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

GUIDELINES FOR IMPORTATION AND RELEASE OF INVESTIGATIONAL MEDICINAL PRODUCTS

1.0 Introduction

1.1 Investigational medicinal products (IMPs), which are unregistered medicines, may only be brought into the country after positive ethical opinion is obtained, the clinical trial application has been approved and a letter of authorization has been issued by NAFDAC.

1.2 The holder of the authorization must ensure that permit to import IMP has been issued by NAFDAC, prior to importation. The quantity(ies) of IMPs to be imported will be dependent on the sample size of the study, in accordance with the approved study protocol.

1.3 The National Regulatory Authority (NRA) of the producing country should be responsible for assurance of compliance with Good Manufacturing Practice (GMP) for the manufacture and lot release of clinical batches of the IMP.

1.4 The Agency should take all appropriate measures to ensure that the holder of the authorization has permanently and continuously at his disposal the services of at least one qualified person who is responsible for ensuring:

1.4.1 In the case of investigational medicinal products that each batch has been manufactured and checked in accordance with internationally accepted standards of good manufacturing practice for medicinal products for human use, the product specification file and the information submitted in the application for authorization;

1.4.2 in the case of an investigational medicinal product which is a comparator product from a third country, and which has a marketing authorization, where the documentation certifying that each production batch has been manufactured in conditions at least equivalent to the standards of good manufacturing practice referred to above cannot be obtained, that each production batch has undergone all relevant analyses, tests or checks necessary to confirm its quality in accordance with the information submitted in the application for authorization.

1.5 In as much as the provisions laid down in (1.1) or (1.2) above are complied with, investigational medicinal products shall not have to undergo any further testing if they are imported into the country in which the clinical trial is to be conducted, together with batch release certification signed by the qualified person.

1.6 In all cases, the qualified person must certify in a register or equivalent document that each production batch satisfies the provisions as stated above. The said register or equivalent document should be kept up to date as operations are carried out and shall remain at the disposal of the agents of the competent authority for a period of not less than five years.

2.0 Scope

2.1 This guideline applies to all investigational medicinal products, including vaccines, which do not have marketing authorization in the country of intended use.

2.2 All procedures should apply to the placebo product, if applicable to the relevant clinical trial.

2.3 During the period of validity of the trial authorization, any subsequent importations should be subject to the same procedures.

3.0 Responsibilities of the Sponsor

3.1 The sponsor should not supply an investigational medicinal product until the sponsor obtains all required documentation (e.g. approval from the appropriate ethics committee and regulatory authority(ies)).

3.2 The sponsor should ensure that the investigational product(s) (including active comparator(s) and placebo, if applicable) is characterized as appropriate to the stage of development of the product(s), is manufactured in accordance with applicable GMP, is coded and labelled in a manner that protects the blinding, if applicable.

3.3 The sponsor should determine the investigational medicinal product(s) acceptable storage conditions (e.g. Temperature, protection from light, etc.), reconstitution fluids and procedures, and devices for product infusion, if any.

3.4 The sponsor should:

3.4.1 Ensure timely delivery of investigational medicinal product(s) to the investigator(s);

3.4.2 Maintain records that document shipment, receipt, disposition, return and destruction of the investigational product(s);

3.4.3 Maintain a system for retrieving investigational medicinal product(s) and documenting this retrieval (e.g. for deficient product recall, reclaim after trial completion, expired product reclaim);

3.4.4 Maintain a system for the disposition of unused investigational medicinal product(s) and for the documentation of this disposition.

3.4.5 Take steps to ensure that the investigational medicinal product(s) are stable over the period of use; this data should be available on request and for inspection purposes (where applicable). If non-compliance with the specifications becomes evident in the stability studies during the period of use in the clinical trial, the sponsor should notify the investigators and arrange to take appropriate steps;

3.4.6 Maintain sufficient quantities of the investigational medicinal product(s) used in the trial to reconfirm specifications, should this become necessary, and maintain records of batch sample analyses and characteristics. To the extent stability permits, samples should be retained either until the analyses of the trial data are complete or as required by the applicable NAFDAC requirement(s), whichever represents the longer retention period.

4.0 Labelling and Packaging

4.1 The labelling of investigational medicinal products should comply with the relevant NAFDAC requirements.

4.2 The particulars should appear in English and any other language on the outer packaging or, where there is no outer packaging, on the immediate packaging.

4.3 The particulars should include at least the following information:

- 4.3.1 State clearly that it is a clinical trial material
- 4.3.2 The product name or unique code
- 4.3.3 Storage temperature and conditions
- 4.3.4 Expiry date
- 4.3.5 Sponsor contact details

4.4 The Investigational medicinal products should be packaged to prevent contamination and unacceptable deterioration during transport and storage.

