outlines warning signs suggesting a medical product may be substandard or falsified. This figure is available in a separate leaflet online and is predominantly for use by healthcare professionals but can be adapted for use by other public health actors.

Fig. 5. Warning signs for substandard and falsified medical products

Substandard and falsified medical products are often difficult to detect. The following signs should raise suspicion. Please note that this guide is not an exhaustive list.

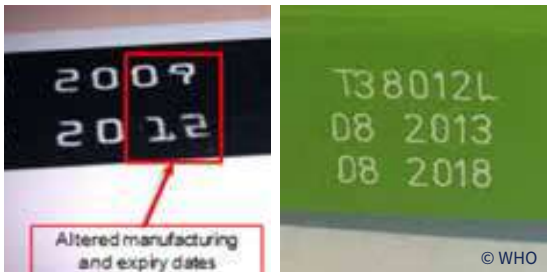
Therapeutic effect	• Patients report that the product is not working properly (unexpected lack of efficacy), and/or • Patients suffer unexpected adverse reaction(s)
Outer packaging	• Packaging is not in good condition, and/or • Manufacturers details are not clearly stated, and/or • Incorrect language, with grammatical and spelling errors, and/or • Batch numbers and expiry/manufacturing dates appear altered
Inner packaging	• Batch numbers, manufacturing/expiry dates on inner packaging (e.g. blister pack) are different from outer packaging, and/or • Patient information leaflet is in the wrong language
Supply source	• Any suspicion is raised on the source or price of a product and authenticity of accompanying documents, and/or • Any suspicion is raised on quantities available, e.g. products that are usually in short supply are suddenly available regularly or in large quantities
Other factors	• Product does not look, smell, taste and feel correct (i.e. texture), and/or • Packaging components are empty or separated, and/or • Product was not properly stored

Substandard example

Degraded antimicrobial tablets.

Collection of falsified antimicrobial medicines.

Falsified example

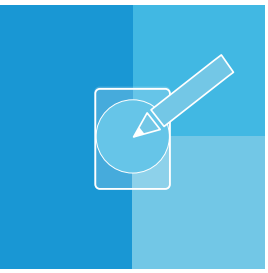


Falsified expiry dates.

Falsified vaccine vials.

If in doubt, please contact your national health authorities, who should then liaise with the WHO Global Surveillance and Monitoring System on SFMP.

Follow guidance provided in the aide memoire on how to manage an SFMP incident.



Notes for healthcare professionals

Therapeutic effect

- Is there an unexpected lack of efficacy? Often the product will not cause a toxic reaction but will fail to treat the condition for which it was intended, with potentially devastating consequences. For example, a patient failing to respond to their anti-infective will rarely consider that the cause of the problem may be their medicine.
- Is there an unexpected adverse reaction? Some SFMPs do cause adverse reactions and sometimes fatalities. A patient may experience an unexpected or unusual worsening of their medical condition.

Outer packaging and inner packaging

- Is the packaging in good condition? The container should protect the medical product inside (e.g. properly sealed and airtight).
- Are the manufacturer's details (e.g. name, logo, hologram, full address and registration number) clearly stated and in the correct language for the market/country in which the product is distributed?
- Are there any spelling or grammatical errors?
- Are the batch/lot numbers and manufacturing and expiry dates altered? They should be clearly shown, not possible to erase and easily readable, and there should be no irregularity in the embossing or imprinting.
- Is the dosage form or product strength clearly indicated on the label and the same on all parts of the packaging?
- Is the information the same on the inner and outer packaging, with no signs of alteration and discrepancies?
- Is there a patient information leaflet and is it in the correct language? The information on the patient information leaflet should match the information on other parts of the packaging. There should be no irregularity in printing quality or colour, shape, texture and size of paper (e.g. smudged ink, overly thick or rough paper).

Supply source

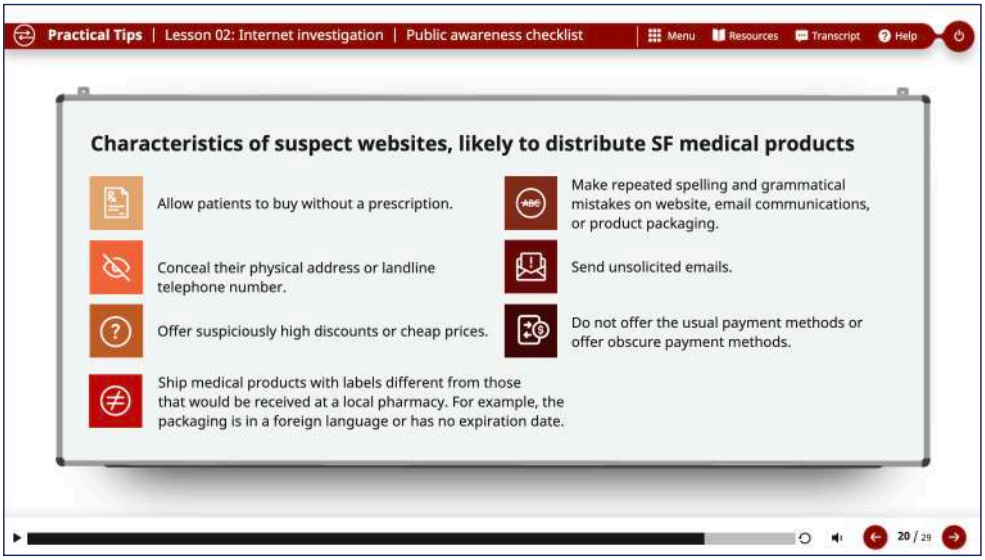
- Are there any suspicions about the source, price and quantities available (e.g. sudden availability of a product that is usually in short supply), or authenticity of accompanying documents? Those engaged in the manufacture, distribution and supply of SFMPs understand the market and respond quickly to demand. SFMPs can penetrate the legal supply chain through hospitals, clinics, pharmacies and wholesalers who have obtained medical products from unknown sources and intermediaries without checking their credentials or conducting any due diligence.

Other factors

- Did the patient (or did you) notice that the medical product looked, tasted, smelt or felt different? Any irregularity in the uniformity of appearance (i.e. colour, shape, texture, size and clarity), flavour and smell should raise suspicion.
- Are there any empty or separated packaging components (e.g. bottle caps, spoons, bottles, flat packs and capsules)? Such incidents may indicate signs of smuggling or tampering.
- Was the product properly stored? Storage conditions (e.g. temperature and humidity) should be stated on the label and maintained. Signs of degradation may include leakage and discolouration.

5.1.2 Characteristics of suspect websites likely to distribute SFMPs

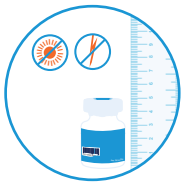
The following three screenshots are from the WHO e-course on SFMPs, and provide guidance on prevention and detection of SFMPs on the internet and social media. Access to the wider e-course is available on request from: rapidalert@who.int



5.1.3 Taking good photographs of suspected SFMP samples

This section is available as a separate leaflet online. Good photographs of a suspect sample are vital to identify SFMPs. A typical set of photographs includes one of each side of the sample, clearly displaying key information. When multiple photographs of multiple products or batch numbers are taken, it is essential to ensure that each photograph is appropriately labelled to match the correct product/batch number when sending the photographs. See example 1 and example 2 in this section.

Set the scene to ensure clear photographs can be taken



To ensure the key information will be clear in the photographs, set the scene with the following tips.

- Use a camera with at least 10 megapixels (most smartphones have this).
- Use a plain background and sufficient indirect lighting.
- Avoid reflections (e.g. disable the flash).
- Prevent blurry photos (e.g. auto focus, stable support and zoom if necessary).
- Include a graduated ruler next to the sample in frame (or another scale).
- Level camera close to and directly above the sample (no oblique views).

Photograph all sides of the packaging to capture key information

Depending on each product, packaging, shape, more than one photograph may be necessary. Take photographs of all sides of the packaging (front, back and sides) to capture the following information:

- product name
- active pharmaceutical ingredient(s)
- dosage strength and formulation
- batch number
- expiry and manufacturing dates
- name and address of manufacturer
- detailed views of key features, including any authentication marks (e.g. hologram, logo, barcode or CE mark).

Check that all information is fully captured

To ensure that all the information is captured, also photograph, if available:

- registration number
- all the different layers of packaging and the patient information leaflet
- market authorization holder name
- import/export licence numbers.

Example 1. Capture maximum information

For the sake of simplicity, different elements are captured in a single frame below; it is better to take multiple photographs with higher definition to capture all details.

1. Product name, manufacturer name, registration number, and dosage clearly displayed

   The example cannot show back of the box

2. Batch number and expiry-manufacturing dates in focus
3. Plain, non reflective background

© WHO

4. Batch number and dates displayed on blister to compare with carton
5. Additional photograph needed for detail side view
6. Dosage form and primary packaging clearly displayed
7. Graduated ruler for scale

Example 2. Ensure information is understandable

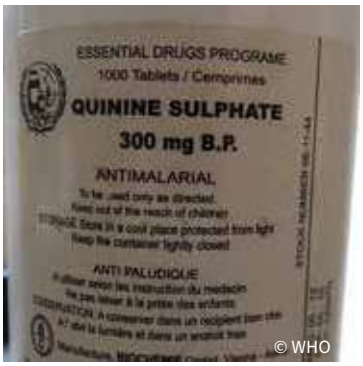
Importance of focus. The photograph below captures some of the key information (including batch number) but it is blurry, because the focus is on the foreground object.

