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Annex 9
Guidelines on packaging for pharmaceutical products

Introductory note

This review of the various elements of the packaging of a pharmaceutical product is aimed at ensuring that medicines arrive safely in the hands of the patients for whom they are prescribed.

In the manufacture of pharmaceutical products, quality assurance is defined as "the totality of the arrangements made with the object of ensuring that pharmaceutical products are of the quality required for their intended use" (*1*).

In addition, the system of quality assurance for the manufacture of pharmaceutical products should ensure that "arrangements are made for the manufacture, supply and use of the correct starting and packaging materials" (*1*).

Public opinion sometimes considers packaging to be superfluous. However, it must be emphasized that packaging preserves the stability and quality of medicinal products and protects them against all forms of spoilage and tampering.

All medicinal products need to be protected and "consequently need to be packaged in containers that conform to prescribed standards, particularly with respect to the exclusion of moisture and light and the prevention of leaching of extractable substances into the contents and of chemical interaction with the contents. . . . However, the limits of acceptability in these various respects depend, at least in part, on climatic variables. Recommendations in *The international pharmacopoeia* can only be advisory; precise quantitative standards will have to be locally determined" (*2*).

The complexity of packaging materials and the highly technological nature of medicinal products is such that manufacturers are confronted with significant problems. Interaction between packaging and such products is possible due to the combination of a multiplicity of container components and active pharmaceutical ingredients, excipients and solvents used in a variety of dosage forms.

The quality of the packaging of pharmaceutical products plays a very important role in the quality of such products. It must:

— protect against all adverse external influences that can alter the properties of the product, e.g. moisture, light, oxygen and temperature variations;
— protect against biological contamination;
— protect against physical damage;
— carry the correct information and identification of the product.

The kind of packaging and the materials used must be chosen in such a way that:

— the packaging itself does not have an adverse effect on the product (e.g. through chemical reactions, leaching of packaging materials or absorption);
— the product does not have an adverse effect on the packaging, changing its properties or affecting its protective function.

The resulting requirements must be met throughout the whole of the intended shelf-life of the product. Given the link between the quality of a pharmaceutical product and the quality of its packaging, pharmaceutical packaging materials and systems must be subject, in principle, to the same quality assurance requirements as pharmaceutical products.

The appropriate system of quality assurance for the manufacture of pharmaceutical products should therefore follow the WHO guidelines for good manufacturing practices (GMP) (*1*).

The requirements to be met by pharmaceutical packaging and packaging materials as described in compendia (pharmacopoeias) and standards (e.g. those of the International Organization for Standardization (ISO)) must be considered only as general in character. The suitability of packaging or packaging material for any particular requirements and conditions can only be ascertained through detailed packaging and stability studies on the product concerned.

Glossary

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

General

bulk product

Any product that has completed all the processing stages up to, but not including, final packaging (*1*).

containers

A container for pharmaceutical use is an article which holds or is intended to contain and protect a drug and is or may be in direct contact with it. The closure is a part of the container. The container and its closure must not interact physically or chemically with the substance within in any way that would alter its quality. The following terms include general requirements for the permeability of containers (*3*):

- *Well-closed containers* must protect the contents from extraneous matter or from loss of the substance under normal conditions of handling, shipment or storage.
- *Tightly closed containers* must protect the contents from extraneous matter, from loss of the substance, and from efflorescence, deliquescence or evaporation under normal conditions of handling, shipment or storage. If the container is intended to be opened on several occasions, it must be designed to be airtight after reclosure.
- *Hermetically closed containers* must protect the contents from extraneous matter and from loss of the substance, and be impervious to air or any other gas under normal conditions of handling, shipment or storage.

Substances and dosage forms requiring protection from light should be maintained in a *light-resistant container* that — either by reason of the inherent properties of the material of which it is composed, or because a special coating has been applied to it — shields the contents from the effects of light. Alternatively, the container may be placed inside a suitable light-resistant (opaque) covering and/or stored in a dark place (*3*).

labels

All finished drug products should be identified by labelling, as required by the national legislation, bearing at least the following information:

(a) the name of the drug product;

(b) a list of the active ingredients (if applicable, with the International Nonproprietary Names (INNs)), showing the amount of

each present, and a statement of the net contents, e.g. number of dosage units, mass or volume;

(c) the batch number assigned by the manufacturer;

(d) the expiry date in an uncoded form;

(e) any special storage conditions or handling precautions that may be necessary;

(f) the directions for use, and any warnings and precautions that may be necessary;

(g) the name and address of the manufacturer or the company or person responsible for placing the product on the market.

marketing authorization (product licence, registration certificate)
A legal document issued by the competent drug regulatory authority that establishes the detailed composition and formulation of the product and the pharmacopoeial or other recognized specifications of its ingredients and of the final product itself, and includes details of packaging, information given on the label, product information and shelf-life (*1*).

materials
A term used to denote starting materials, process aids, intermediates, active pharmaceutical ingredients, packaging and labelling materials.

packaging material
Any material, including printed material, employed in the packaging of a pharmaceutical product, excluding any outer packaging used for transportation or shipment. Primary packaging materials are those that are in direct contact with the product (*1*).

packaging process
All operations, including filling and labelling, that a bulk product has to undergo in order to become a finished product (*1*).

production
All operations involved in the preparation of a pharmaceutical product, from receipt of the starting materials, through processing and packaging, to completion of the finished product (*1*).

quarantine
The status of starting or packaging materials, intermediates, or bulk or finished products isolated physically or by other effective means while a decision is awaited on their release, rejection or reprocessing (*1*).

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