4.5 The investigational medicinal product(s) should be stored as specified by the sponsor, and in line with NAFDAC Good Distribution Practice (GDP) and Good Manufacturing Practice (GMP guidelines), and other NAFDAC regulations and conditions (if applicable).

4.6 In blinded trials the coding system for the investigational medicinal product(s) should include a mechanism that permits rapid identification of the product(s) in case of a medical emergency but does not permit undetectable breaks of the blinding.

5.0 Importation and Release

5.1 Shipping of investigational medicinal products should be conducted according to instructions given by/or on behalf of the sponsor in the shipping order.

5.2 A pre-clearance inspection should be carried out at the port of entry by the Agency. This should include the shipping documentation and overall physical condition of the consignment. (See point 6 below.)

5.3 If specific storage conditions are essential to ensure the quality of the product, e.g. maintenance of cold chain in the case of vaccines, a device that will confirm that storage temperatures were not exceeded during transport should be included with the shipment.

6.0 Application

6.1 All applications for importation of Investigational medicinal products should be made on the NAFDAC electronic Clinical Trial Application Platform (eCTAP) which is available on the NAFDAC website at https://nafdac.smapply.io/

6.2 All relevant documents should be uploaded with the application

7.0 Documentation

Documentation that should accompany each consignment of IMP should enable NAFDAC at the port of entry to release the product to the investigator(s) responsible for conducting the clinical trial in the country.

7.1 This documentation should include at least:

7.1.1 A valid Import Permit stating the quantity(ies) of IMPs to be imported.

7.1.2 The CoA of each batch of the investigational medicinal product(s) as well as comparator(s), if relevant

7.1.3 A copy of NAFDAC letter of authorization of clinical trial

7.1.4 A copy of a valid Certificate of Manufacture issued by the competent Regulatory Authority in the country of origin

7.1.5 A copy of a valid WHO certificate of a pharmaceutical product issued by the competent Regulatory Authority in the country of origin

7.2 The Cover Sheet should be completed by the sponsor and should accompany each consignment of investigational medicinal products. ***See Annex 1***

7.3 The Checklist may be used by the sponsor to ensure that the required documents are attached and correct, but a blank document should be submitted with the Cover Sheet for use by the Agency staff responsible for authorizing the importation of the IMP. ***See Annex 2***

8.0 Destruction/Exportation of IMP

Destruction

8.1 Any IMP remaining after conclusion of a Clinical Trial may either be destroyed or exported to sponsor site where applicable.

8.2 For IMPs to be destroyed, the applicant shall forward a detailed letter of request for approval to destroy such IMP to the Agency via email at derheadquarters@nafdac.gov.ng or submit in hard copy to the office of the Director, Drug Evaluation and Research Directorate.

8.3 The letter should contain amongst others, the following:

8.3.1 Details of Sponsor

8.3.2 Details of Trial Site(s)

8.3.3 Details of Principal Investigator

8.3.4 Reconciliation schedule/list showing items imported as approved, used and left (These items should match the total when added up or if there is a variance in the sum, an explanation or justification should be presented.

8.3.5 Current GMP Certificate of the facility where product was manufactured

8.3.6 Evidence of study completion (Notification/end of study report)

8.3.7 If products are expired, a copy of the shipment including batch number where applicable and expiry date

8.4 Evidence of Payment (where applicable)

8.5 Following satisfactory submission of all documents, the Agency shall process application further and proceed to witness such destruction as applicable

Exportation.

8.6 Upon completion of the study or in a situation where products have expired and applicant wishes to export same to the sponsor site, the following documentation have to be made and forwarded to the office of the Director as in 7.1 above:

8.6.1 Letter of application stating reason for exportation. (This justification must be approved by the Agency before further processing of such process)

8.6.2 Reconciliation schedule/list/ Utilization report duly signed by the PI

8.6.3 GMP Certification/compliance letter of facilities where IMP was manufactured

8.6.4 Evidence of Payment where applicable

8.6.5 Notification of study closure/end of study report

N/B: Revalidation of an IMP for re-use by the sponsor is not encouraged. If there should be any reason for such, a well-designed stability study with supporting document as requested by the Agency must be submitted to support such application.