© WHO

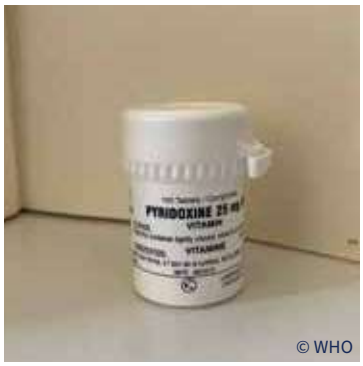
Clear labelling. The photograph underneath is not associated with a product or manufacturer name. The information is useless because some information is not visible.

© WHO

Importance of scale. The photographs below show how a product's size can be misleading if it is taken out of context or without indication of scale.



© WHO



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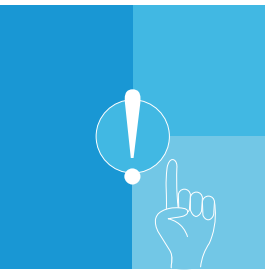
© WHO



5.1.4 SFMP incident management aide memoire

Table 34 outlines the steps that should be followed in managing SFMP incidents.

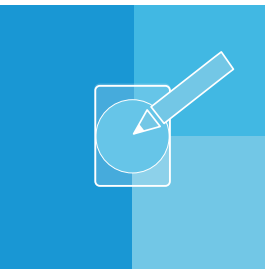
This table is available in a separate leaflet online and is predominantly for use by staff from national health regulatory authorities but can and should be adapted for use by other public health actors.

[Remember these incidents attract a lot of attention, unnecessary delays are difficult to explain, and public health and the reputation of your organization may be at risk.]

Table 34. SFMP incident management

Step	Action
1. SFMP incident is notified 	Identify and contact focal points within your organisation who have been trained to manage SFMP incidents. National health authorities must liaise with the WHO Global Surveillance and Monitoring System on SFMPs. Contact rapidalert@who.int in case of doubt
2. Establish facts 	It is essential to: • Contact the source of the information. • Assess the reliability of the source (see notes on next page). • Assess the credibility of the information received (see notes next page). • Document any available information and list outstanding questions (consider the "what, when, where, how, why" approach). • Obtain evidence (e.g. product samples and photographs).
3. Identify and assess risks 	The public health risk must be identified and assessed as soon as possible to determine the appropriate response and resources to be deployed. Please also consider the separate documents: *Prioritization and risk parameters,* and *Questions to consider when assessing risk*. Consult with the stated manufacturer of the reported product (see notes on next page).
4. Immediately protect public health 	Once risks are identified, public health must be protected by removing the source of the risk represented by the SFMP. This include the following immediate actions. • Quarantine or seize any suspected medical product dependent on risk. • Ensure the product is stored securely and in compliance with storage conditions. • Ensure appropriate treatment is available for affected patients.
5. Control quality 	The composition of the product may present additional risks to health. Use field screening devices or laboratory analysis to identify appropriate mitigation actions such as replacement treatements (see notes on next page).
6. Coordinate mitigation actions 	To efficiently respond to SFMP incidents, consider the following actions. • Establish a team of relevant regulatory specialists, appoint a lead person and invite relevant external stakeholders/experts. • Keep strict records of all meetings and all decisions that are made. • Focus on protection of public health, mitigating the risk posed by the product and investigating the origin. • Consider a recall of the medical product and issuing associated communications and media messages (e.g. alerts or public notices). • Verify stocks/availability of genuine (quality-assured) replacement product.

SFMP: substandard and falsified medical product; WHO: World Health Organization.



Notes health care professionals

Health and care providers are encouraged to identify national focal points who can conduct a search of the WHO Global Surveillance and Monitoring System database when dealing with a suspected SFMP at the earliest opportunity.

Irrespective of whether there is a match with other products in the database, the suspected or confirmed medical product should be reported to WHO as soon as possible. Other Member States may be seeing the same product in circulation and this report will assist them.

Remember that search results can match with your product on a separate continent or in another region. This information will help you assess risk, manage and respond to your incident more efficiently and effectively, and, in serious cases, save lives.

Assessing the reliability of a source

Anonymous information should be treated with caution and the following information should be ascertained.

- Is the source of the information a whistle blower or a current or ex-employee of a company they are reporting?
  - What is the motivation for supplying the information?
  - Is the source easily contactable?
  - If contact details are supplied, are they accurate (e.g. dialling codes, telephone numbers, email addresses and physical addresses)?
- Has information been received from the same source previously? If so, was it accurate?
- Is the source willing to be contacted and met, or to supply further information?

Assessing the credibility of the information

- Can the product registration number be verified through a national regulatory authority register?
- Has any similar information been received from different sources?
- Are there any other sources that can corroborate the information provided?
- Is there an approved package insert on the national regulatory authority/manufacturer website?
- Are there any obvious inaccuracies in the information?

Questions to manufacturers

- Did you manufacture this product? If yes, does the product and packaging look genuine? Photographs and samples should be provided if available.
- Are the manufacturing/batch/expiry dates authentic? If the batch number is genuine, where and when was it distributed?
- Have you had falsified or substandard versions of this batch reported previously? If so, when and where?
- Have you received any complaints about this batch? If so, from whom, where and when?
- Have you received any reports of unexpected adverse reactions relating to this product or batch? If so, when, where, how many and how severe?
- Is there any other information we should be aware of?

5.1.5 Prioritization and risk parameters

This section is available as a separate leaflet online and must be used in conjunction with the leaflet entitled Questions to consider when assessing risk (section 5.1.6 of the trainer's toolkit)

The parameters given are only suggestions that may be used to:

- assess the level of different risk types, and
- prioritize resources to deploy appropriate mitigation and control measures.

The information given in this section can be adapted to different contexts of conducting risk assessment of an incident of SFMP, taking into account factors such as response capacity, socioeconomic environment and reliance opportunities.

Note. This document does not cover medical devices, including in vitro diagnostics.

Risk assessment and management of SFMP incidents

The goal of risk assessment is to identify and prioritize actions that will mitigate the threat.[3] Risk assessment is a systematic process of gathering, assessing and documenting information to assign a level of risk (Table 35). It provides the basis for taking action to manage and reduce the negative consequences of SFMPs.

The risk management cycle includes the identification and prioritization of mitigation measures, taking into account the likelihood of success, the feasibility of implementation and unintended consequences. Resources are never unlimited and this applies to any organization. Resource management determines the quality of the SFMP incident response.

Multistakeholder engagement is always encouraged to establish all necessary facts. There may not be full confidence in the information available initially. In this case, further information should be sought, and the risk assessment repeated as appropriate. Risk assessment is a continuous (but not always sequential) process, and each new piece of information will help refine the assessment. Risk management also requires continuous monitoring and evaluation as the incident unfolds.

Handling SFMP incidents in a professional, consistent, timely and proportionate manner requires sound risk assessment and will reflect well on the organization(s) involved.

[3] Threat is the potential harm that can occur. Risk is the likelihood that the harm will be realized.

Table 35. Prioritization and risk parameters by type

Type of risk	Risk level	Criteria
Critical		
Public health	High	Fatalities or serious adverse reactions, or Immediate or likely threat of fatalities or serious adverse reactions, or Multiple numbers of persons affected (> 500, or depending on population size)
	Medium	Severe adverse reactions, or Threat of severe adverse reactions, or Multiple numbers of persons affected (> 100, or depending on population size)
	Low	Threat of severe adverse reactions, and Low numbers of persons affected (< 100 or depending on population size), or Isolated incident
Supply chain	High	Product already in the regulated/licensed supply chain, and Reached hospitals, clinics, pharmacies or patients, or Recall likely to lead to a considerable shortage
	Medium	Product available only through unlicensed and unregulated outlets
	Low	Product not thought to be available to the public
Geographic	High	Product available on an inter-regional or global basis, including unregulated websites
	Medium	Product restricted to one region
	Low	Product restricted to a small area
Environmental	High	Serious or immediate risk to the environment
	Medium	Potential risks to the environment
	Low	No environmental risks identified
Associated		
Public interest	High	Widespread and escalating international media interest, or Patient group or other major stakeholder interest, or Risk of serious reputational damage to public authorities or organizations
	Medium	Regional or national media interest, or Subject of complaints to/from stakeholders
	Low	No significant public interest
Political	High	Subject of significant national government interest
	Medium	Affecting or likely to affect, change or undermine policy
	Low	Non-contentious issue
Economic	High	Major financial gain or serious loss > US$ 1 million (or depending on socioeconomic environment)
	Medium	Financial gain or loss < US$ 1 million (or depending on socioeconomic environment)
	Low	No significant gain or loss
Legal	High	Organization(s) exposed to litigation or other legal challenges
	Medium	Weakness exposed in the regulatory or legislative systems
	Low	No perceived legal risks
Historical		
Product history	High	Same batch/lot of product previously notified
	Medium	Same product previously notified
	Low	No previous reports
Supply-chain elements	High	Same importer, exporter, broker, wholesaler, distributor or retailer
	Medium	Similar method or pattern of transportation, concealment of products or payment
	Low	No previous reports

5.1.6 Questions to consider when assessing risk

This section is available as a separate leaflet online and must be used in conjunction with the leaflet entitled Prioritization and risk parameters (section 5.1.5 of the trainer's toolkit).

