FOOD AND DRUGS AUTHORITY

GUIDELINES FOR CONDUCT OF CLINICAL TRIALS IN PAEDIATRIC POPULATION

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1.0 INTRODUCTION

Children represent a vulnerable population with developmental, physiological and psychological differences from adults, which make age and development related research important for their benefit. Medicinal products, including vaccines, for children need to be tested scientifically before widespread use. This can only be achieved by ensuring that medicinal products which are likely to be of significant clinical value for children are fully studied.

It is a well-known fact that children are not small adults. Pharmacokinetics and pharmacodynamics between adults and children are different with adverse reactions being more common in children than in adults. Growth and maturation processes, as well as certain specific diseases are unique to children. Specific consequences of medical interventions may be seen in children and may only appear long after exposure. Unfortunately this has been demonstrated by previous catastrophies with the use of medicinal products.

2.0 SCOPE

The provisions of these guidelines aim to contribute to the promotion and protection of the dignity, the well-being and the rights of children.

The document is intended for all persons involved in any stage of a clinical trial, including sponsors of clinical trials, ethics committees, regulatory authorities, pharmaceutical companies, insurance companies, investigators of clinical trials performed in children of all ages.

3.0 GLOSSARY

Adult: Any person aged 18 years and above is considered an adult.

Assent: When a subject deemed legally incompetent, such as a child, is able to give assent to decisions about participation in research, the investigator must obtain that assent in addition to the consent of the legally authorized representative.

Benefits: The observation of progress in diagnosis, treatment or prevention in the child or group of children affected.

Child: A child is an individual aged below 18 years.

Generally, children may be considered under the following categories according to their age:

- Newborn infants / neonates (birth to 27 days)
    - Preterm (delivered before 37 completed weeks of gestation)
    - Full term (delivered after 37 completed weeks of gestation)
- Infants (from 1 month to 12 months)
- Toddler (from 1 year to 2 years)
- Early childhood (from 2 years to 5 years)
- Late childhood (from 5 years to11 years)
- Adolescents (from 12 years to 18 years)

Ethics committee: An independent body constituted of medical, scientific, and non-scientific members, whose responsibility is to ensure the protection of the rights, safety and well-being of human involved in a trial by, among other things, reviewing, approving, and providing continuing review of trial protocol and amendments and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects.

Informed consent: A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of

the trial that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed and dated Informed Consent Form.

Investigational Product: A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial including a product with a marketing authorization when used or assembled in a way different from the approved form, or when used for an unapproved indication or when used to gain further information about an approved use.

It may be physical, psychological, or social, and may be immediate or delayed.

Legal representative of a child The legal representative will be one or both parents or guardian.

Paediatric Population: The term 'paediatric population' refers to the part of the population aged below 18 years.

Placebo: An inactive substance or a sham form of a therapy administered as a control in testing experimentally or clinically the efficacy of a biologically active preparation or procedure.

Principal Investigator: A person responsible for the conduct of the clinical trial at the clinical trial site(s), who is entitled to provide health care under the laws of the Country**.**

Risk: Potential harm (real or theoretical) or potential consequence of an action

4.0 GENERAL CONSIDERATIONS

4.1 Considerations of clinical trial applications involving paediatrics shall be in relation to the underlisted existing Guidelines for the conduct of clinical trials in Ghana:

1. Guidelines for Authorization of Clinical Trials of Medicines, Food Supplements, Vaccines and Medical Devices in Ghana.
2. Guidelines on Good Clinical Practice
3. Guidelines for Conduct of Clinical Trials During Emergencies
4. Guidelines for Conduct of Clinical Trials in Other Vulnerable Populations

4.2 Because of the special protection they deserve, children shall not be the subject of clinical trials when the research can be done in legally competent subjects.

4.3 Where a trial involving children is proposed, the Authority shall determine whether the research might be equally informative if carried out with consenting adults.

4.4 Children shall participate in clinical trials only where their participation is indispensible and of relevance to children.

4.5 If clinical trials with children prove necessary, the least vulnerable among them shall be included.

4.6 The choice of subsets of the paediatric population to be included shall be made on the basis of the likely target population for the medicine being tested, the possibility of extrapolation, and the scientific validity of such an approach.

4.7 The Authority shall at all times require strong justification for the inclusion of children.

5.0 PROCESS OF INFORMED CONSENT INVOLVING CHILDREN

5.1 Informed consent from the legal representative

5.1.1 As the child is unable to provide legally binding consent, informed consent shall be sought from the legal representative on the child's behalf.