9.0 Compassionate use /Expanded access

9.1 Compassionate use program also known as expanded access allows for patients with serious or life-threatening diseases to access investigational medicinal products outside of clinical trial based on the following:

9.1.1 Patients with serious or life-threatening disease who lack alternative therapeutic option

9.1.2 The study must have been concluded with a positive Benefit-Risk profile of the IMP as evaluated by NAFDAC

9.1.3 Product is undergoing/will undergo product registration in Nigeria

9.1.4 There are no alternatives to such products

9.1.5 The use is limited to only patients with life threatening disease who participated in the trial but could not have access to such IMP upon completion of the active phase of the trial

9.1.6 The IMPs are available at the site upon conclusion of the trial and not imported/manufactured for purposes of expanded access use

9.1.7 The Procedures/processes to be implemented for patients' benefit must be approved by NAFDAC for a stated period.

9.1.8 Approval must have been sought from NHREC/HREC as applicable

9.1.9 Routine monitoring of the use must be carried out by NAFDAC, which might also include site visits where necessary.

9.1.10 Patients must have consulted with their Physician and have a recommendation by the Physician that the IMP is the only option available for use in this instance

9.2 Following the criteria above, if the applicant met such criteria, the applicant would forward a letter stating why the IMP should be used for Extended Access or Compassionate Use

9.3 The use of the IMP for such purpose can only be implemented upon approval by NAFDAC

10.0 Definitions and Abbreviations

eCTAP: electronic Clinical Trial Application Platform
CoA: Certificate of Analysis
GMP: Good Manufacturing Practices
Investigational Medicinal Product: It is a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including products already with a marketing authorization but used or assembled (formulated or packaged) in a way different from the authorized form, or when used for an unauthorized indication, or when used to gain further information about the authorized form.
NRA: National Regulatory Authority
NAFDAC: National Agency for Food and Drug Administration and Control.
Sponsor: An individual, company, institution or organization which takes responsibility for the initiation, management and/or financing of a clinical trial.

ANNEXURE 1

COVER SHEET ***(to be completed by the sponsor)***	
IMPORTATION AND RELEASE OF INVESTIGATIONAL MEDICINAL PRODUCTS	
Fees (if applicable)	
Study Title and phase of the study	
Protocol Number	
Study Drug	
Manufacturer's Name and Address	
NAFDAC approval number of clinical trial	
Name of Comparator Drug (if applicable)	
NAFDAC registration number(s) of comparator drug(s) (if applicable)	
Name of Concomitant drug(s) – If applicable.	
NAFDAC registration number(s) of concomitant drug(s) (if applicable)	
Sponsor	
Principal Investigator	
Applicant	
Trial site(s)	
Sponsor Contact Person: Address Telephone number Fax number Cell number E-mail address	
Principal Investigator's Information: Address: Tel. No: Email:	
Batch number(s) and expiry date: Study drug Comparator drug(s)	

Quantities	
Blinding done or not	
Recommended storage temperature	

ANNEXURE 2

Checklist of required documentation
To be supplied by the sponsor for use by the NAFDAC staff responsible for authorizing the importation of the IMP

IMPORTATION AND RELEASE OF INVESTIGATIONAL MEDICINAL PRODUCTS			
CHECK-LIST of required documentation			
Are the following documents attached and correct, as indicated:		**YES**	**NO**
1	Copy of NAFDAC letter of approval of clinical trial		
2	Certificate(s) of Analysis (CoA) i. Study drug ii. Comparator (if applicable) iii. Concomitant Drug (if applicable)		
3	Does the CoA reflect at least the following information: Product name or code Name of company / Sponsor Batch number Expiry date Date of issue Signature, qualification and title of responsible person Results of physical and analytical tests		
4	Copy of valid Certificate of Manufacture issued by the competent Regulatory Authority in the country of origin		
5	WHO certificate of a pharmaceutical product issued by the competent Regulatory Authority in the country of origin		
6	Device / Proof of maintenance of cold chain (if applicable)		

7	Labelling: *outer packaging, immediate container* Does the label clearly indicate:		
7.1	That the product is clinical trial material, e.g. "For use in clinical trial only"		
7.2	Product name or unique code (if blinded) *Does this concur with the information on the Cover Sheet*		
7.3	Storage temperature *Does this concur with the information on the Cover Sheet*		
7.4	Storage conditions (e.g. protection from light)		
7.5	Batch number *Does this concur with the information on the Cover Sheet*		
7.6	Date of Manufacture		
7.7	Expiry date *Does this concur with the information on the Cover Sheet*		
7.8	Sponsor contact details *Does this concur with the information on the Cover Sheet*		
8	Is the physical condition of the consignment acceptable?		

CORRESPONDENCE

All correspondence should be addressed to:
The Director-General (NAFDAC)

Attn: The Director,
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NAFDAC website: www.nafdac.gov.ng
E-mail address: der.headquarters@nafdac.gov.ng
Telephone Number: