User's Guide for control of pharmaceutical products

Annex 1 & 2

Annex 1

Technical check-list for pharmaceutical products

1. **Regulatory status**

The supplier (distributor)

- It is authorized by the competent regulatory authorities
- It can show a valid (not expired) copy of this authorization

The distributor definitely needs to be able to show a copy of this authorization in his country of origin. Otherwise he will not be retained.

The manufacturer

- The manufacturer is known and its name is clearly mentioned on the packaging
- The manufacturer or supplier (if different from the manufacturer) can prove that the manufacturer - is approved of by the competent regulatory authorities
- The manufacturer or supplier can show a copy of a valid GMP certificate (WHO Model Certificate) for the concerned manufacturing site

If one of the above points is not fulfilled, the supplier (distributor or manufacturer) cannot be considered.

- The manufacturer or supplier (if different from the manufacturer) can prove that the manufacturing site has been approved by the inspectors of the Pre-qualification Project of the World Health Organization (WHO) or by the inspectors of PCS (Pharmaceutical Inspection Cooperation Scheme)

If this last point is fulfilled, this is considered to be an asset. However this is not a mandatory requisite.

The product

First of all, the regulatory status of the product must be verified. These are some of the possibilities:

- The medicine is registered in the country of origin, but NOT MARKETED (We ask for the registration number. and the date: …)
- The medicine is registered AND marketed in the country of origin (We ask for the registration number. and the date: …)
- The medicine is registered AND marketed in an ICH country (International Conference on Harmonization = EU + US + Japan) (We ask for the country, the registration number and the date: …)
- The drug is manufactured for export only (We ask for a copy of the export certificate)

The supplier (distributor) needs to have a recent/specific CPP (WHO Model Certificate of a Pharmaceutical Product) for the product he is proposing/selling, and he has to be able to show a copy on demand.

Specifications of the final product

There are two possibilities:

a. A monograph of this product exist in an accepted international Pharmacopoeia (British Pharmacopoeia or BP, United States Pharmacopoeia or USP, International Pharmacopoeia)

- The proposed product complies with the specifications of the monograph one of these reference pharmacopoeias (specify the Pharmacopoeia and which edition).
- On the assumption that the product is in accordance with the specifications of the monograph of another pharmacopoeia (e.g. Indian, Chinese, Russian, …), please specify which Pharmacopoeia and which edition.
- On the assumption that the *in house* specifications have been developed, the analytic method has to be communicated to us upon demand.

b. A monograph of this product does not presently exist in accepted international Pharmacopoeia (BP, USP, International)

- On the assumption that the product is in accordance with the specifications of another pharmacopoeia (e.g. Indian, Chinese, Russian, …), please specify which Pharmacopoeia and which edition.
- On the assumption that the *in house* specifications have been developed, the *in house* specifications and the analytic method have to be communicated to us upon demand.
- Can the supplier prove that the *in house* specifications have been accepted by the competent national authorities?

A certificate of analysis needs to be provided for every sold batch.
The analysis has to be made by:

- ○ the manufacturer
- ○ an independent accredited laboratory

2. Stability

- The manufacturer (or distributor, if different from the manufacturer) has a report of stability studies performed in compliance with the recommendations of the WHO.
  In the absence of a stability study, the product cannot be purchased. The impossibility of providing a written report has to be justified.

- The product has been tested under climatic conditions of Type IV.
  This test is advisable, but it is not a mandatory requisite.
- A summary report of the stability studies has to be communicated upon demand.
- The expiry date has to be consistent with the result of the stability studies.
- The proposed/sold product has to be identical (active ingredients, packaging, size of batch) with those used for the stability studies.

3. **Labels/packaging**

Basic rules:
* The primary and secondary packaging must ensure the preservation of the medicine until the expiry date declared by the manufacturer.
* The labeling has to be clear and has to guarantee a safe usage of the medicine.

The manufacturer (or distributor, if different from the manufacturer) has to communicate upon demand the accurate technical information on the proposed packaging (materials, specifications).
The primary packaging has to be labeled or printed in indelible ink. The following information has to be clearly indicated:

- International Non-proprietary Name (INN)
- The batch number
- The expiry date in explicit form (no coded)
- The administration route
- The name of the manufacturer and the country of manufacturing

The secondary packaging has to be labeled or printed in indelible ink.

- The labels or printing have to be preferably written in French/English/ Spanish and, in any cases, they have to be written in a language which is clearly understandable for the health personnel who will have to use it.
- Self-adherent labels are preferred
- Paper labels have to be attached in such a way that they won't detach in warm and humid climatic conditions
- At least the following information has to be on the labels or printing:
  - → The International Non-proprietary Name (INN)
  - → The complete list of the active pharmaceutical ingredients and the precise amount of each, by the respective dosage unit
  - → The manufacturer's name and address
  - → The name and the country of location of the license holder (if different from the manufacturer)
  - → The registration number of the product in the country of origin (when applicable)
  - → Any special storage conditions or handling precautions that may be necessary, preferably in English, French and Spanish
  - → The instructions for use, and any warnings or precautions that may be necessary, preferably in English, French and Spanish.
  - → The batch number assigned by the manufacturer
  - → The manufacturing in a clearly understandable form (month/year; coded forms are not acceptable)
  - → The expiry date in a clearly understandable form (month/year; coded forms are not acceptable)
  - → The information given in the labelling or printed on the packaging, must comply with the recommendations of the WHO
  - → The storage conditions and the expiry date given in the labelling or printed on the packaging, should be consistent with the results of the stability studies, performed by the manufacturer in accordance with the WHO recommendations.

4. Active pharmaceutical ingredients (APIs)

- The name of the manufacturer of every API has to be known by the supplier and has to be communicated on demand, by the manufacturer or distributor.
- The manufacturer(s) of the **APIs** has/have to be authorized in their country of origin. A copy of their authorization has to be shown on demand.
- The supplier has to make sure that the **APIs** comply with the specifications of at least one of the following pharmacopeia: European Pharmacopoeia (EP), British Pharmacopoeia (BP), United States Pharmacopoeia (USP) or International Pharmacopoeia of WHO
- In case the API isn't described in one the Pharmacopeias mentioned here above, the *in house* analytic methods must have been evaluated and approved of by the manufacturer.
- A copy of the Certificate of Analysis (CoA) of each **API** has to be shown on demand.

5. Therapeutic equivalence

The therapeutic equivalence:

- ○ Has been demonstrated *in vivo*
- ○ Has been demonstrated *in vitro*
- ○ Does not need to be demonstrated for this product (justify why)
- ○ Has not been demonstrated

6. Commitment

The manufacturer and/or distributor must commit himself on his word of honor to guarantee that all the communicated information is genuine and accurate.

Annex 2

In vitro diagnostic medical devices

For the products that do not meet the criteria previously mentioned in this Charter (not qualified or pre-qualified by the WHO, not qualified by the ISBT, not authorized in a high-regulated country, not included in the Annex II A and B of the Directives 98/79/EC from the European Union) and while waiting for more adapted international norms, the manufacturer has to provide:

(i) Proof of certification, issued by an independent competent body, of compliance with quality standards established for *in vitro* diagnostic medical devices, as for instance in ISO norms 13485:2003 or in FDA 21 CFR 820.

(ii) Proof of stability of the *in vitro* diagnostic medical device, carried out in accordance with the norms issued by the WHO.

We reserve ourselves the right to ensure the conformity of these products with the quality criteria mentioned above.