Critical risks

Public health risks

- Have there been any reports of health events associated with the reported/suspected SFMP, for example, suspected adverse reaction? What is the severity?
- How many people/patients have been affected or may be affected in the future?
- What is the profile of the population exposed to the risk (e.g. children, vulnerable populations and difficult-to-reach people)?
- Were all the adverse reactions reported from the same location/point of care/health care professional?
- Is it likely that the adverse reaction was caused by method of administration or use (e.g. injection device, self-administration or self-medication) instead of the therapeutic itself?

Supply-chain risks

- Is the reported/suspected SFMP in the regulated or illicit/unregulated supply chain? Was it properly registered and imported?
- At what point in the supply chain was the incident discovered (e.g. by the patient, pharmacy, hospital, wholesaler or manufacturer)?
- How many different batch numbers (and unique combinations of variable data) are involved?
- What volumes of product have been reported? How many doses/treatment regimens?
- Who supplied the reported/suspected SFMP, and who else may have received it (e.g. public/government procurement agency, NGOs or aid organizations and private sector)?
- What other products have been procured through the same supply route?
- How many production sites of the reported/suspected SFMP exist? What is their production capacity?
- Could the issue affect other products produced in the same sites?

Geographic risks

- Where was the incident discovered (e.g. border area, major transport hub or in transit)? Where else is the reported/suspected SFMP likely to be available?
- Is the reported/suspected SFMP available in a wide range of locations? In what quantities?
- Could the reported/suspected SFMP have been smuggled/stolen/in transit (i.e. a consignment such as a container temporarily in one port or location before reaching its final destination)?
- Are there packaging elements that suggest the reported/suspected SFMP may be widely available geographically (e.g. packaging in multiple languages or multiple registration numbers)?

Environmental risks

- Are there factors associated with the environment, health status, behaviours, social or cultural practices, health infrastructure and legal and policy frameworks that increase a population's vulnerability to the reported/suspected SFMP?
- Would the services of a specialized laboratory be required? Is there any risk of environmental contamination if the reported/suspected SFMP is disposed of inappropriately?

Associated risks

Public interest

- Would a recall cause panic/distrust/other significant reaction from the public (alert versus alarm)?
- Are the media likely to report on the incident? Is the subject material likely to generate media interest (e.g. involves children, high profile organizations, a relatable story or multiple sources)?
- Has the incident been reported by multiple independent sources (e.g. residents, news media and health care workers)?
- How likely is the situation to get out of control or cause significant alarm in terms of public communication? Is there an effective system for communication between incident managers and other stakeholders?
- Who supplied the reported/suspected SFMP (e.g. public/government procurement agency, NGO or aid organization)?

Political

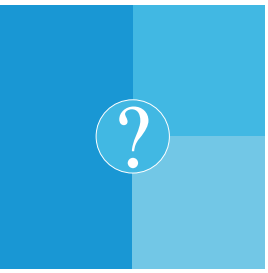
- Who reported/discovered the product in the first place? Could there be ulterior motives?
- Who has been involved in and informed of the incident at this stage? For example, are local authorities taking action; if so, what are the local political implications to be taken in account?
- Is the reported/suspected SFMP manufactured/distributed/procured by organizations or individuals who may have conflicts of interest?

Economic

- What is the volume/size of the seizure/discovery of the reported/suspected SFMP?
- Is the reported/suspected SFMP comparatively expensive? Will replacement by a good-quality and safe version have a substantial economic impact (and on whom)?
- Is the population who uses the product exposed to risk of financial hardship when procuring the product (economic vulnerability)?
- Would the response/mitigation/control measures have a substantial cost (e.g. recall, laboratory analyses and replacement therapies)?
- Are there many pharmaceutical production/distribution sites that are affected?

Legal

- Is there a legal framework that empowers/enables the implementation of mitigation/response/control measures, especially if immediate/urgent action is required?
- Is your organization at risk of litigation in relation to the reported/suspected SFMP? Could any such legal process hinder the implementation of mitigation measures?
- Does your organization have any legal obligations related to the quality and safety of the reported/suspected SFMP? Were there any quality management processes that could have been overlooked?
- Who is legally responsible for the manufacture/distribution/quality/authorization of the reported/suspected SFMP?



Historical risks

Previous history of product

- Is it likely that the same adverse reaction may have occurred before elsewhere and not be noted?
- Is there a previous similar record (e.g. finished product, active ingredient or therapeutic indication) in your own database, the WHO GSMS database, the database of another similar organization, or in the media/open-source intelligence?

Previous history of supply-chain element or stakeholder

- Has a similar incident been reported previously (e.g. with a similar presentation, affecting a similar population and geographical area, over the same time period)?
- Is there a previous similar record (e.g. manufacturer's name or importer's name) in your own database, the WHO GSMS database, the database of another organization, or in the media/open-source intelligence?
- Does the incident present a recurring pattern in the supply-chain distribution and/or operational method?
- Have there been any associated or previous events (e.g. product recalls or similar events in neighbouring countries)?

General questions to assess response capacity and impact

Mitigation/control measures to prioritize

- Can the treatment be continued with an alternative product?
- What type of product is affected? For example, is the product on an essential medicines list, is it a life-saving product? Is this product marketed/distributed/available abroad, either formally or informally? Can help be obtained from colleagues in other organizations to support resource planning and risk mitigation (e.g. analysing information, distributing alternative treatments)?
- Could there be any form of contamination in different batches/lots (e.g. pathogenic microorganisms or another active ingredient)? Is the issue at the level of finished product or active pharmaceutical ingredients?
- Is specialized and/or lengthy and/or costly laboratory testing required? Can WHO assist?

Consequences of response measures

- Can the same number of doses be easily replaced and/or alternative treatment be provided? What would be the impact of a recall?
- What is the availability and acceptability of effective preventive measures and treatment?
- Are there any access issues related to the reported/suspected SFMP (e.g. existing or projected shortage or likelihood of medication being shared between patients)?
- What is the market turnover and the shelf life of the reported/suspected SFMP?

5.2 Supplementary training resources

5.2.1 Glossary of terms

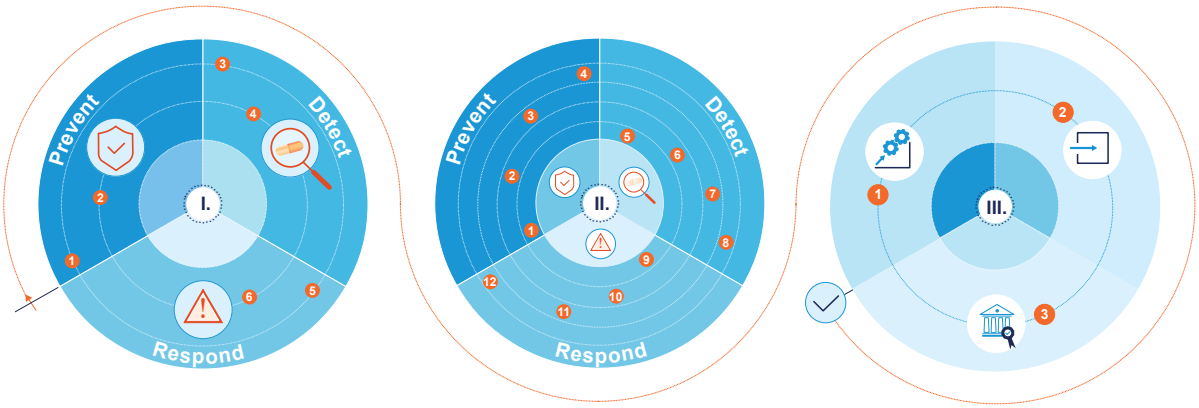
Term (acronym)	Definition
Adverse event	Any untoward medical occurrence in a clinical trial subject administered a pharmaceutical product; it does not necessarily have a causal relationship with the treatment.
Batch number	A defined quantity of starting material, packaging material or product, processed in a single process or series of processes, so that it is expected to be homogeneous. It may sometimes be necessary to divide a batch into a number of sub-batches, which are later brought together to form a final homogeneous batch. In continuous manufacture, the batch must correspond to a defined fraction of the production, characterized by its intended homogeneity. The batch size can be defined either as a fixed quantity or as the amount produced in a fixed time interval.
Benchmarking	A measurement or point of reference at the beginning of an activity which is used for comparison with subsequent measurements of the same variable.
Competency	Competency combines knowledge, skills and attitudes. Competencies describe how the work is to be carried out, while objectives indicate what must be accomplished. They also provide a sound basis for consistent and objective performance standards by creating a shared language for what is needed and expected by the organization.
Expiry date	The expiry date placed on the container of a product designates the date up to which (including) the product is expected to remain within specification, if stored correctly. It is established for every batch by adding the shelf-life period to the manufacturing date.
Global benchmarking tool (GBT)	A WHO developed tool and the primary means by which WHO assesses regulatory systems for the regulation of medical products. The tool and benchmarking methodology enable WHO and regulatory authorities to: identify areas of strength as well as areas for improvement; facilitate the formulation of an institutional development plan to build upon strengths and address identified gaps; aid in the prioritization of investments in the institutional development plan; and help monitor progress. The WHO GBT is the first truly global tool for benchmarking regulatory systems, unified from previous WHO tools.
Global Surveillance and Monitoring System (GSMS)	A comprehensive initiative by WHO aimed at preventing, detecting and responding to substandard and falsified medical products. GSMS plays a crucial role in enhancing the global response to substandard and falsified medical products by providing a robust framework for data collection, analysis, reporting and capacity-building. GSMS also provides key services to WHO Member States, including: data collection and analysis; reporting and communication; risk assessment and surveillance; capacity-building and training; technical assistance and support; and global collaboration and coordination.
Governance	Refers to the different ways that organizations, institutions, businesses and governments manage their affairs. Governance is the act of governing and thus involves the application of laws and regulations, but also of customs, ethical standards and norms. Good governance means that affairs are managed well, not that the laws, regulations or norms are themselves necessarily good.
Manufacturer	A company that carries out operations such as production, packaging, repackaging, labelling and relabelling of pharmaceuticals.

