Annex 5

Guidelines on import procedures for medical products

Background

This document is a revision of the 1996 publication:

- Guidelines on import procedures for pharmaceutical products. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations, thirty-fourth report. Geneva: World Health Organization; 1996: Annex 12 (WHO Technical Report Series, No. 863; http://apps.who.int/medicinedocs/documents/s21962en/s21962en.pdf).

1. Introduction

1.1 Public health considerations demand that medical products should not be treated in the same way as ordinary commodities. Their manufacture and subsequent handling within the distribution chain, both nationally and internationally, must conform to prescribed standards and be rigorously controlled. These precautions serve to assure that patients receive quality-assured medical products, and to prevent the infiltration of substandard and suspected falsified medical products into the supply system.

1.2 The availability of medical products is sometimes limited, owing to economic constraints, difficulty in meeting norms and standards in their production, and lack of resources in their supply chain. These conditions lead to market penetration by substandard and suspected falsified medicines, which poses hazards for public health and forces the diversion of public health resources from other uses. In light of this, investments towards strengthening strategies at the customs level are deemed crucial to ensure quality-assured medical products for patients (*1*, *2*).

1.3 The global economy of scale and scope that characterizes modern trade requires continuous improvement in border control. This includes a departure from the traditional reactive control system to a risk-based and proactive approach. A country's risk-based surveillance scheme should identify risks and define the controls that will protect patients from substandard, falsified and unregulated medical products. A risk-based approach can improve the cost–benefit ratio with existing or reduced resources, through more effective and efficient controls. These guiding principles were endorsed in 1994 by the World Health Assembly in resolution WHA47.17 as having global relevance (*3*).

1.4 Within the context of its revised medicines strategy adopted in 1986 by the Thirty-ninth World Health Assembly in resolution WHA39.27 (*4*), the World Health Organization (WHO) developed *National drug regulatory legislation: guiding principles for small drug regulatory authorities* (*5*), which established a regulatory approach in line with the resources available within a small national regulatory authority (NRA), and were intended to assure not only the quality, but also the safety and efficacy of medical products distributed under its aegis.

1.5 The principles emphasize the need for the effective use of the *WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce* (*6*, *7*). This constitutes a formal agreement between

participating Member States to provide information on any medical products under consideration for export, notably on its marketing authorization in the country of origin and whether or not the manufacturer complies with the *WHO good manufacturing practices for pharmaceutical products* (*8*).

1.6 To be fully effective, the WHO Certification Scheme needs to be complemented by administrative and other safeguards aimed at ensuring that imported products are in conformity with all particulars with the relevant marketing authorization, or for specific intended use, such as clinical trials, named patient programmes, emergencies or other means, as appropriate, within the importing country and that they remain secure within the distribution chain. Storage and transit facilities must provide protection against tampering and adverse conditions, and relevant controls must be applied at every stage of transportation (*9*, *10*).

1.7 Medical products containing substances controlled under international conventions have long been subjected to rigorous border control. Some of these controls, and particularly those designed to prevent the diversion and illicit interchange of products during transit, are relevant to all medical products and are therefore included in these guidelines. Only those medical products falling under the category of narcotic and psychotropic substances that are permitted by the relevant authorities shall be allowed to be imported as foreseen in the national and regional legislations and international treaties signed by the country.

2. Scope

2.1 These guidelines, which stem from the above considerations, were first developed in 1996 in consultation with NRAs, the pharmaceutical industry, the World Customs Organization and the United Nations International Drug Control Programme.[1] Following the recommendation of the 52nd Expert Committee on Specifications for Pharmaceutical Preparations (ECSPP), these guidelines were reviewed, adding critical and contemporary topics, such as: the e-commerce/internet-mediated distribution and the alert systems mechanism that should be in place between entry ports/ NRAs/WHO, in case of unregistered, unlicensed, substandard and falsified medical products. Lastly, the glossary was revised and cross-references were added to other established WHO guidance documents.

[1] Since 1997, this has been part of the United Nations Office for Drug Control and Crime.

