

National Code of Health Research Ethics



FEDERAL MINISTRY OF HEALTH

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Foreword

The National Code of Health Research Ethics represents the collective concern of the government and the people of Nigeria to ensure the protection of human participants in scientific research to the highest ethical standard that is possible.

The Accra Ministerial meeting on Health Research, a meeting I initiated, highlighted various challenges inhibiting African and other developing countries in harnessing the full benefits of research and made recommendations on the way forward. One such recommendation was to establish systems for the protection of human participants in research.

There is now increased global, regional and local commitment to strengthening health research in developing countries in order to provide evidence that will serve as the quintessential driver to strengthen health systems, achieve the Millennium Development Goals (MDG) and improve overall health status at all levels. As a result, we are witnessing massive investments from multilateral agencies, global philanthropies and foundations in the development of new tools and methods for the control of our major diseases such as malaria, HIV/AIDS and vaccine-preventable diseases of childhood. It is expected that this trend of increased investment in research that is relevant to our National health issues will continue.

However it is common knowledge that despite the potential of research to contribute to improvements in health care services and training, it also carries a risk that participants, communities, local researchers and even the country may be exploited and exposed to egregious harm. A system of ethical regulation of research ensures that research is conducted in a manner that will maximize the benefits of research while limiting its potential harms and exploitation of research participants.

Nations have statutory responsibility of ensuring the protection of its people from exploitation. As we continue to promote health research in order to contribute towards improving the health

status of Nigerians, we have taken it upon ourselves to strengthen our National Health Research Ethics Committee, to provide and ensure adherence to a regulation for protection of human participants in research – The National Code of Health Research Ethics.

This code clearly defines the roles and responsibilities of the National Health Research Ethics Committee, Institutional Health Research Ethics Committees; Healthcare Professionals; Universities; Health Researchers and Research Sponsors in the protection of human research subjects.

As a national code, all stakeholders in health research including our partners in the international community are expected to respect and abide by its tenets, in the spirit of promoting and defending human rights.

I therefore, wish to emphasize the need for all stakeholders to collaborate with my ministry and health authorities at the state and local government levels to ensure the successful implementation of this code. This will promote best practices, maintain public trust and result in improvement in the performance of our health system.

I recommend this document as an indispensable companion for all stakeholders in health and health research, health researchers, the Nigerian public as well as the international community.



Prof. Eyitayo Lambo
Hon. Minister of Health

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About NHREC

The National Health Research Ethics Committee (NHREC) is the apex body responsible for the provision of and ensuring adherence to guidelines that govern ethical research practice in order to ensure the protection of human research participants in Nigeria.

The committee was inaugurated in October 2005 by the Hon. Minister of Health in line with Mr. President's directive for the strengthening of a mechanism that will ensure the protection of Nigerians as they participate in researches.

The committee was an offshoot of the dormant Health Research Ethics Committee which had been in existence since early 1980's.

The terms of reference for the committee are to:

- (a) Determine guidelines for the functioning of health research ethics committees;
- (b) Register and audit health research ethics committees;
- (c) Set norms and standards for conducting research on humans and animals, including norms and standards for conducting clinical trials;
- (d) Adjudicate in complaints about the functioning of health research ethics committees (HREC) and hear any complaint by a researcher who believes that he has been discriminated against by a health research ethics committee;
- (e) Refer to the relevant statutory health professional council matters involving the violation or potential

violation of an ethical or professional rule by a health care provider;

- (f) Institute such disciplinary action as may be prescribed against any person found to be in violation of any norms and standards, or guidelines, set for the conduct of research under this Bill; and
- (g) Advise the Federal Ministry of Health and State Ministries on any ethical issues concerning research.

Section A

To whom does this code apply?

This code applies to all health research involving human participants, conducted, supported or otherwise subject to regulation by any institution in Nigeria.

Definition of Research and Coverage of Code:

Research here is defined as systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. It may consist of:

- (a) Therapeutic procedures – interventions administered with the intent of providing direct benefit to the research participant
- (b) Non-therapeutic procedures – interventions that are not administered with therapeutic intent and are only intended to answer the scientific question of the study

Activities which meet this definition constitute research for purposes of this code, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

Health research that is conducted anywhere in Nigeria must comply with all sections of this code.

Section B

Exemption

Research activities in which the only involvement of human participants will be in one or more of the following categories are exempt from health research ethics committee oversight:

(a) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as:

(1) Research on regular and special education instructional strategies, or

(2) Research on the effectiveness of or comparison among instructional techniques, curricula, or classroom management methods.