Term (acronym)	Definition
Market surveillance	The activities carried out and measures taken by public authorities to ensure that products comply with the requirements set out in legislation and do not endanger health, safety or any other aspect of public interest protection (based on European Union Council Directive EC No 756/2008 of 9 July 2008 concerning the requirements for accreditation and market surveillance relating to the marketing of products and repealing Regulation (EEC) No 339/93).
Medical product	Products including, but not limited to, finished pharmaceutical products, medical devices, vaccines and in vitro diagnostic products.
Member State Mechanism	This mechanism was established at the 2012 World Health Assembly to address substandard and falsified medical products in a transparent and inclusive way from a public health perspective and expressly excluding considerations of intellectual property rights. A World Health Assembly resolution was passed against a backdrop of increasing concern about such products and the health and socioeconomic harms they cause. WHO serves as the Secretariat of the Member State Mechanism. The mechanism aims to protect public health and promote access to affordable, safe, efficacious and quality medical products, and to promote through effective collaboration among Member States and the Secretariat, the prevention and control of substandard and falsified medical products and associated activities
Monograph	In the context of WHO, monographs provide detailed information on specific medicinal substances or products, including their properties, uses, dosage forms, quality standards and safety information. Monographs serve as authoritative references for health care professionals, manufacturers, researchers and regulatory authorities to ensure the quality, safety and efficacy of medicines.
National medicines regulatory agency (NMRA)	The NMRA is responsible for the registration of and other regulatory activities concerning medical products, such as medicines, vaccines, blood products and medical devices.
National regulatory system (NRS)	The NRS provides the framework that supports WHO. The system is composed of entities responsible for the registration, marketing authorization and other regulatory functions concerning medical products. The number of regulatory entities responsible for different regulatory functions may vary from one country to another.
Packaging	Packaging relates to all operations, including filling and labelling, that a bulk product has to undergo in order to become a finished product. Sterile filling would not normally be regarded as part of packaging, the bulk product being the filled, but not the finally packaged, primary container.
Pharmaceutical product	Any product intended for human use, or a veterinary product intended for administration to food-producing animals, presented in its finished dosage form, which is subject to control by pharmaceutical legislation in either the exporting or the importing state. This includes: products for which a prescription is required; products that may be sold to patients without a prescription; biologicals; and vaccines. It does not include medical devices.

Term (acronym)	Definition
Pharmacopoeia	A pharmacopoeia is an official publication containing a list of medicinal products with their effects and directions for use. The main objective of a pharmacopeia is to protect public health by creating and making available public standards to help ensure the quality of medicines. Pharmacopoeia standards support regulatory authorities in controlling the quality of pharmaceutical substances, their finished pharmaceutical products and related materials. It provides a tool with which the user or procurer can make an independent judgement regarding quality, thus safeguarding the health of the public.
Process	A set of interrelated or interacting activities that use inputs to deliver an intended result. In the context of NRAs [national regulatory authorities], the production and service provision processes should coincide with basic regulatory functions.
Quality control	Quality control relates to all measures to ensure that specifications, sampling, testing and analytical clearance of raw materials, intermediates, packaging materials and finished pharmaceutical products conform with established specifications for identity, strength, purity and other characteristics.
Rapid alert	An urgent notification submitted by an NRA [national regulatory authority] participating in the rapid alert system on measures taken against a product placed on the market that poses a risk to consumer health and/or safety.
Recall	A process for withdrawing or removing a pharmaceutical product from the distribution chain because of defects in the material or complaints of a serious nature. The recall might be initiated by the manufacturer/importer/distributor or a responsible agency.
Regulation	A written instrument containing rules having the force of law.
Regulatory authority	A government body or other entity that exercises a legal right to control the use or sale of medical products within its jurisdiction, and that may take enforcement action to ensure that the products marketed within its jurisdiction comply with legal requirements.
Regulatory framework	The collection of laws, regulations, guidelines and other regulatory instruments through which a government controls the manufacture, clinical evaluation, marketing, promotion and post-marketing safety benchmarking of medical products.
Stakeholder	Any individual, group or organization that can affect, be affected by, or perceives itself to be affected by a risk. Primary stakeholders are the patient, health care professional, medicines regulatory authorities and the pharmaceutical industry.
Substandard and falsified (medical products)	A substandard medical product is an authorized product that fails to meet either its quality standards or its specifications, or both. A falsified medical product is one that deliberately and fraudulently misrepresents its identity, composition or source.

WHO: World Health Organization.

5.2.2 WHO prevent–detect–respond strategy to combat SFMPs



I. Objectives

Prevent
1. Demand quality
2. Secure supply

Detect
3. Improve detection
4. Increase reporting

Respond
5. Protect public health
6. Prevent recurrence

II. Actions

Prevent
1. Supply chain integrity
2. Education and awareness
3. Multi-stakeholder engagement
4. Comprehensive legal framework

Detect
5. Border control
6. Reporting system
7. Risk-based inspection and surveillance
8. Access to laboratories and screening technologies

Respond
9. Alerts and recalls
10. Regulatory strenghtening
11. Transparent legal process
12. Evidence-based policy and procedure

III. Impact

Safety and quality
1. Increased technical capacity
2. Improved access
3. Strengthened governance

Prevent

Supply chain integrity

A track and trace system with an authentication process has been implemented for medical products.

The supply chain has been mapped from point of manufacture or importation through to public outlets, pinch points identified and staff trained to identify, report and respond to suspected substandard and falsified medical products.

Education and awareness

There are focused education, media and awareness programmes, for non-health professionals, the general public and civil society groups on substandard and falsified medical products.

The issue of substandard and falsified medical products is integrated as part of the core medical, pharmacy and regulatory curriculum.

Multistakeholder engagement

There is clear and regular communication with civil society groups, health care professional organizations, the pharmaceutical industry and actors within the supply chain, specifically focusing on substandard and falsified medical products.

There are documented and implemented procedures for regular engagement with the relevant government departments and agencies, including national pharmacovigilance centres, national poison centres and national quality control laboratories.

Comprehensive legal framework

There are legal provisions in place enabling the national medicines regulatory authority (NMRA) to seize, quarantine, sample, analyse, recall and destroy substandard and falsified medical products.

There are legal provisions in place for the inspection, investigation, enforcement and proportionate sanctioning of those engaged in the manufacture, distribution, storage, supply and sale of substandard and falsified medical products.

There is a documented strategy and guidelines in place and implemented relating to the prevention, detection and response to substandard and falsified medical products.

Detect

Border control	There are designated ports for the importation and export of medical products, and a regulatory presence at those ports. There are documented and implemented procedures for allowing the exchange of information concerning suspected substandard and falsified medical products between customs, police and the regulatory agency.
Reporting systems	Effective public reporting systems exist, enabling the reporting of suspected substandard and falsified medical products and adverse drug reactions to the NMRA.
Risk-based inspection chains and surveillance	A risk-based strategy is documented and implemented for conducting regular targeted and random market surveillance for substandard and falsified medical products within the regulated and unregulated supply There is a documented and implemented risk-based inspection programme for those entities engaged in the manufacture (including relabelling/repackaging), importation, distribution/wholesale and supply/sale of medical products.
Access to laboratories and screening technologies	There is access to an externally accredited national quality control laboratory and documented procedures are in place and implemented regarding the analysis and reporting of substandard and falsified medical products. There is access to field screening equipment (and relevant reference material), which staff have been trained to use, and procedures are documented and implemented for the use of such equipment.