2.2 These guidelines are directed to all parties involved in the importation of medical products, including NRAs, competent trade ministries, customs authorities, port authorities and importing agents.

2.3 They are intended to promote efficiency in applying relevant regulations, to simplify the checking and handling of medical products for import and, inter alia, to provide a basis for collaboration between the various interested parties.

2.4 They are applicable to medical products destined for use within the country of import and are intended to be adopted into prevailing national procedures and legal requirements.

3. Glossary

The definitions given below apply to the terms used in these guidelines. They may have different meanings in other contexts.

falsified medical products.[2] Medical products that deliberately or fraudulently misrepresent their identity, composition or source. Any consideration related to intellectual property rights does not fall within this definition. Such deliberate or fraudulent misrepresentation refers to any substitution, adulteration or reproduction of an authorized medical product or the manufacture of a medical product that is not an authorized product.

import authority. The national agency responsible for authorizing imports (e.g. the ministry or department of trade or of imports and exports).

importation. The act of bringing or causing any goods to be brought into a customs territory (national territory, excluding any free zone).

importer. An individual or company or similar legal entity importing or seeking to import a medical product. A "licensed" or "registered" importer is one who has been granted a licence for the purpose.

marketing authorization (product license, registration certificate). A legal document issued by the competent national regulatory authority that authorizes the marketing or free distribution of a medical product in the respective country after evaluation for safety, efficacy and quality. In terms of quality, it establishes, inter alia, the detailed composition and formulation of the medical product and the quality requirements for the product and its ingredients. It also includes details of packaging, labelling, storage conditions, shelf-life and approved conditions of use.

[2] This definition reflects the ongoing discussion in the Member State mechanism under the auspices of the World Health Assembly; see Appendix 3 in reference (*11*).

medical product. A term that includes medicines, vaccines, diagnostics and medical devices.

national regulatory authority. The national agency responsible for the marketing authorization of, and other regulatory activities concerning, medical products.

screening technologies. The qualitative and/or semi-quantitative technologies that could rapidly acquire the analytical information or data for preliminary identification of suspect medical products in the field.

standard operating procedure. An authorized written procedure giving instructions for performing standardized operations – both general and specific.

starting material. Any substance of defined quality used in the production of a medical product, but excluding packaging materials.

substandard product. An authorized product that fails to meet either its quality standards or its specifications, or both.[3]

unregistered product. A medical product that has not undergone evaluation and/or approval by the NRA for the market in which it is marketed/ distributed or used, subject to permitted conditions under national or regional regulation and legislation. This medical product may or may not have obtained the relevant authorization from the national/regional regulatory authority of its geographical origin.

4. Legal responsibilities

4.1 The importation of medical products should be done in accordance with national and regional legislation and should be enforced by the NRA, customs and other relevant authorities.

4.2 National and regional guidelines providing recommendations on the implementation of legislation should be drawn up by the NRA or the ministry of health, if a NRA is not formally established, in collaboration with the customs authority and other responsible agencies and organizations.

4.3 The import of medical products should be undertaken by an importer or agency authorized by the NRA as per national and regional legislation. This normally does not include medical products in transit.

[3] These standards and specifications are normally reviewed, assessed and approved by the applicable national or regional regulatory authority before the product is authorized for marketing (*11*).

4.4 The import of all medical products should be channelled exclusively through custom posts or ports specifically authorized for this purpose. This is also applicable to medical products moving through the networking global e-commerce (such as the World Wide Web/internet).

4.5 All formalities on importation of medical products should be coordinated by the relevant authorities (customs, border control, or other as appropriate), NRA and/or ministry of health, as relevant. When justified by the workload, NRA officials may be stationed in a full-time position at such designated ports of entry. In carrying out the duties and formalities, the impact of possible delays on, for example, access to medicines and storage conditions of medical products, should be considered (for storage facilities, please see Section 9).