5.1.2 The specific and written informed consent of a legal representative shall be sought prior to enrolling a child in a trial.

5.1.3 For an 'emancipated child', a written informed consent shall be required as for any adult capable of giving consent. Under these conditions, informed consent is no longer required from a legal representative.

5.2 Informed consent of families with different cultural background

Where appropriate, a cultural mediator, familiar with medical terminology, independent from the sponsor and investigator, experienced in the language, social habits, culture, traditions, religion and particular ethnic differences shall be made available during the informed consent process.

5.3 Assent from children

5.3.1 Prior to enrolling a child into a clinical trial, informed consent shall be obtained from the legal representative before obtaining the child's assent.

5.3.2 The child's assent is not sufficient to allow participation in research unless supplemented by informed consent of the legal representative.

5.3.3 The evaluation of whether or not a child can give assent shall not solely be based on age, but shall also depend on other factors such as developmental stage, intellectual capacities, life / disease experience, etc.

5.3.4 If the child's assent is not obtained, this shall be documented with justification in the consent form which is signed by the legal representative and investigator.

5.3.5 Assent, like consent, is a continuous process and shall be sought throughout the conduct of the trial.

5.3.6 Objections raised by a child at any time during a trial shall be considered and the will of the child respected.

5.4 Assent according to age groups and level of maturity

5.4.1 Children from birth to 3 years of age

In this age group, understanding of research is not expected and it is not possible to obtain assent.

5.4.2 Children from 3 to12 years

Within this age group there is the emergent capacity to agree. Where the child has some capacity to understand, age- and maturity-appropriate information is still needed and shall be given even if after giving information, assent is evaluated not to be obtainable.

5.4.3 Adolescents

5.4.3.1 The emerging capacity of an adolescent for independent decision-making shall be balanced with the need for continued special protection as provided by legal representatives.

5.4.3.1 When an adolescent is legally emancipated (emancipated child), informed consent must be sought directly from the adolescent.

5.5 Difference of opinion between the child and the legal representative

Every effort shall be made to understand and respect differences of opinion between the child and his/her legal representative. Strong and definitive objections from the child should be respected.

5.6 Withdrawal of the consent/assent

5.6.1 In all circumstances, legal representatives and children shall be made aware of the rights to refuse participation in a clinical trial and are entitled to freely withdraw their informed consent or assent, respectively, without giving reasons.

5.6.2 Legal representatives and children shall be reassured that the withdrawal from the trial will not result in any prejudice or detriment especially to their treatment.

5.6.3 After a child withdraws from a trial, the investigator is still responsible for reporting trial-related events. In addition, the investigator shall provide assurance of appropriate treatment and follow-up.

6.0 SPECIAL CONSIDERATIONS ON THE PROTOCOL

6.1 Considering the need for additional protection of children involved in trials and with a view to providing an opinion on the protocol, the Authority shall also check for the inclusion of paediatric experts in the review of the protocol by the IRB/IEC and conduct of the study.

6.2 In particular, the following points shall be examined:

6.2.1 The trial uses age-appropriate formulations of the investigational product(s).

6.2.2 An independent Data and Safety Monitoring Board (DSMB) with appropriate expertise in the conduct of clinical trials in children is identified in the protocol, unless otherwise justified.

6.2.3 The Principal Investigator shall be a paediatric expert.

6.3 The design and analysis of clinical trials in children shall adhere to the general principles of Good Clinical Practice.

6.4 The size of the trial conducted in children shall be as small as possible but large enough to demonstrate the appropriate efficacy with sufficient statistical power.

6.5 Use of placebo in children shall be restricted.

6.6 Special precautions shall be taken with respect to the amount and frequency of blood sampling amongst children. Especially in preterm and term neonates because they have very limited blood volume, are often anemic due to age and frequent sampling due to underlying pathological conditions

7.0 RISK ASSESSMENT AND MONITORING

7.1 The investigator shall make a thorough analysis of the risks in the trial and describe this in the protocol.

7.2 Risk assessment shall include the evaluation of the risk of the investigational product tested or the control, the risk of withholding active treatment (if applicable) and the risk of the disease itself.

7.3 The accumulation of clinical trials in the same population should, as much as possible, be avoided in trials involving children.

7.4 Risk shall be continuously monitored and pre-specified in the protocol.

7.5 Use of a Data and Safety Monitoring Board (DSMB) is strongly recommended in trials involving children. If a DSMB is not used, this shall be justified.

7.6 The DSMB shall include pediatric experts.

8.0 REPORTING TRIALS INVOLVING PEDIATRICS

Reporting of clinical trial data shall comply with standard protocols.