Respond

Alerts and recalls	A documented and implemented procedure exists concerning the issuing, receipt and response to Rapid Alerts concerning substandard and falsified medical products. A designated and trained focal points) within the NMRA has been established to receive and respond to reports of suspected substandard and falsified medical products and has access to the WHO Global Surveillance and Monitoring System for substandard and falsified medical products.
Regulatory strengthening	Regulatory personnel are designated and trained in the response to substandard and falsified medical products and documented procedures have been established and implemented. The prevention, detection and response to substandard and falsified medical products has been embedded in core regulatory responsibilities across departments and government agencies and is included in regulatory assessment indicators.
Transparent legal process	The use of regulatory or criminal law sanctions is justified and applied in a consistent and proportionate way. The application and use of sanctions is published by the national or regional regulatory authority.
Evidence-based policy and procedure	Each incident involving substandard and falsified medical products has been reviewed with a view to identifying weaknesses in the system, vulnerabilities in the supply chain and making appropriate changes to improve the safety of patients. There is clear use of data from a wide range of sources in developing evidence-based policy and procedures to prevent, detect and respond to substandard and falsified medical products.

Source: WHO, 2017 *(1)*.

5.2.3 Exercises and case studies

This section provides six exercises and case studies. These are linked to the modules of the curriculum guide, along with learning points that align with the competency framework. Trainers may adopt and adapt these exercises based on the objectives of learners, as well as local context and resources. Additional exercises and case studies will continue to be developed and made available by WHO through the online portal for this toolkit, where trainers will also be invited to share their exercises.

The exercises and case study are:

- 1: understanding risk analysis of SFMPs
- 2: undertaking good procurement, storage and distribution practices
- 3: understanding visual inspection of medical products
- 4: completing the reporting form and SFMP report
- 5: counselling patients affected by SFMPs
- 6: case study of SFMPs based on a real WHO Medical Product Alert.

Exercise 1. Risk analysis of SFMPs

1. Identify and analyse the products most at risk of being substandard or falsified in your country.
   (a) How could you identify products that are likely to be substandard or falsified?
   (b) What information sources are available to you to identify substandard or falsified medical products?
   (c) What are the characteristics of the medical products at risk?

Deliver a short presentation to the group listing the medical products you consider to be most at risk of being substandard or falsified. Describe the steps you took to identify these at-risk products (including the information sources you used) and list what their characteristics are.

1a. How could you identify products that are likely to be substandard or falsified?

Consider the risks that lead to the production of SFMPs and undertake a desktop analysis of the information sources.

Shortage of medicines provides incentives to buy from unregulated suppliers. Both patients and physicians may respond to these shortages by looking outside the regulated supply chain to secure the medicines they need.

Unmet demand for medical products with high perceived quality can create incentives to buy from unregulated suppliers. Marketing and prescribing practices that create unmet demand for higher-margin products usually raise costs to patients. Patients who want, but cannot afford, a premium product that is not covered by their insurance may look outside the regulated supply chain and source the product online or in informal markets.

In an attempt to protect profit margins, commercial strategies combine to create unmet needs and demand, and to drive people to sellers outside the regulated supply chain. This creates a niche in the market for criminals who wish to sell falsified products.

Factors that contribute to the proliferation of SFMPs include both the unintentional and deliberate neglect of GMP. This stimulates the circulation of substandard products, while falsification has its roots in crime and corruption. Both types of products circulate because of the unpredictable supply and constant demand for medicines and insufficiencies in the regulatory system. This illegal operation thrives in places where regulation is weak, technical capacity is lacking and the risk of detection is low. A poor understanding of the issue among health professionals and the public contributes to the problem.

SFMPs are most likely to be circulating in supply chains when:

- access to affordable, good-quality, safe and effective medicines is limited;
- standards of governance are low, ranging from a lack of ethical practices in health care and medicine outlets to corruption in both the public and private sectors; and
- the tools and technical capacity to ensure good practices in manufacturing, quality control and distribution are limited.

A high proportion of cases of SFMPs so far reported to WHO occur where these problems overlap.

- Constrained access to affordable, safe and good-quality medical products
  - affordability
  - availability
  - acceptability

- Lack of good governance
  - overstretched regulatory frameworks
  - absence of transparency and accountability
- Weak technical capacity and tools
  - not following standard procedures: the first step to quality products

1b. What information sources are available to you to identify substandard or falsified medical products?

Identify and refer learners to select material from the list of technical resources (section 5) and bibliography references (section 5.3) of this toolkit.

1c. What are the characteristics of the medical products at risk?

Substandard production and falsification affect all types of medical products. Common classes of SFMPs include antimalarials, antibiotics, vaccines, HIV treatments, medicines affecting the central nervous system, cardiovascular medicines, and medicines for diabetes and cancer.

In developed countries, mostly life-style medicines such as slimming pills, treatment for impotence, hormones or steroids can be substandard or falsified. In developing countries, however, life-saving medicines such as antibiotics and antimalarials are more likely to be substandard or falsified. Life-saving medicines are now the fastest growing category of falsified medicines. Additionally, medical devices such as contact lenses, condoms, syringes, surgical instruments and wheelchairs are also affected.

SFMPs can be both prescription and over-the-counter medicines; moreover, they can also be proprietary or generic. Both expensive and inexpensive medical products can be substandard or falsified. In addition, much prescribed and in-demand medicines, products used off-label and parenteral products (in developing countries) are prone to being falsified. Medical products that are in short supply are also candidates for falsification.

The importance of WHO Medical Product Alerts should be stressed, and examples of alerts provided.

Conclusions. Why is risk analysis of SFMPs important?

Gathering as much information about SFMPs as possible is important to validate the information. An analysis should seek to identify the medical products most at risk, vulnerabilities in supply chains and weaknesses in capacity and health systems.

Data analysis equips policy-makers and regulators with detailed information on emerging trends, thus better informing post-market surveillance and allowing more focused investment for capacity-building and regulatory strengthening.

A system of risk analysis facilitates a more accurate assessment of the scope and scale of SFMPs and the socioeconomic harm they cause and contributes to combating these products.

Exercise 2. Procuring medicine and ensuring compound safety

Exercise 2.1 Identify and describe safety issues related to the supply chain of medical products

(a) List the main safety issues related to the pharmaceutical supply chain when SFMP become part of it.

(b) Describe the challenges in securing a safe pharmaceutical supply chain.

(c) Discuss how these challenges can be overcome and how SFMPs can be prevented from entering the supply chain.

Illustrate and present the above in the form of a diagram/picture/infographic that includes steps in the supply chain.

1a. Main safety issues related to the pharmaceutical supply chain

These issues include:

- infiltration of SFMPs
- adverse reactions of patients to the medicines
- increased number due to greater complexities of supply-chain operations
- manufacturing, such as mixing incorrect raw materials, cross-contamination due to manufacturing more than one product in the same facility or improper labelling of the final product
- retailer, including improper temperature controls and handling
- transportation, caused by mishandling, improper temperature controls and the use of improper shipping modes
- storing and warehousing, such as using improper temperature controls, incorrect handling in the warehouse and mixing products with raw materials
- raw material supplier, such as improperly prepared raw material, raw material with high impurity levels and mislabelling of raw material shipments.

1b. Challenges in the pharmaceutical supply chain

The key stakeholders in the supply chain include multiple government agencies, hospitals, clinics, pharmaceutical manufacturers and distributors, pharmacies, research organizations and national regulatory authorities. Many other organizations (e.g. insurance companies) may increase the complexity further. Many pharmaceutical supply chains have grown in an uncontrolled fashion.

Challenges in the pharmaceutical supply chain include:

- order management
- warehouse management
- avoidance of shortages
- lack of coordination
- inventory management
- absence of information on demand
- constraints in health workforce capacity
- expiry of medicines
- temperature control
- shipment visibility.

1c. Preventing SFMP from entering the supply chain

Three steps should be followed to properly qualify suppliers and protect the supply chain (Fig. 6).

Fig. 6. Steps for preventing substandard and falsified medical products from entering the supply chain

Step 1

The first step is to verify that supplies of medicinal products only come from legitimate businesses that have a wholesale distribution authorization, or that have a manufacturing authorization which covers the product in question.

Copies of licences can be requested from suppliers. In addition, details of a licence of a supplier can usually be seen on the website of the national regulatory authority. It is important that these registers are updated regularly, although they must not be relied on as the sole means of confirming suppliers' authority to supply. A practical way to prove legitimacy of suppliers is to obtain a printed copy of the appropriate pages of licences and certificates, signed and dated, as confirmation that the checks were made, when they were made and by whom.

For supplies obtained from wholesalers and manufacturers based in other countries, the same checks should be made on relevant websites and via licences that have been translated and authenticated by a notary. Some countries also have their own registers and these can also be referenced to support qualification.

Step 2

The second step requires that wholesalers confirm that they comply with good distribution practices. To ascertain compliance with GSDP, the GSDP certificate of the wholesaler should be viewed on the relevant website. The certificate should have a valid date and the certificate expiry should be recorded.

Check conditions attached to GSDP certificates for new applicants and companies where the inspection indicated a more frequent inspection schedule was required and limiting certificate expiry to a specified period.

If there is no GSDP certificate available, then other evidence of GSDP compliance by the wholesalers should be obtained, such as a copy of their latest inspection completion letter confirming GSDP compliance.