5. Legal basis of control

5.1 Subject to the exemptions specified in the national and regional legislation, and mentioned in paragraph 5.5 below, only medical products approved by appropriate documentation to be duly registered or authorized, as appropriate for marketing, should be cleared by relevant authorities.

5.2 The NRA should publish an updated list of authorized medical products and authorized importers permitted to import into the country for marketing. This does not include a list of exempted products and importers as per national or regional legislation. In all cases, close collaboration with the NRA is needed to verify that the product is authorized for importation and that there are no restrictions, temporary suspensions or withdrawals of marketing authorizations.

5.3 NRAs should be empowered to take legal actions and should collaborate closely with customs, police, judiciary and others to detect substandard and falsified products and to avoid the import of such products. Efficient and confidential channels for communicating information on these products and other illicit activities should be established between all responsible official bodies.

5.4 In countries where no formal system of product marketing authorization has been established, the importation of products is most effectively controlled by issuing permits in the name of the NRA to the authorized importing agency or agent. Within the framework of the WHO Certification Scheme, WHO provides a list with names and full addresses of those government organizations authorized to sign and issue a certificate of a

medical product (CPP).[4] NRAs receiving a CPP can use this list to check and verify whether the certificate they are receiving has been issued by the authorized organization (*6*, *7*). Additional measures that may be taken under these conditions include:

- provision by the NRA to the customs authorities and to the importing agency and agents of official lists of medical products permitted and/or prohibited to be imported;
- provision by the importing agent of certified information to establish that the product is authorized by licence for sale in the country of export.

5.5 The NRA should reserve discretionary powers to waive product authorization requirements in respect of consignments of medical products imported in response to emergency situations, specific intended use as in clinical trials, donation (*13*) and in response to requests from clinicians for limited supplies of an unlicensed product needed for the treatment of a specific named patient.

6. Required documentation

6.1 As a prerequisite to border and customs clearance, the importing agency or agent should be required to furnish the customs authority with the required documentation in respect of each consignment, except in cases of exemptions as per national or regional legislation (see also paragraph 5.5). For example, the following documents can be considered:

- documents issued by the NRA in the importing country, attesting that:
  - the importer is duly authorized to import the medical products;
  - the product is duly authorized to be marketed or permitted to be imported into the importing country;
- a batch-release certificate issued by the manufacturer;
- a safety data sheet, where applicable;
- a relevant invoice, bill or delivery slip for the batch, including the product name, batch number, quantity and expiry date;

[4] Information on competent authorities of countries participating in the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce can be found in reference (12).

- any other documentation required by national or regional legislation for customs clearance, e.g. a certificate in accordance with the WHO Certification Scheme;
- any other document that should be issued by the competent authority of the exporting country, as applicable.

6.2 The NRA may grant exemptions to the above if the distribution is taking place through regional hubs or by international organizations.

7. Implementation of controls

7.1 Visual examination and preliminary screening technologies should be routinely undertaken by the customs authorities. Where possible, this should be done in collaboration with an inspector or enforcement officer of the NRA. The size of the consignment should be checked against invoices, bills or delivery slips, and attention should be given to the nature and conditions of the packaging and labelling. The external package should be compared with a standard when this is possible. (*Note*: spelling errors, low-quality printing and other defects may be signs of a substandard or falsified product. The external package should be intact and should not show any signs of damages or infiltrations that may change the inner content (*2*, *14–16*).)

7.2 Arrangements should be made by the NRA and other relevant authorities (i.e. national official control laboratories, ministry of health) for the sampling and subsequent physical and chemical analysis of medical products, based on established procedures following a risk-based approach.

7.3 When samples are taken for analysis to a governmental or other accredited quality control laboratory, prior to the release of the consignment as per national and regional legislation, the consignment should be placed in quarantine at approved sites. During this procedure, and throughout the time that the consignment is held legally under customs control, particular care must be taken to ensure that packages do not come into contact with potential contaminants. In addition, the package should be stored under appropriate conditions, as recommended on the label or in the safety data sheet, such as temperature, light and humidity limits (*14–16*).

