Guidance To Applicant

For Pack Submission

This guideline aims to help biological product manufacturers and importers understand and comply with EDA rules about the biological product pack labeling and insert requirement.

This guidance addresses the requirements for review and approving the pack (outer pack & inner label) and insert could be met.

This guidance will provide information about pack and insert submission and approval for biological products submitted through new registration or renewal pathway.

I- General considerations

1- All biological products are required by Egyptian Pharmacy law (127/1955) to be accompanied by outer and inner labelling texts and a package leaflet setting out comprehensive information which is accessible to and understandable by those who receive it, so that they can use their medicine safely and appropriately.

2- EDA presidential decree (343/2021) article 9 mentions the following obligations about package labelling:

For outer pack:

- the site address of manufacturer
- the name license holder
- the manufacturing date and expiry date
- the batch number
- the barcode
- the product license number
- the product price

For inner label:

- the site address of manufacturer
- the manufacturing date and expiry date
- the batch number

3- for any changes undertaken for registered products regarding packs & inserts, the applicant should submit the variations for variation department of biological registration administration for review and assess to issue a variations approval.

II- Information That Should Be Submitted in the Biological Product (whether new or renewal product) pack and insert submission:

1- Local Product:

- **Product Trade Name**, the company write the trade name typically as in Inquiry Approval, biological application forms, insert and stability approval. The generic name shall be printed in letters that are at least half as large as the letters comprising the trade name

- **Active ingredients or generic name**, the company should mention their quantities or strengths identical to the approved insert, the product composition certificate submitted with the core file and stability approval.

- **The Pharmaceutical Dosage Form** (e.g.: PFS, Vial, PFP, ….), identical to Inquiry Approval, biological application forms, insert and stability approval.

- **Full List Composition of all inactive ingredients**, identical to the product composition certificate submitted with the core file, insert and stability approval.

- **Route of administration (e.g.: IV, IM. SC, infusion…)**, as mentioned in product insert and approved from scientific committee.

- English speaking pack in addition to Arabic language

- **Warning for all drugs** "Keep out of reach of children" must be mentioned / & **In case of presence of some ingredients** (for exp.: Aspartame. Sunset yellow, Benzalkonium chloride, Benzyl alcohol and others) they should be mentioned.

- If the dosage form or the product is related **to special population** (infant, Children, adults), it should be mentioned on the pack.

- **Number of Units of the dosage form** present in the container or box. If the product contains a lyophilized part and Water for injection part, should mention each unit with its number of units.

- **Different concentration** should have **different printing color** for easier identification and avoid medication error.

- **Manufacturer of the finished product:** full site address should be mentioned and identical to r inquiry approval, manufacturing license and biological product application.

NOTE:
a- the manufacturer is named on the label; the name shall be qualified by one of the following phrases: "**Manufactured by _____** " or "**Manufacturer of finished product is _____** ".
b- the packager is different from the manufacturer of finished product and named on the label; the name shall be qualified by the following phrase: "**Packaged by _____** ".
b- If the Toll manufacturer is named on the label, the name shall be qualified by the following phrase: "**Manufactured by _____ for _____".**

- Solvent manufacturing site (if needed): full site address should be mentioned and identical to inquiry approval, manufacturing license and biological product application.

- **Product License Holder**: full company address should be mentioned and identical to request inquiry approval, manufacturing license and biological product application.

- Batch number

- Manufacturing date

- Expiry date

- Name and number of accessories (if available) (e.g. needles, tubes, swabs, ….)

- Storage conditions

It is recommended to contain the following information (if needed)

a- Precautions about shaking, freezing, handling.

b- Single use or multiple usage.

c- Storage temperature.

d- After reconstitution state.

e- After opening state.

f- Preparation for use, i.e., shaking, dilution, adjustment of temperature or other manipulation or process.

g- special storage precautions

h- specific precautions relating to the disposal of unused medicinal

- **Quantity of dose delivered** may be mentioned, including usual quantities for each of the uses for which it is intended and usual quantities for persons of different ages.

- **the barcode** (complying the ministerial decree 29/2016 for track and trace inside Egypt)

- the product license number: identical to the number mentioned in the EDA product license

- the product price: identical to the pricing certificate

- the company logo (if needed)

- refer to the insert for any further information that is critical to the patient.

- Pack description in case of Multi packs which are composed of several single packs of the same strength of a medicinal product.

2 - Imported Product:

- **Product Trade Name**, the company write the trade name typically as in CPP, Inquiry Approval, biological application forms, insert and stability approval. The generic name shall be printed in letters that are at least half as large as the letters comprising the trade name

- **Active ingredients or generic name**, the company should mention their quantities or strengths identical to the approved insert, the product composition certificate submitted with the core file, CPP and stability approval.

- **The Pharmaceutical Dosage Form** (e.g.: PFS, Vial, PFP, ….), identical to Inquiry Approval, biological application forms, insert, CPP and stability approval.

- **Full List Composition of all inactive ingredients**, identical to the product composition certificate submitted with the core file, insert, CPP and stability approval.

- **Route of administration (e.g.: IV, IM. SC, infusion…)**, as mentioned in CPP, product insert and approved from scientific committee.

- Multilingual or English-speaking pack in addition to Arabic language (if available)

- **Warning for all drugs** "Keep out of reach of children" must be mentioned / & **In case of presence of some ingredients** (for exp.: Aspartame. Sunset yellow, Benzalkonium chloride, Benzyl alcohol and others) they should be mentioned.

- If the dosage form or the product is related **to special population** (infant, Children, adults), it should be mentioned on the pack.

- **Number of Units of the dosage form** present in the container or box. If the product contains a lyophilized part and Water for injection part, should mention each unit with its number of units.

- **Different concentration** should have **different printing color** for easier identification and avoid medication error.

- **Manufacturer of the finished product:** full site address should be mentioned and identical to request inquiry approval, manufacturing license, CPP and biological product application.

- Solvent manufacturing site (if needed): full site address should be mentioned and identical to request inquiry approval, manufacturing license, CPP and biological product application.

NOTE:
*** - if the pack is country specific pack:**
a- the manufacturer is named on the label; the name shall be qualified by one of the following phrases: **"Manufactured by _____ "** or **"Manufacturer of finished product is _____ "**.
b - If the batch releaser is identified on the label, the name shall be qualified by the phrase **"Batch Releaser site is _____".**
c- the packager is named on the label; the name shall be qualified by one of the following phrases: **"Packaged by _____ "**.
*** - if the pack is country of origin pack, international or shared pack:**
a- the company will stamp the manufacturing site by inkjet on outer pack (according to technical committee 9/7/2020) in case of not mentioning the manufacturer of finished product.

- **Product License Holder**: full company address should be mentioned and identical to request inquiry approval, manufacturing license, CPP and biological product application.

- **the importer:** full company address should be mentioned and identical to biological product application and importer register

- Batch number

- Manufacturing date

- Expiry date

- Name and number of accessories (if available) (e.g. needles, tubes, swabs, ….)

- Storage conditions

It is recommended to contain the following information (if needed)

a- Precautions about shaking, freezing, handling.

b- Single use or multiple usage.

c- Storage temperature.

d- After reconstitution state.

e- After opening state.

f- Preparation for use, i.e., shaking, dilution, adjustment of temperature or other manipulation or process.

g- special storage precautions

h- specific precautions relating to the disposal of unused medicinal

- **Quantity of dose delivered** may be mentioned, including usual quantities for each of the uses for which it is intended and usual quantities for persons of different ages.

- **The barcode** (complying the ministerial decree 29/2016 for track and trace inside Egypt)

- The product license number: identical to the number mentioned in the EDA product license

- The product price: identical to the pricing certificate

- The company logo (if needed)

- **Refer to the insert** for any further information that is critical to the patient.

III-Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors to promote safe administration and use of the product:

A. Poor Design of Product Container Labels and Carton Labeling Can Obscure Critical Safety Information

Poor label design can contribute to medication errors by making it difficult for healthcare professionals and/or patients to readily locate and understand critical safety information. Examples from reports of medication errors include:

• Key information, such as the product name, strength, and dosage form expressed in a confusing manner; or is not properly located and displayed.

• Key information does not appear in the same field of vision (i.e., the information is not readable without having to turn or rotate the container).

• Container labels and carton labeling look similar across multiple strengths of the same product or across multiple products within a company's product line.

• Container labels and carton labeling look similar among multiple products from different manufacturers.

• Container labels and carton labeling are visually cluttered by extraneous text or distracting images and graphics.

B- Error-prone abbreviations or symbols

Text is difficult to read because of font size or style, insufficient color contrast, or other design elements.

• Overlapping text is printed on both sides of a clear, transparent, or translucent container label such as those that might be found on syringes, ampules, vials or intravenous bags

- Critical Product Information Should Appear on the pack layout

•Trade name

•generic name

•Product strength

•Route(s) of administration

•Warnings (if any) or cautionary statements (if any)

The information listed above should be the most prominent information on the pack layout. Other information on the pack layout such as the net quantity statement, manufacturer name, and logo should not compete in size and prominence with the important information listed above. Information such as the product strength equivalency statement, “each vial contains” statement, and manufacturer name and logo is best placed on the side or back of pack layout to maximize the prominence of the important information listed above.