Step 3

The third step is the timely rechecking of the information obtained and due diligence.

Wholesalers must be aware of issues that could affect their suppliers' continued authorization to supply. A procedure must be in place that ensures that there are regular documented checks of lists of suspended licence holders and appropriate websites for GMP and GSDP statements of non-compliance. A full revalidation of the information held on suppliers should be done at least annually.

When entering a new contract with new suppliers, the wholesale distributor should carry out due diligence checks to assess their suitability, competence and reliability. The following checks should be made.

- Check, for example, the financial status of the supplier, length of trading and credit history.
- Check audits of the supplier, or results of a visit.
- Identify where stock is coming from and if a new product is being offered.
- Check if the product is being offered in very large quantities or volumes, or if the price offered is much lower than usual.
- Check transparency of the supply chain.
- Check methods of transportation.

Due diligence checks should be implemented and documented when dealing with a company or transaction that is outside an established trading pattern.

Criminals actively look for weak points in the supply chain so they can profit. Criminals may illegally copy the licence and address details of a legitimate company but set up a fake website and bank account that is similar to the real operation. Typically, this fake company will offer some enticing stock and send information using genuine company details but from a different email account, possibly substituting ".com" for ".net", or from a closely related website name. The bank account information will be for the fake company. Caution is needed if the supplier advises that its bank details have changed.

Shortages of medical products should always be considered a warning sign. Health authorities and others should make regulators aware so that they can increase their alertness around those products, working with customs officials at ports and through surveillance of the supply chain.

Clear and regular communication is needed with civil society groups, health care professional organizations, the pharmaceutical industry and organizations within the supply chain, specifically focusing on SFMPs.

In addition, documented and implemented procedures are needed for regular engagement with the relevant government departments and agencies, including national pharmacovigilance centres, national poison centres and national quality control laboratories.

A track and trace system with an authentication process should be implemented for medical products. The supply chain should be mapped from point of manufacture or importation through to public outlets, pinch points identified, and staff trained to identify, report and respond to suspected SFMPs.

The following actions and issues should be considered.

- Conduct independent research into the company: review official sources of information, such as national records.
- Check details provided by an organization match online details.
- Call telephone numbers or test contact details.
- Validate bank details.
- Ensure internal training programmes include individuals/departments which may be approached outside your direct knowledge, such as finance, and equip staff with mechanisms to report changes to supplier or customer details about which you may not be aware.
- Ensure processes and assessments are in place to confidently establish the identity of a prospective supplier.
- Be aware that unexpected types, volumes and prices of products being offered and unusual availability can be a potential risk.

- Understand that risk management processes minimize the possibility of falsified medicines entering the supply chain.
- When requalifying suppliers, consider if any significant changes in directorship or ownership have occurred.
- Ensure staff and management can be confident that replies are only sent to approved and valid e-mail addresses.
- Promote sound information management, including awareness that integrating reporting mechanisms from goods in processes introduces deviations into the quality management system.
- Review new contact details.

Procurement in community settings

Procurement should provide a medicine which is of an appropriate quality, and which is safe to use at all stages of its lifetime, that is, prescribing, dispensing, preparation, administration and disposal. Capabilities of the supply chain should be assessed to ensure products are genuine, stored correctly and available when required.

Exercise 2.2 You are a pharmacist working in a community pharmacy. Describe the steps you would take to ensure that procurement practice is safe?

What documentation would be necessary?

The following are the steps of correct procurement.

1. **Need for a product.** During procurement, the organization should be able to determine the need for a product. Some industries have standards they use to help determine product specifications.

   In the pharmaceutical supply chain, medicines for procurement should be based on the national essential medicines list. The latest WHO Expert Committee on Selection and Use of Essential Medicines, and WHO Technical Report Series No. 895 on use of essential medicines *(33)* can also be consulted.

   In addition, a reliable system for quantification of needs is required to avoid wastage or scarcity. Most small countries usually base their requirements on past consumption. It is also possible to compare reports of consumption versus stock documentation to identify the medicines that are scarce.

2. **Source determination/vendor selection.** Procurement should be from suppliers registered, evaluated and qualified by the country's regulatory authorities. The standard specifications of the pharmaceutical products should be specified in the supplier contract with regard to quality, storage conditions and the type or method of delivery. It is advisable to have a limited range of suppliers to procure from to avoid infiltration of SFMPs.

   Ensure there is no conflict of interest, as open and fair competition attracts good suppliers. A lack of transparency might cause suppliers to disengage and withdraw from future tenders, which will reduce the numbers of bidders and the competition. Written procedures for all procurement actions should be established and followed. Additionally, the information about the tender process and the results should be made public as far as the law permits.

3. **Adequate price check and terms.** The buyer (e.g. wholesaler, hospital or pharmacy) will examine all relevant information to determine the best price and terms for the product. The aim is to provide good-quality products in the right quantities, at the lowest cost and when needed.

   After thoroughly evaluating the offers from suppliers, a special committee or tender board usually awards the tenders. It is important that a pharmacist or a person with technical and clinical knowledge of pharmaceutical products and their manufacture is a member of this board.

4. **Purchase order.** The purchase order is used to buy materials from a seller. It defines the price, specifications and terms and conditions of the product or service and any additional obligations. For medicines, information such as dosage form or strength is also important.
5. **Purchasing order delivery.** The purchase order must be delivered by fax, mail, courier or email or other electronic means. The recipient/provider of the medicines then acknowledges receipt of the order.
6. **Receipt and inspection of purchases.** After receiving the order of medical products, the buyer should compare the medicines with the supplier's receipt and the purchase order.
7. **Invoice approval and payment.** The supplier of the medical products should make a request for payment in writing, accompanied by an invoice describing the products delivered and services provided and the shipping documents. Payment should be made promptly. The agreement on payment procedure and conditions should be clearly stated in the contract and even in the bids from potential suppliers while procurement takes place.
8. **Record maintenance.** Proper records should be maintained, particularly for audit. These include purchase records to verify any tax information and purchase orders. The supplier's performance should be recorded as well, with emphasis on timely and correct delivery, quality of medicines and their shelf life after delivery. These records may guide future procurement and purchases as well.

It is important to monitor and store procurement documentation provided by suppliers or other parties to allow products (that may be SFMPs) to be tracked.

Procurement in hospital settings

Exercise 2.3 You are a pharmacist working in a hospital. What are the differences and similarities with safe procurement in a community pharmacy?

The operational steps are similar to the community settings. They also include strategic procurement that is more risk-based, taking account of, for example, local capacity and resources.

1. **Source determination/vendor selection.** It is necessary to determine where or from whom to obtain the product. The procurer (e.g. company, wholesaler or hospital) may have an approved vendor list. Procurement methods include tenders, competitive negotiations or direct procurement. Selection of reliable suppliers of good-quality medical products is essential. New suppliers should be alerted on product quality issues when procuring, in addition to existing suppliers.

   In hospital pharmacies, adopting pre-qualifying and post-qualifying systems for suppliers reduces the risk of infiltration of SFMP. Specification of storage conditions of medicines and their proposed quality standard should be known by suppliers during procurement.

   Pharmaceutical tendering involves different stakeholders and steps in the process are regulated by national authorities. This inevitably means adapting different PDR strategies to different countries (e.g. increasing the use of screening devices if access to quality control laboratories is limited). These processes are also guided by publications of other international organizations such as WHO and the Organisation for Economic Co-operation Development.

   The procurement process should be part of the hospital quality system. It should be assessed regularly, and quality improvement actions taken to improve the outcomes of clinical effectiveness, cost–effectiveness and patient safety. A judicious tendering procedure has the potential to achieve substantial cost savings depending on the purchasing power of the organization and the market diversity for the products involved. Negotiations driven mainly by costs may achieve short-term savings but there is a risk of medicines shortages and long-term price increases.

Manufacturing capacity may not meet potential need and if other suppliers drop out of the supply chain due to loss of tenders, this can cause weaknesses. Tendering should include impact assessment tools and continuous monitoring of supply-chain vulnerability and sustainability.

2. **Receipt of medicines.** The internal supply chain should also be robust and fit for purpose, that is, the arrangements ensure products are available for patients and are of the appropriate quality.

Discussion. You have received a delivery of commercial products in your hospital pharmacy consisting of sterile components. What do you need to check before accepting the product?

Sterile products contain active and inactive ingredients, intermediate containers (e.g. a syringe used to transfer a medicine from one container to another), final containers, closures and seals. When sterile products are delivered, they should be transferred to their manufacturer-designated storage environment as soon as possible. This is especially important for temperature- and humidity-sensitive products that may become unstable and even degraded within minutes to hours depending on the product, packaging and/or environmental conditions. Delivery documents should be reviewed at the receiving area to ensure that the sterile products have not been subjected to any delays during shipment which could result in exposure of the article to elevated temperatures or other undesirable conditions. Sterile products requiring specific handling or refrigerator temperature storage conditions should have documented evidence provided by suppliers to show that the specified temperature range has been maintained throughout transportation. Staff receiving sterile products should contact the product manufacturer to determine the significance of deviations from the specified temperature range during shipment.

