National Agency for Food & Drug Administration & Control (NAFDAC)

Drug Evaluation & Research (DER) Directorate

GUIDELINES FOR LABELING OF INVESTIGATIONAL MEDICINAL PRODUCTS

1.0 INTRODUCTION

Labeling is an important and integral part of the approval of a medicinal product. This also applies to the Investigational Medicinal Product (IMP) in clinical trials (CTs).

The purpose of regulatory labeling requirements for investigational medicinal products (IMPs) in clinical trials (CTs) is to provide added value regarding:

• Protection of the subjects

• Identification of the IMP

• Traceability of the IMP

• Proper use of the IMP

• Identification of the trial

• Proper documentation of the trial

The compliance with these requirements is important for drug development as non-compliance may cause problems during the approval process.

The IMP should be correctly labeled according to the mandatory information required by NAFDAC. The label has to be permanently affixed to the container. The challenge is increased in multinational trials in which the necessity arises to give information in several languages (multi-lingual trials) as well as in trials in which several IMPs and/or medicinal products are used.

2.0 PRINCIPLE

Investigational medicinal products should be produced in accordance with the principles and the detailed NAFDAC Good Manufacturing Practice Guidelines for Medicinal Products. Other NAFDAC Guidelines published should be taken into account where relevant and as appropriate to the stage of development of the product.

In clinical trials there may be added risk to participating subjects compared to patients treated with marketed products. The application of GMP to the manufacture of investigational medicinal products is intended to ensure that trial subjects are not placed at risk, and that the results of clinical trials are unaffected by inadequate safety, quality or efficacy arising from unsatisfactory GMP.

The production of investigational medicinal products involve added complexity in comparison to marketed products by virtue of the lack of fixed routines, variety of clinical trial designs, consequent packaging designs, and the need, often, for randomization and blinding and increased risk of product cross-contamination and mix up.

3.0 GLOSSARY

3.1 Blinding

A procedure in which one or more parties to the trial are kept unaware of the treatment assignment(s). Single-blinding usually refers to the subject(s) being unaware, and double blinding usually refers to the subject(s), investigator(s), monitor, and, in some cases, data analyst(s) being unaware of the treatment assignment(s). In relation to an investigational medicinal product, blinding shall mean the deliberate disguising of the identity of the product in accordance with the instructions of the sponsor. Unblinding shall mean the disclosure of the identity of blinded products.

3.2 Clinical trial

Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamics effects of an investigational product(s) and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of one or more investigational medicinal product(s) with the object of ascertaining its/their safety and/or efficacy.

3.3 Comparator product

An investigational or marketed product (i.e. active control), or placebo, used as a reference in a clinical trial.

3.4 Investigational medicinal product

A pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when 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.

3.5 Investigator

A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.

3.6 Manufacturer/importer of Investigational Medicinal Products.

A company that carry out operations such as production, packaging, repackaging, labeling and relabeling of pharmaceuticals.

3.7 NAFDAC

National Agency for Food and Drug Administration and Control

3.8 **Randomization**

The process of assigning trial subjects to treatment or control groups using an element of chance to determine the assignments in order to reduce bias.

3.9 **Randomization Code**

A listing in which the treatment assigned to each subject from the randomization process is identified.

3.10 **Sponsor**

An individual, company, institution or organization that takes responsibility for the initiation, management and/or financing of a clinical trial.

4.0 LABELING

4.1 The following information should be included on labels, unless its absence can be justified, e.g. use of a centralized electronic randomization system:

- 4.1.1 Name, Address and Telephone number of the sponsor, contract research organization or investigator (the main contact for information on the product, clinical trial and emergency unblinding);
- 4.1.2 Pharmaceutical Dosage form, Route of Administration, Quantity of dosage units, and in the case of open trials, the Name/Identifier and Strength/Potency;
- 4.1.3 The batch and/or code number to identify the contents and packaging operation;
- 4.1.4 A trial reference code allowing identification of the trial, site, investigator and sponsor if not given elsewhere;
- 4.1.5 The trial subject Identification Number/Treatment Number and where relevant, the visit number;
- 4.1.6 The name of the investigator (if not included in (i) or (iv));
- 4.1.7 Directions for use (reference may be made to a leaflet or other explanatory document intended for the trial subject or person administering the product);
- 4.1.8 “For clinical trial use only” or similar wording;
- 4.1.9 The storage conditions for the product;
- 4.1.10 Period of use (use-by date, expiry date or re-test date as applicable), in month/year format and in a manner that avoids any ambiguity.
- 4.1.11 “keep out of reach of children” except when the product is for use in trials where the product is not taken home by subjects.

4.2 The address and telephone number of the main contact for information on the product, clinical trial and for emergency unblinding need not appear on the label where the subject has been given a leaflet or card which provides these details and has been instructed to keep this in their possession at all times.

4.3 Labeling of investigational medicinal product should be in English language. Other languages may be included especially for multinational trials.

4.4 When the product is to be provided to the trial subject or the person administering the medication within a primary package together with secondary packaging that is intended to remain together, and the secondary packaging carries the particulars listed in "4.0", the following information shall be included on the label of the primary package (or any sealed dosing device that contains the primary packaging):

4.4.1 Name of sponsor, contract research organization or investigator;

4.4.2 Pharmaceutical dosage form, route of administration (may be excluded for oral solid dose forms), quantity of dosage units and in the case of open label trials, the name/identifier and strength/potency;

4.4.3 Batch and/or code number to identify the contents and packaging operation;

4.4.4 A trial reference code allowing identification of the trial, site, investigator and sponsor if not given elsewhere;

4.4.5 The trial subject identification number/treatment number and where relevant, the visit number.

4.5 If the primary packaging takes the form of blister packs or small units such as ampoules on which the particulars required in "D" cannot be displayed, secondary packaging should be provided bearing a label with those particulars.
The primary packaging should nevertheless contain the following:

4.5.1 Name of sponsor, contract research organization or investigator;

4.5.2 Route of administration (may be excluded for oral solid dose forms) and in the case of open label trials, the name/identifier and strength/potency;

4.5.3 Batch and/or code number to identify the contents and packaging operation;

4.5.4 A trial reference code allowing identification of the trial, site, investigator and sponsor if not given elsewhere;

4.5.5 The trial subject identification number/treatment number and where relevant, the visit number;

4.6 Symbols or pictograms may be included to clarify certain information mentioned above. Additional information, warnings and/or handling instructions may be displayed.

4.7 If it becomes necessary to change the use-by date, an additional label should be affixed to the investigational medicinal product. This additional label should state the new use-by date and repeat the batch number. It may be superimposed on the old use-by date, but for quality control reasons, not on the original batch number. This operation should be performed at an appropriately authorized manufacturing site. This additional labeling should be properly documented in both the trial documentation and in the batch records.

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