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NATIONAL AGENCY FOR FOOD AND DRUG ADMINISTRATION AND CONTROL (NAFDAC)

REGULATORY AND REGISTRATION (R&R) DIRECTORATE

GUIDELINES FOR THE REGISTRATION OF BIOSIMILARS IN NIGERIA

A. GENERAL

- These guidelines are for the interest of the general public and in particular, pharmaceutical industries in Nigeria.
- It is necessary to emphasize that, no medicinal product shall be manufactured, imported, exported, advertised, sold or distributed in Nigeria unless it has been registered in accordance with the provisions of decree 19 of 1993 and the accompanying guidelines.

- **Biotechnology [1]Product** is any product prepared from cells cultivated from cell banks, excluding microbial metabolites such as antibiotics, amino acids, carbohydrates and other low molecular weight substances.
  They may be isolated from a variety of natural sources - human, animal, or microorganism - and produced by biotechnology methods.

- **Reference Biotechnology Product (RBP)** is a product used as the comparator for head-to-head comparability studies with a Biosimilar in order to show similarity in terms of quality, safety and efficacy. Only a biotherapeutic product that was licensed on the basis of a full registration dossier in Nigeria and / or by a stringent Regulatory Authority can serve as a RBP.

[1] Reference Biotechnology Product (RBP) can also refer to Reference Biotherapeutic Product and Reference Biopharmaceutical Product

Note: See below the appropriate circumstances under which a biotherapeutic product that is not licensed in Nigeria may be used as a RBP.

- **Biosimilar:** A product is said to be a biosimilar if it demonstrates similarity in terms of quality, safety and efficacy to a named reference biotherapeutic product licenced in Nigeria and or / a by stringent regulatory authority.

Appropriate Circumstances for the Use of a Reference Biotechnology Product (RBP) not Licensed in Nigeria

In instances where the RBP used is not licensed in Nigeria, the following should be considered:

a. The applicant is responsible for showing that the RBP not licensed in Nigeria, used for the purposes of demonstrating similarity is registered in a jurisdiction that formally adopts International Conference on Harmonization (ICH) guidelines and has regulatory standards and principles for evaluation of medicines, post-market surveillance activities, and approach to comparability that are similar to Nigeria;

b. The applicant has the responsibility of ensuring that the chosen RBP not licensed in Nigeria has associated with it sufficient information and data to support the submission;

c. The RBP not licensed in Nigeria is from a jurisdiction that has an established relationship with Nigeria.

B. APPLICATIONS

1. (a) The manufacturer shall be represented by an applicant - a duly registered pharmaceutical company - who must be in possession of a notarized Power of Attorney from the manufacturer authorizing him to speak for the principal on all matters relating to the product.

(b) The manufacturer must show:

I. **Manufacturer's Licence / Certificate**

This is the documentary evidence issued by Competent Health Authority of the country of manufacture that the company is licenced to manufacture biotechnological products which may be used in the country of origin and / or exported.

II. **Product License/Certificate of Registration**

This is the documentary evidence of registration of such product by the competent Health Authority of the country of manufacture.

III. **Certificate of Pharmaceutical Product (COPP) in conformity with WHO format**

This is the documentary evidence by the competent Health Authority that the sale of the product does not constitute a contravention of the drug laws of the country of manufacture.

IV. **Valid WHO GMP Certificate**

NOTE: The documents in respect of (I), (II), (III) and (IV) shall be authenticated by the Nigerian Mission in that country. In countries where no Nigerian Embassy or High Commission exists, any other Embassy or High Commission of any Commonwealth or West African country can authenticate the documents.

2. (a) An application for registration of a Biosimilar product shall be made by the applicant who procures the prescribed application form which must be duly completed with all required information.

This form shall be obtained from the office of the Director (R & R) upon payment of prescribed fee and submitted with a formal application letter, stating the name of the manufacturer, International Non-proprietary Name(INN)/scientific name, brand name (where applicable), strength, pack size and indication of product.

(b) A separate application form shall be submitted for each Biosimilar product. In this context, the application for registration of one dosage form with different strengths, of same formulations with different dosage forms, shall be made on different application forms.

(c) i. The applicant shall be responsible for ensuring that the product that will be imported after licensing shall comply with the approved label, quality and other conditions of approval.

ii. The applicant shall be responsible for importation, good distribution and storage of the product.

iii. The applicant shall also be responsible for submitting a detailed Risk Management Plan (RMP) as well as provide Periodic Safety Update Report (PSUR) in line with the Guidelines for Post Marketing Surveillance (PMS).

C. PRODUCT

1. There must be evidence to demonstrate similarity to a named Reference Biotechnology Product of assured quality, safety, and efficacy in respect to the indication(s), route of administration and dosage forms that has been licensed based on a full registration dossier in Nigeria and / or by a stringent Regulatory Authority (please see 'A' above, under **Appropriate Circumstances...**).

2. Any product that shall not comply with (c) 1 above shall not be considered for registration.

3. An applicant shall not be allowed to register a formulation in more than one brand name even where different doses of the active ingredient(s) are used.

4. The product information dossier shall be submitted in International Conference on Harmonization (ICH) Common Technical Document (CTD) format with the relevant sections duly completed and signed by both the Managing Director and Superintendent Pharmacist. The content of the dossier must be in compliance with the sections on the format. This should be submitted in 2 copies (hard and electronic copies).

D. LABELLING REQUIREMENTS

1. Labeling shall be informative and accurate.

2. The minimum labeling requirements on the primary and secondary package labels are;
   (a) Name of product- INN/scientific name and brand name (where applicable). The INN/scientific name must be written directly under the brand name and in same character.
   (b) Manufacturer's name and factory location address.
   (c) Provision for NAFDAC Registration Number.
   (d) Batch Number/Lot Number.
   (e) Manufacturing and Expiry dates.
   (f) Quantitative listing of all the active ingredients per unit dose.
   (g) Precisely defined storage conditions.

3. The minimum requirements on the leaflet insert are:
   (a) Name of product- INN/scientific name and brand name (where applicable). The INN/scientific name must be written directly under the brand name and in same character.
   (b) A statement indicating that the product is a biosimilar.
   (c) The leaflet shall carry advice / caution stating that interchangeability or substitution of a biosimilar with another biosimilar or a reference biotechnology product with a biosimilar, is not advisable.
   (d) Manufacturer's name and factory location address.
   (e) Dosage regimen.
   (f) Indications, frequency, route and conditions of administration.
   (g) Quantitative listing of all the active ingredients per unit dose.
   (h) Precisely defined storage conditions.
   (i) Adequate warnings where necessary.

4. Any Biosimilar product whose name, package or label bears close resemblance to an already registered product or is likely to be mistaken for such registered product, shall not be considered for registration.

5. Any Biosimilar product which is labeled in a foreign language shall NOT be considered for registration unless an English translation is included on the label and package insert (where applicable).

6. Information on indication carried on packages and leaflet insert of product shall not differ from that in other countries, and in particular the country of origin of the product.

E. DOCUMENTATION

Applicants shall be required to submit the following documents (original and two (2) copies) along with the duly completed application form(s) to the Liaison Office of Director (LOD):

(1) Power of Attorney or Contract Manufacturing Agreement:

Power of Attorney shall be:

a) Notarized by a Notary public in the country of manufacture.
b) Issued by the manufacturer of the product.
c) Signed by the MD, GM, Chairman or President of the Company.
d) Stating the names of the products to be registered.
e) Stating the name and address of the applicant
f) Stating the owner of the trademark (where applicable).

Contract Manufacturing Agreement shall be:

a) Notarized by a notary public in the country of manufacture.
b) Signed by both parties- the manufacturer and the applicant stating names and designations of the signatories.
c) Stating the names of all the products to be registered and other relevant clauses clearly explained in an unambiguous language.

(2) Manufacturer's License / Certificate indicating:

a) The name of products to be registered.
b) The name and address of manufacturer.

(3) Certificate of Pharmaceutical Products (COPP – WHO FORMAT)

(4) Valid WHO Good Manufacturing Practice (GMP) Certificate

NOTE: The documents in respect of (2), (3) and (4) shall be issued by the relevant health/regulatory body and authenticated by the Nigerian Mission in that country. In countries where no Nigerian Embassy or High Commission exists, any other Embassy or High Commission of any Commonwealth or West African country can authenticate.

(5) Evidence of Trademark approval from Federal Ministry of Commerce & Tourism / Certificate of Registration of Brand Name with the trademark Registry in the Ministry of Commerce in Nigeria.
This shall be done in favor of the trademark owner (manufacturer or applicant), as the case may be.

(6) Comprehensive Certificate of Analysis, issued by the manufacturer indicating the name, designation and signature of the analyst.

(7) Evidence of membership of approved sectoral group.

(8) Certificate of Business Incorporation of the importing company with the Corporate Affairs Commission in Nigeria.

(9) Current Superintendent Pharmacists License to practice issued by the Pharmacists Council of Nigeria.

(10) Valid Pharmaceutical Premises License Issued by the Pharmacists Council of Nigeria.

(11) Application letter for Import Permit by the applicant.

(12) An Invitation Letter for GMP inspection of manufacturing facility written by manufacturer which shall state;

a) The name and full location address of the manufacturer.
b) Name, e-mail address, current phone number & fax number of contact person in the country of origin of product.
c) Guide map (illustrating the shortest land/air route to the manufacturing factory).

d) Name(s) of product(s) intended for registration).

e) The applicant's information (Name of company, full location address, functional telephone number, fax number, e-mail address.

(13) Proposed distribution channels for the product intended for registration.

(14) Name(s) and location address(es) of cold chain storage facility(s) (where applicable).

Note: Failure to comply with these requirements may result in the disqualification of the application or lead to considerable delays in processing of registration.

F. FEES SCHEDULE

Total payment for registration of Biosimilar is ₦350,000:00 plus 5% VAT. Breakdown as follows:

a. ₦10,000.00 for Import Permit
b. ₦240,000.00 for Processing Fee
c. ₦100,000.00 for Product License

Please note that every fee is subject to review and attracts 5% VAT.

G. ISSUANCE OF CERTIFICATE OF REGISTRATION

Upon registration, the applicant shall be issued a Notification of Product Registration with the registration number which shall subsequently be used to obtain the registration certificate.

H. VALIDITY OF APPROVAL

The Certificate of Registration for a Biosimilar shall be valid for a period of five (5) years. However the Agency may suspend, withdraw or cancel the certificate of registration of Biosimilar product if found to have any of the following flaws:

i. Data/document with which the product was registered was found to be false or falsified.

ii. The circumstance under which the product was registered no longer exists.

iii Any of the conditions under which the Biosimilar product was registered has been contravened.

iv. The standard of quality, safety or efficacy as prescribed in the documentation for registration is not being complied with.

v. The premises, in which the product is processed, manufactured or stored on behalf of the holder of the certificate of registration is found to be unsuitable.

Note:

1. Procurement and submission of an application form or payment of processing fees does not confer registration status on product.
2. NAFDAC reserves the right to revoke, suspend or vary the certificate during its validity period.
3. Failure to respond promptly to queries on enquiries raised by NAFDAC on the application, will automatically lead to suspension of further processing of the application.
4. Registration of a product does not automatically confer Advertising permit. A separate approval by the Agency shall be required if the product is to be advertised.
5. NAFDAC may withdraw the Certificate of Registration in the event that the product is advertised without express approval from Agency.
6. All applicants are required to submit functional e-mail address(es) and telephone number(s).

STEPS TO PRODUCT REGISTRATION

STEP I: DOCUMENTATION

All documents (originals and two (2) copies) as stated in E above except document No. 13, are to be submitted to the Liaison Office of Director (LOD), Regulatory and Registration Directorate.

STEP II: IMPORT PERMIT

Upon satisfactory documentation,

i. Import Permit (i.e permit to import samples for registration) shall be issued by the Drug Registration Division on payment of ten thousand five hundred naira (N10, 500) only, 5% VAT inclusive.
ii. A letter for cold chain inspection shall also be issued to the company (if applicable).

STEP III: PRODUCT VETTING:

The following shall be submitted:

i. One (1) well labeled sample.
ii. Two (2) packaging materials of the product(s) or artwork.
iii. Hard & electronic copies (CD-ROM) of Common Technical Document (CTD).
iv. Hard & electronic copies (CD-ROM) of Risk Management Plan (RMP)
v. An invitation Letter for GMP inspection.
vi. A copy of the import permit.
vii. The receipt of payment for the import permit.

STEP IV: DOSSIER REVIEW:

STEP V: LABORATORY ANALYSIS

Upon satisfactory review and payment of two hundred and forty (₦240,000:00) naira only plus 5% VAT for processing, samples shall be sent to the laboratory for analysis.

STEP VI: ISSUANCE OF NOTIFICATION OF REGISTRATION

The company(s) shall be issued a Notification of Product Registration following satisfactory laboratory analysis; satisfactory cold chain inspection report (where applicable) and approval by various levels of Products Approval Committees.

All correspondence in respect of the Guidelines should be addressed to:

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