When the products are received in the pharmacy, a standard operating procedure should specify the visual inspection of sterile products, and sterile ready-to-use containers and devices (e.g. syringes and needles). All items must be free from defects, within the manufacturer's expiry dating and appropriate for their intended use. Records should be maintained to explain the reason for deviation from specified storage conditions and the resulting action taken. Defective medical products should be promptly reported.

Exercise 3. Visual inspection of medical products

The trainer should go through the visual inspection checklist (section 5.1.1) and distribute it as a handout to pharmacy undergraduates.

All photographs in this exercise were taken by Professor Lutz Heide (University of Tübingen, Germany) and are used with permission of the author, as published in PLoS One *(34)*.

1) Which of the medicines photographed (A or B) is legitimate? Give reasons.

A **B**

Answer

Product A is falsified Clomid tablets. Note the misspelling “Citrate de clomifère” instead of “Citrate de clomifène”. Product B is falsified azithromycin tablets. The indicated manufacturer – IP Hamburg GmbH Germany – does not exist.

2) Which of the examples photographed (A or B) is likely to be genuine and which falsified?

A **B**

Answer

Product A is a genuine Maloxine. Product B is falsified (logo with incorrect colours, as well as lack of information about the product).

3) Which of the examples photographed (A or B) is likely to be genuine and which falsified?

A **B**

Answer

Box B is genuine (see hologram). Box A is fake (no hologram, no trade mark ®) and incorrect spelling.

4) Which of the tablets (A or B) is likely to be of concern and why?

A **B**

Answer

Tablets A are discoloured and degraded, and likely to be substandard.

Exercise 4. Completing the reporting form and report of SFMP

Instruct trainees to complete a reporting form based on the Arsumax example from Exercise 3.

The reporting form will depend on the one used by the relevant national authority.

National reporting is recommended in the first instance, but reports can also be made to WHO. For the purpose of this exercise, an adapted version of the WHO form used to report to the GSMS is presented in Table 36.

Table 36. Reporting form for SFMP

Reporting person	
Name	Organization
Type of organization	Country
Telephone number	Email
Discovery details	
Date discovered	Discovered by
Address or location where the suspect product was discovered (geographic)	Is the suspect product in distribution within your country?
Countries imported from	Is the suspect product available within the regulated or unregulated supply chain
If available within the supply chain, at what level?	Method of distribution to the public
If available via the internet, please record the website address.	
Suspect product details	
Suspect product name	Type of product
Is the suspect product registered in the reporting country	Registration, product or marketing authorization number shown on the suspect product
All active pharmaceutical ingredients in the product	
Main intended medical use	Other uses
Manufacturer	Dosage form
Container type	Dosage strength
Batch/lot number	Expiry date
Date of manufacture	Packaging language
Method of administration	Quantity discovered
Type of medical product	Are photographs of the suspect product available?

Product analysis	
Laboratory analysis undertaken	Type of laboratory analysis undertaken
Email address of laboratory	
Results of analysis — packaging	Results of analysis — dose
Impact on public health	
Have adverse reactions been reported?	Severity of adverse reactions
Symptoms	Estimated number of patients affected or at risk
Communication	
Has any public statement been made?	Date of public statement
Has any product been withdrawn or recalled?	Date of product recall

Exercise 5. Managing patients affected by an SFMP

Case study 1

JM is a 46-year-old male who has just arrived in your pharmacy seeking advice. He reports that 1 week ago he was injured in a construction site accident. An infection developed in one of his wounds and he was prescribed an antibiotic to treat it. Today in your pharmacy, JM admits that he did not get his antibiotic prescription dispensed at your pharmacy because he needed to save money while he is not able to work. Instead, he obtained the antibiotic from an online source that had the medicine he needed at a much cheaper price. Since receiving his internet-ordered medicine, he has been taking it as directed, but he now has generalized weakness, a fever and a rash.

Factors to consider

What medical issue(s) could JM be experiencing? It is possible JM is experiencing increased side-effects and/or a lack of efficacy in managing the infection in his wounds. It could be that there is an increase in the number of infections and the lack of effective treatment could signal the development of resistance due to the use of an SFMP.

What does the JM's medical history say about allergies? Could the patient's current condition be an allergic reaction?

What other information is needed to fully analyse the case? What additional questions need to be asked of the patient and other health care professionals?

What parts of the case are indicative of JM having potentially received an SFMP? He obtained the antibiotic medicine from an online source and at a much cheaper price than usual.

If JM has received an SFMP, what is the next step in treatment? He needs to be referred for reassessment of his wounds and an evaluation of the subsequent symptoms that may have resulted from receiving an SFMP.

What considerations in treatment are needed now that JM may have received an SFMP? Whether the current treatment will still be effective is questionable. He should have his wounds swabbed and sent for sensitivity testing.

Is resistance more of a concern now? Yes — if the SFMP (antibiotic) was inactive or subtherapeutic, resistance is likely. Once sensitivities of the infecting organisms to antibiotics are identified, the correct antibiotic can be selected. JM may require intravenous antibiotics.

What reporting and documentation procedures need to occur? There should be full documentation of events in the patient's health record. If possible, the suspected SFMP (antibiotic) should be sent for laboratory analysis. A report should be completed for the national medicines regulatory authority.

How can a situation like this be prevented in the future? Discuss the checklist in the World Health Professions Alliance's tool for visual inspections *(35)* with JM.

Case study 2

YW is a 24-year-old female who is returning to the HIV adherence clinic today for her 3-month HIV monitoring appointment. She has been stable on her medication and her viral load has been undetectable throughout the course of treatment. In accordance with the clinic's adherence policies, YW brought her medicines with her to the clinic to show that she has been taking them properly and consistently. On inspecting the medicines, you realize that there are some small differences in the markings on one of the antiretroviral products. After referencing a medicine standards resource, you confirm that the product is not genuine, and appears to be a sophisticated falsified product (i.e. able to deceive and/or bypass visual inspection).

Factors to consider

YM has been receiving a SFMP for up to 3 months, and it appears to still be effective at controlling her disease, so should it still be discontinued? The risks posed by the spurious medicines should be evaluated versus the cost–benefit of disrupting treatment. The health care professional will have to decide whether the risk of potentially harmful substances in the spurious medicine outweighs the risk posed by interrupting the patient's treatment regimen. This consideration is of particular concern in medical conditions where interruption of therapy is harmful.

What follow-up questions can you ask YM to find out more information about the SFMP?

- Where was the medicine obtained?
- How long have you been taking the medicine?
- When was the medicine purchased?
- Do you have any of the original packaging that the medicine came in?

As a pharmacist, should you report the discovery of the SFMP? Yes, to the national medicines regulatory authority.

This SFMP was used to treat HIV. What sort of dangers does a community face when medicines such as these are being used as therapy by chronically ill, contagious patients? There is a risk with subtherapeutic treatment that viral loads increase, and this makes it easier to pass on HIV with the result that infection rates may rise.

Exercise 6. Case study of an SFMP based on a real WHO Medical Product Alert

This exercise is based on the WHO Medical Product Alert No. 4/2015.

In December 2014, more than 1000 people in the same region suffered from a strange symptom: neck spasms. As a result, 30 children younger than 5 years died.

Question 1. To whom should the information be circulated? Who should be informed in such circumstances? What conduct should be adopted?

A clinical examination must be carried out systematically on all patients by the medical staff of health centres or hospitals. A summary of the diagnoses should be held by the pharmaceutical regulatory authority in order to provide an overview of the situation. Additionally, given the large number of patients, an epidemiological study needs to be done.

Following clinical investigations (lumbar punctures and laboratory analyses), meningitis was finally ruled out. Another diagnosis was proposed, that of mass poisoning.

Question 2. If a meningococcal epidemic has been ruled out, what investigations should be carried out and by whom?

- Epidemiological field survey: examination of patient data/registers; interviews with health care professionals, patients and their families; search for products, medicines and food consumed by patients.
- Pharmacovigilance investigation: examination, completion (if necessary) and analysis of the pharmacovigilance reports received.
- Clinical examination: collection of biological samples (urine and blood) for toxicological analysis to look for a toxic agent causing extrapyramidal reactions.
- Pharmaceutical inspection: collection of samples of medicinal products.

Question 3. What criteria should be used when taking medical product samples?

The following types of samples should be taken:

- medicines taken at patients' bedsides, ideally consumed by the patients themselves
- products used by a large number of patients suffering from the disease
- main medicines commonly self-medicated locally
- medicines collected from the places where patients usually buy them (pharmacies, public health centres, if possible, street vendors)
- new products in circulation in the region
- random sample.

These purchases/samples should be taken by inspectors (pharmaceutical inspectorate) as a matter of priority. Police support may be considered for obtaining samples from the informal market.

Question 4. What types of analysis should be carried out on medical product samples? Where should this be done?

The samples should be analysed by a prequalified accredited ISO/WHO laboratory (national quality control laboratory). If necessary, the samples can be sent to a subcontracted quality control laboratory if the capacity is not available nationally.

