PROCEDURES

FOR ASSESMENT OF A

CLINICAL TRIAL RELEASE

OR

GENERAL RELEASE

OF

A HUMAN VACCINE

SECTION I

INTRODUCTION

A vaccine is a biological preparation that improves immunity to a particular disease. It typically contains an antigenic substance that resembles a disease-causing agent. It is often made from nucleic acid, viral vectors, recombinant fusion proteins and genetically altered or attenuated live agents. The agent stimulates the body's immune system to recognize the agent as foreign, destroy it, and "remember" it, for easy recognition and destruction in case of post-vaccination infections with the real organism. Vaccine development is not limited to identification of suitable antigens, adjuvants and delivery methods, but includes regulatory, technical and manufacturing hurdles in translating a vaccine candidate to the clinic. To evaluate safety and efficacy data for health interventions, vaccine clinical trial release protocols must be adequately reviewed at both institutional and national levels.

This document sets out points that have to be considered by the investigator in the preparation and assessment of a proposal for the trial release or general release of a human vaccine. It should be considered in conjunction with the National Biotechnology Authority (NBA) Act and the Biosafety Guidelines. In terms of the NBA Act *[Chap.14.31]* of 2006, all institutions involved in biotechnological applications and/or processes must be registered with the NBA and should set up an Institutional Biosafety Committee (IBC). The proposal shall be prepared by the responsible investigator and reviewed by the IBC before submission to the Authority.

It is recognised that questions relating to possible risks may not be answerable with certainty. However, it is the responsibility of those engaged in the preparation of the proposal to give the fullest and best consideration of which they are capable, to the possible impacts of the proposed introduction, and to make full disclosure of relevant matters to the IBC and the NBA. The impacts to be considered include those on public health and biosafety, other organisms and the environment. Full regard is to be paid to the experience gained in contained work on the vaccine, and to the results of a search of the relevant literature and consultation with appropriate experts and public authorities.

Answers are to be supported by appropriate data and references. If none are available, the basis on which the answer is given should be stated. Where any doubt exists about the appropriate answer to a question, the nature of the doubt is to be stated. Where a potential hazard is noted the clearest possible description of the relative risks involved shall be provided, and where appropriate, possible steps to eliminate or manage the hazard are to be considered and suggested.

Accidental release

All procedures for handling the vaccine shall be designed to ensure so far as possible that no accidental release occurs, and that all releases are planned. Should any accidental release of the vaccine occur, it shall be reported immediately to the respective IBC and the NBA, together with details of mitigating action taken, if appropriate and, the persons or authorities who have been notified. *Reporting a matter to the NBA does not relieve the applicant of any other obligations he or she may have under law or statute to notify relevant authorities or persons who may be affected.*

Submission of proposal

The applicant shall provide answers to all questions in Section II appropriate for the vaccine to be released. When the IBC is satisfied with the proposal, it shall forward it to the NBA. Where a proposal includes commercially sensitive information, the applicant may mark relevant portions as “Commercial-in-confidence”. Substantial reasons why specific sentences or passages should be so treated shall be given. Where material is clearly so marked, the NBA will treat it as confidential unless it forms the view that some disclosure is necessary. In that event, the NBA will notify the applicant in writing and subsequently negotiate a mutually agreed resolution. If agreement is not reached the proposal may be withdrawn, without disclosure or prejudice, at any time prior to the necessary disclosure in pursuit of approval.

SECTION II:

QUESTIONARRE

A. AIMS AND OBJECTIVES

1. What phase of clinical trial is it?

2. What are the primary objectives of the trial?

3. If the clinical phase is successful, is it intended that a general release of the product is to be proposed? If so, when, where and by who is it proposed that the general release takes place?

4. What is the target population for the vaccine and what criterion is being used to select the individuals?

5. In case of live microbe form of vaccine, can the vaccine affect non target population, if so in what way and what are the likely effects?