7.4 A consignment suspected of being substandard, falsified or not authorized should be placed in quarantine pending the analysis of samples and forensic investigation. During this procedure, particular care must be

taken to ensure that packages do not come into contact with potential contaminants. In addition, the package should be stored under appropriate conditions as recommended on the label or in the safety data sheet, such as temperature, light, and humidity limits (*14–16*). Time is often saved if materials and reagents needed to undertake simple analytical tests and screening technologies are available at the customs border. The consignee should immediately be informed of such action; ideally, the authorized manufacturer or importer should also be promptly involved in the investigation.

7.5 National or regional regulations should define the responsibilities of the respective parties and the precise procedures to be followed by representatives from the NRA, police, border control, or ministry of health, as appropriate, for the relevant investigation and legal actions.

7.6 Falsified medical products and other products that have been imported in contravention of the law must be forfeited and destroyed, or otherwise dealt with in accordance with the procedures established by national and regional legislation, the records of which should be appropriately archived (*17*). The relevant authorities must be indemnified against any consequent legal actions and proceedings.

7.7 NRAs should notify other national or regional authorities and the WHO Global Surveillance and Monitoring System[5] of confirmed cases of imported substandard or falsified products, without delay, on the appropriate form.

7.8 The WHO Member State mechanism has prepared an overview on the different field screening devices, authentication and verification technologies, and "track and trace" models that can facilitate responses (*11*). Overt/covert technologies, forensic chemical markers, bar-coding and other forms of serializations can support the seamless tracking of products through the supply chain. The implementation of these and upcoming new technologies is considered one of the most prominent preventive measures to tackle substandard and falsified medical products.

[5] The WHO Global Surveillance and Monitoring System collects reports from focal points in the NRAs and international procurement agencies, which will forward the report via email to rapidalert@who.int where necessary. Focal points are encouraged to send any photographs, laboratory reports or other relevant documents as attachments. For further information, see reference (*18*).

8. Procedures applicable to pharmaceutical starting materials

8.1 When considering finished medical products, the responsibility for the quality assurance of starting materials (active pharmaceutical ingredients [APIs] and excipients) used in that product is vested in the manufacturer of the finished pharmaceutical product. Few NRAs have introduced authorization requirements for APIs and excipients (*10*).

8.2 Some national and regional authorities also exercise documentary and (in some cases) quality control through laboratory testing of APIs as a prerequisite to customs clearance.

8.3 Each imported pharmaceutical starting material should be accompanied by a warranty (or batch certificate) prepared by the manufacturer, for example, as recommended by the WHO pharmaceutical starting materials certification scheme (SMACS) (*19*).

8.4 Pharmaceutical starting materials purchased and imported from third-party vendors should be appropriately labelled in accordance with national regulations and accompanied by a certificate of analysis from the original manufacturer.

9. Storage facilities

9.1 Many medical products tend to degrade during storage and some need to be stored under specified conditions, such as 2–8 °C. All customs posts designated to handle consignments of medical products should be provided with secure storage facilities, with the required conditions including cold storage areas.

9.2 Customs and NRA officials should ensure that the appropriate environmental conditions are maintained for storage, and monitor that the equipment is maintained and in good working order. The facilities should be inspected periodically by the NRA.

9.3 The importer should inform the customs authorities in advance of the anticipated arrival of medical products, in order that they may be transferred from the international carrier to the designated storage facility without delay and, in appropriate cases, without breaking the cold chain.

9.4 Consignments of medical products and pharmaceutical starting materials, especially those requiring cold chain, should be accorded high priority for clearance through customs, to avoid extended storage.

10. Training requirements

10.1 When implementing these guidelines, the performance of the established procedures (including but not limited to personnel, documentation, procedures, and equipment) should be reviewed on an open-ended basis and improved in the light of on-site monitoring and evaluation. Workshops designed to facilitate efficient implementation of the guidelines and established procedures, and to foster collaborative approaches between the various responsible parties, should be organized by the NRA at intervals, in collaboration with the customs authority and other parties.

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