C. Labels Should Be Legible, Readable, and Easy to Understand

EDA recommends that the text on the container label and carton labeling should be (1) generally oriented in the same direction; (2) placed in the same field of vision (i.e., readable without having to turn or rotate the container); and (3) surrounded by adequate white space to improve readability and avoid crowding. Important factors to consider include the following:

- Contrast of Text and Background Color

The color contrast between the text and the container label background color should be chosen to afford adequate legibility of the text. Companies should avoid color combinations that do not afford maximum legibility of text (e.g., pale yellow text on white container label background)

- Information Crowding and Visual Clutter

When labels are crowded, text size generally decreased, and important information may be difficult to read. Lines or blocks of text should be separated by sufficient white space to avoid crowding or clutter. EDA recommend placing less important information on a side or back panel of the container label and carton

labeling. Apart from required information about a product's manufacturer, distributor or packer, information about business partnerships should not appear on the label or labeling .

- The graphic design should not compete with, interrupt, or distort important information.

Images of dosage form can help pharmacists or Doctors confirm they are dispensing the correct medication when comparing the product to be dispensed against the product contained in the commercial container closure system. the image better to be appeared at the bottom of the label and should not compete in size or prominence with the proprietary and/or nonproprietary name and strength information. Images should represent the actual dosage form.

D .Dangerous Abbreviations, Acronyms, and Symbols

Certain abbreviations, acronyms, and symbols are dangerous and should not be used because they are frequently misinterpreted and can lead to mistakes that result in patient harm. For example, the abbreviation µg for microgram should not be used because it has been mistaken as mg, meaning milligram. The abbreviation mcg is an appropriate abbreviation for microgram.

The abbreviation IU for international unit also should not be used because it has been confused for the intravenous route of administration.

Mistakes can also result from the use of abbreviations, symbols, and dose designations whose meaning is non-standardized and/or unfamiliar to the healthcare professional or other target reader. For these reasons, sponsors should avoid using error-prone abbreviations or symbols for product names, doses, and strength designations on container labels and carton labeling.

E. Avoid Look-alike Container Labels and Carton Labeling

Look-alike container labels and carton labeling have frequently contributed to product selection errors and administration of the wrong drug, wrong strength and/or wrong dose. Companies should create a container label and carton labeling design that is sufficiently distinct from that of their other products and the products of other manufacturers so that the end user is able to correctly identify, select, dispense, and administer the appropriate medication, strength, and dose.

EDA recommends the usage of Color Differentiation, Color differentiation is an effective tool that can (1) differentiate products within a manufacturer's product line; (2) differentiate strengths within a manufacturer's product line; and (3) highlight certain aspects of the label, such as important warning statements.

IV-Pack and insert submission for review and approval:

A- the biological Reception Unit is responsible for pack review and approval for new registration products or Renewal licenses:

B- biological registration specialist receives the following from applicant:

- in case of new products:

1- Seven layouts of proposed outer pack and inner label for each concentration from each manufacturing site (if more than one site)

2- Pricing certificate (not required in case of products comply 820 decree)

3- If the trade name is a registered trade name, the company will submit the approval certificate

4- Request inquiry approval

6- Official declaration (from scientific office or from manufacturer) stating the type of the submitted pack (COO pack, country-specific pack, international pack …..ect) with differences in a tabulated form.

7- Administrative data include (Composition certificate, importer register, contracts, CPP, GMPs, Manufacturing Licenses, tax card and commercial register).

8- site abroad inspection approval for non-reference & non-WHO prequalified.

- in case of renewal products:

1- Seven layouts of proposed outer pack and inner label for each concentration from each manufacturing site (if more than one site).

2- Official declaration (from scientific office or from manufacturer) stating the type of the submitted pack (COO pack, country-specific pack, international pack …..ect) with differences in a tabulated form.

3- If there is updated pack approved previously from variation unit, the company will submit the variation approval and declaration that the pack is the most updated one and this will be attached with renewal license.

4-the most updated original pack that marketed in Egypt

5- If the trade name is a registered trade name, the company will submit the approval certificate

6- Official declaration (from scientific office or from manufacturer) stating the type of the submitted pack (COO pack, country-specific pack, international pack …..ect) with differences in a tabulated form.

7- Administrative data include (Composition certificate, the updated pricing certificate, importer register, contracts, CPP, GMPs, Manufacturing Licenses, tax card and commercial register).

8- site abroad inspection approval for non-reference & non-WHO prequalified.

C- the biological reception specialist starts to assess and approve the pack after Inspection file approval, Stability file approval, scientific file approval and insert approval.

D- Biological Reception Specialist performs a detailed review on the packs and layouts according to packs requirements and ensures the consistency of the data on the outer and inner labels with the data in the stability decision, approved insert and the CPP for imported products.

E- If comments are present, BRS sends an email with listing the required documents.

F- Once documents are completed, concerned BRS approves the submitted layouts by signing and stamping the layouts and writing the obligations that should be stated on outer and inner labels.