6. What measures have you put in place to minimise such risks?

B. THE NATURE OF THE VACCINE

1. Components of the vaccine?
    a. What type of vaccine is it (dead, attenuated, toxoid, protein subunit conjugation, DNA vaccine, viral vector, genetically modified or any other novel combinations)?
    b. What health concerns are associated with any vaccine components?

2. Are there any adjuvants, excipients, primers, boosts or preservatives in the vaccine preparation and use? If so, indicate the name, characteristic, use and safety level in the vaccine.

3. If microbes have been used, is it known whether the culture media has any adverse effect on humans? If so, provide details of those effects, including any applicable reports.

4. Does the vaccine formulation have any potentially unstable genotypes? If yes, what measures have been put in place to minimise risks that may arise due instability of the genotypes?

5. a. What methods are to be used to test for batch to batch consistency?

    b. Comment on the relative stability of vaccine over time under named appropriate storage conditions.

6. On the basis of contained experiments/preclinical trials, please describe
    a. Animal model used and the vaccine life span in the subjects.
    b. The possibility of the vaccines or resulting immunological response products to be transmitted from the subject and the mode of transmission.
    c. Therapeutic efficacy and pathophysiological observations observed in animal studies.
    d. Effects expected when the vaccine interacts with target and non-target species in the internal and external environment.
    e. Any other relevant information.

7. If vaccine is a product of genetic modification
    a. Give a detailed description of the steps taken in vaccine development.
    b. Explain based on previous data and/or research, likelihood of transferability of inserted gene, including likely targets.
    c. Provide data if any to suggest that inserted trait has no deleterious effects on any other organisms especially in the internal environment.

C. POPULATION SIZE AND LOCATION OF RELEASE

1. Describe the population size and trial location giving reasons for the choice of area. Include a map where relevant.

2. Provide relevant data on age, sex and the health status of sample individuals.

3. Are there any special conditions (e.g individuals' health, diet) that may exacerbate any undesirable effects? If yes, what are the likely effects and how can they be minimised?

D. HABITAT AND ECOLOGY

In case of microbe based vaccines,

1. What is the natural habitat of the organism?

2. State where the organism was originally isolated.

3. Is the organism present in Zimbabwe or its exotic? If present, please give the geographic distribution of the organisms.

4. Are the organisms already present in the both internal and external environment at or near population sampling area? If so, provide available data on populations.

5. Are there any known predators or parasites of the organisms in Zimbabwe? If so, describe them.

6. Could the introduction of the organisms prejudice any beneficial function of other organisms in the internal and external environment?

E. GENERAL DETAILS AND PROVISIONS

1. a. What route of administration will be used?
   b. What are the safety concerns affecting route of administration and how have they been addressed?
   c. Indicate treatment regimes involved together with doses to be used.

2. Will the subjects carry any vaccines at the end of the trial? If so
   a) What is the likelihood that they may disseminate the vaccine to the general population e.g by faecal route?
   b) What are the likely effects and what measures have been put in place to minimise such risks?

3. What is the existing evidence regarding level and duration of immunity produced in the target species?

4. What guidelines have been put in place to dispose waste containing any vaccine and/or vaccine residues?

5. What is the likelihood that the host vaccine organism would be used in other human or animal vaccines? Would the use of this vaccine preclude the future use of the host vaccine organism for immunisation purposes?

F. PUBLIC INFORMATION

The information provided under this subsection is for possible public distribution. It should be written in plain language. No commercial-in-confidence information should be included. Applicants should

ensure that information provided does not prejudice their rights to patent protection. The information required must include:

1. The name of the applicant's organisation;

2. Address of the applicant's organisation;

3. Name of contact person;

4. E-mail address, telephone and fax number of contact person;

5. Vaccine to be released;

6. Location and size of planned introduction;

7. Purpose of planned introduction;

8. Brief summary of the nature and results of any genetic modification. Use of technical terms should be minimised, and

9. Agencies consulted before introduction.