The active ingredients indicated on the packaging of the medicines sampled should be looked for and analysed. The presence of impurities and toxic substances should be checked and microbiological controls carried out. Several laboratory techniques (e.g. spectrophotometry, liquid chromatography and nuclear magnetic resonance) should be used to analyse the urine and product samples.

Medicines that were taken by those who fell sick included:

- paracetamol
- cough syrups
- malaria tablets
- diazepam tablets.

Two types of diazepam products were identified. Both products were tablets branded "AGOG" and were sold in bottles branded "Centaur Solina Diazepam" or in bottles branded "AGOG Diazepam".

The two analyses gave the following results.

- Biological and toxicological analysis of biological samples.
  - Haloperidol was detected in several urine samples (median urine concentration of 4 µg/L (range < 1–49 µg/L)).
- Chemical analysis.
  - The samples of the various products taken were clear except for tablets identified as diazepam tablets from the manufacturer AGOG.
  - In the diazepam from the manufacturer AGOG, diazepam was absent, no toxic substances were found and haloperidol was present.
  - The median haloperidol dose per tablet was 13.1 mg (range 9.5–19.9 mg).
  - No haloperidol was detected in the other product samples, which all contained the appropriate active pharmaceutical ingredients.

Diazepam tablets containing haloperidol

Question 5. What do these results mean?

- Epidemiological survey
  - Investigate the origin of the tablets. Trace back to where the tablets were taken. Check which patients were affected by these diazepam tablets?
  - Rule out any other cause.
  - Check the concentrations and adverse effects of haloperidol.
- Survey results
  - No other explanation was found to explain the clinical features observed.
  - The tablets marked AGOG were obtained from patients who had ingested them, and 30% of the samples came from three private pharmacies, 20% from two public health centres, 10% from the local hospital and 40% from street samples.
- Pharmaceutical analysis
  - 15 mg of haloperidol is 20 to 25 times the maximum recommended daily dose for a child weighing 5 kg.
  - The presence of this concentration of haloperidol in the tablets explains why the children died and why it was mainly children who were ill.

Question 6. Who are the key players in clarifying the origin of medicines?

- The national regulatory authority must coordinate the investigation into the origin of the medicines.
- It is the responsibility of the inspecting pharmacists to clarify the origin of the products in collaboration with the people who took the medicines. If the products are imported, collaboration with the customs authorities will be necessary, and the police may also be able to help with investigations.
- The public prosecutor must be informed, and if necessary, the investigation carried out under his supervision.
- The case should be presented and discussed at a meeting of the national coordination committee responsible for combating highly pathogenic avian influenza, to agree on a field investigation plan and define roles.
- It is also important to look for similar cases in other parts of the country.
- Authorities in neighbouring countries should also be contacted and informed to look for similar cases and possibly conduct joint investigations. The WHO global surveillance and monitoring database should be consulted to look for similar cases in other parts of the world.

Question 7. How would you clarify the origin of the medicines used and how they entered the supply chain?

AGOG is the name of a pharmaceutical company. Find out more about this company, its real existence, its location and the products it officially manufactures. Consult the register of pharmaceutical establishments approved in the country of origin and recipient country, the register of medicines approved in the country and the company's website (using a search engine).

- Outcome. There is an AGOG laboratory in India.
- Action:
  - Contact the pharmaceutical company concerned directly for information on the products and batches manufactured.
  - Contact and inform the local authorities of the company involved.
- Result. AGOG Pharma Ltd (Vasai, India) has stated that it does not manufacture diazepam but supplies haloperidol in blister packs labelled "AGOHAL, Haloperidol tablet BP 10 mg".

The diazepam tablets found with the brand name "AGOG" taken by the patients thus appear to be falsified products sold in bottles labelled "AGOG Diazepam".

The investigation must continue with customs to trace the route of these products across the borders.

- Find out about the supply chain used to transport these medicines, for example, retailers, wholesalers and resellers.
- Gather information from (hospital) pharmacists and patients on the source of the supply they used.
- Contact the intermediaries identified to check the origin of the products. The inspection may involve an on-site investigation.

Investigations revealed the origin of the medicines. They originated in Uganda: after examining the distributors used and other countries in the region, the same product distributor based in Kampala (Uganda) was identified as selling falsified AGOG products.

Question 8. What measures should be taken at this stage?

- Take action at the national level.
- Inform the WHO GSMS through the NRRA focal point.
- If the case has not been referred to a public prosecutor at a previous stage, forward the investigation file to the judicial authorities for prosecution on the grounds of, for example, endangering others and marketing medicines that have caused death, depending on the country's legislation (see MEDICRIME Convention).
- WHO to publish the case in its alert on medical products.

Question 9. Would it have been possible to detect these falsified diazepam tablets at the border? What import controls should have been put in place to detect them?

- Implement import permits, in accordance with the WHO GBT market control function of national regulatory authorities.
- Limit entry points for health products and consider all imports through other entry points as illegal, with controls at entry points (customs and inspection).
- Communicate risks to international stakeholders, including the role of customs, available tools (e.g. Asykuda databases) and relevant relationships (e.g. between NRRAs and customs).

Question 10. What international actions could be taken?

- Contact the Ugandan authorities.
- Share knowledge of this distributor with NRRAs in the East African Community.
- Request to inspect the distributor in Uganda or to carry out a joint inspection.
- Request to inspect the Indian manufacturers or search for information on this manufacturer in international databases, from WHO or national regulatory authority colleagues in India.

Question 11. What general advice on investigation and inspection can be drawn from this case?

- SFMPs are present in the legitimate supply chain.
- Multidisciplinary approaches are needed, including collaboration between disciplines and organizations in the investigations (e.g. pharmacovigilance, clinical, toxicology, laboratory, police and national regulatory authorities).
- A structured investigation plan is needed: complex cases cannot be solved by chance.
- Joint action alerts can be used to identify the spread of these products to other countries, thereby preventing further deaths.
- Visual inspection can provide valuable information.

This case highlights the importance of investigating atypical clinical effects and the need for a multidisciplinary approach. Meningitis was a reasonable working diagnosis in an isolated community by primary care workers unfamiliar with dystonia. Further investigation revealed that patients in this area frequently receive over-the-counter diazepam to treat a wide range of conditions for which diazepam should not have been used as part of rational prescribing. Joint action led to the publication of an international alert by WHO on the circulation of falsified diazepam.

5.2.4 WHO e-course on SFMPs

In 2023, WHO launched a self-paced and dynamic e-course on SFMPs, with three modules that included support documents, videos and simulation exercises. Initially designed for NRRAs, as well as WHO staff and focal points to its GSMS, access to the e-course has since been made available on request (See Fig. 7). Requests for access to the e-course should be sent to ilearn@ilearn.who.int

In spring 2025, the trainer's toolkit will also see the launch of a complementary website that will include more comprehensive training resources and a modular approach to developing customized training courses.

Fig. 7. Screenshot of the WHO e-course on SFMPs

5.2.5 Assessment questionnaire for learners

Learners are encouraged to complete a questionnaire at the end of the course to give their assessment of the training. A sample questionnaire is shown in Table 37.

Table 37. Sample end-of-course questionnaire for participants of the training to complete

No.	On a scale of 1–4 circle the best answer that indicates your level of agreement (circle only one).				
1	To what extent, before coming to the SFMP training and/or course, were you informed about its **purpose**?	**Not at all**		**Completely**	
		1	**2**	**3**	**4**
2	Was the SFMP training and/or course content **consistent** with the stated objectives?	**Not at all**		**Completely**	
		1	**2**	**3**	**4**
3	To what extent did the SFMP training and/or course meet your **expectations**?	**Not at all**		**Completely**	
		1	**2**	**3**	**4**
4	To what extent do you expect this SFMP training and/or course will **make a difference** in the way you do your job?	**Not at all**		**Big difference**	
		1	**2**	**3**	**4**
5	Overall, how would you rate the **usefulness** of this SFMP training and/or course?	**Not useful**		**Very useful**	
		1	**2**	**3**	**4**
6	To what extent did the SFMP training and/or course **provide** the following?	**Very poor**		**Excellent**	
	Applicable theoretical information	**1**	**2**	**3**	**4**
	Practical examples	**1**	**2**	**3**	**4**
	Time for discussion	**1**	**2**	**3**	**4**
	Appropriate exercises for learning the content	**1**	**2**	**3**	**4**
	Additional comments about these topics:				
7	Overall, how would you **rate** the following aspects of the training/course?	**Very poor**		**Excellent**	
	Organization of the training/course	**1**	**2**	**3**	**4**
	Organization of the training manual	**1**	**2**	**3**	**4**
	Training/workshop content in the manual	**1**	**2**	**3**	**4**
	Additional comments about these topics:				
8	**Circle the module letter (circle only one).** *(Module A – Background; Module B – Prevent; Module C. – Detect; Module D – Respond)*				
9	Which module (A, B, C or D) did you learn the most from based on the competencies?	**A**	**B**	**C**	**D**
10	Which module (A, B, C or D) did you find the least useful?	**A**	**B**	**C**	**D**
11	Rate the top three competencies that you felt you learned the most. *(For the full list of competencies, see Table 1 in Section 2 on the competency framework).*	1. 2. 3.			
12	Do you have any additional suggestions?				