(b) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behaviour, unless:

(1) Information obtained is recorded in such a manner that human participants can be identified, directly or through identifiers linked to the participants; and

(2) Any disclosure of the human participants' responses outside the research could reasonably place the participants at risk of criminal or civil liability or be damaging to the participants' financial standing, employability, or reputation.

(c) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are *publicly*

available (note that this refers to availability of data and not the status of the custodian of the information/data) or if the information is recorded by the investigator in such a manner that participants cannot be identified, directly or through identifiers linked to the participants.

(d) Studies that are meant to evaluate the outcome of procedures, programs and services are exempt because they are designed to produce information leading to improvement in delivery of procedures, programs and services. Such studies usually evaluate measures that are already in use and considered part of standard practice. They may include collection and analysis of data or collection of new data but they do not involve allocation into groups or randomisation.

(e) Studies that are designed to evaluate or assess quality of services, programs and procedures and formulate guidelines leading to their improvement are exempt. Such studies may involve the collection and analysis of some data.

(f) Innovative or non-validated medical treatment – treatment that is designed solely for the benefit of the patient but in which the ability of the treatment to result in the desired result is to some degree not proven. Such activities are exempt while recommending that they should be subjected to research in order to generate information about their efficacy as soon as possible.

(g) Clinical audit, where the study is designed and conducted solely to define or judge only current care, without reference to a standard. It may involve the collection and analysis of data but there is no allocation to intervention groups or randomisation and the services have been delivered before the audit is initiated.

Who determines exemption?

All exemptions shall be determined by the Health Research Ethics Committee (HREC) - *vide infra*. In summary, applicants conducting research that may be exempt shall submit the proposal or a written summary that contains enough information for judgement to be made, to the HREC. The HREC Chairperson or his designee, in consultation with HREC Administrative Officer – where one exists, shall decide whether the research is exempt. Where the Chairperson is uncertain and the uncertainty is unresolved after request for and provision of more information by the applicant, the proposal or summary should be referred to HREC. All applications for exemption must be brought to the notice of HREC at its regular meeting for discussion as may be deemed necessary by members of HREC.

Section C

Registration of Health Research Ethics Committees

In order for an institution to be able to conduct health research, the institution must have a registered health research ethics committee (HREC). The following are the guidelines for registration:

(a) Registration with National Health Research Ethics Committee (NHREC) shall require:

(1) An application by the authorized head of the institution or their authorized designee which among other things should include that the line of reporting authority of the Chairman of the HREC is directly to the Chief Executive of the proposing institution.

(2) A list of members of the proposed health research ethics committee identified by:

(i) Name

(ii) Qualifications

(iii) Representative capacity

(iv) Indications of experience such as trainings, certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to HREC deliberations.

(v) Any employment or any other relationships (including stock ownership, receipt of grants, honorariums or support from potential research sponsors) that may be construed as conflict of interest within the context of membership of the HREC.

(3) All members of the proposed HREC must have completed NHREC approved training programs in research ethics. Additional training in research methodology and research administration is recommended. Copies of the certificates of completion of such programs must be submitted along with the application. The institution setting up the HREC must provide resources for such training.

(4) Statement of agreement to comply with the Nigerian Code of Health Research Ethics subsequently referred to as "the code", governing HREC in the discharge of its responsibilities for protecting the rights and welfare of human participants of research conducted at or sponsored by the institution.

(5) Statement of commitment to provide meeting space of sufficient quality, office and storage space, sufficient staff and funds to support the HREC review and recordkeeping duties in order to guarantee that these duties can be accomplished with sensitivity and confidentiality.

(6) A statement of commitment to take full responsibility for all actions of each member of HREC in the course of performance of duties related to membership. The institution shall provide coverage for any liability of any member arising from service on HREC.

(b) The lifespan of any HREC shall be two years, after which the institution shall apply for re-registration. The application for re-registration must be submitted within the last 6 months of the expiry of the current registration. During the re-registration process, the institution shall submit:

(1) A current list of members of the health research ethics committee identified by:

(i) Name

(ii) Qualifications

(iii) Representative capacity

(iv) Indications of experience such as trainings, certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to HREC deliberations.

(v) Any employment or any other relationships (including stock ownership, receipt of grants, honorariums or support from potential research sponsors) that may be construed as conflict of interest within the context of membership of the HREC.

(2) Certificates of completion of National Health Research Ethics Committee approved training programs in research ethics completed within 6 months of the expected start date of the registration of the HREC. Additional training in research methodology and research administration is recommended. Copies of the certificates of completion of such programs must be submitted along with the application.

(3) Copy of the primary statement of agreement to comply with the National Code of Health Research Ethics previously endorsed by the institution and the NHREC.

(4) Report of fulfilment of previously stated commitment to provide infrastructure and logistics to support the HREC review and recordkeeping duties.

(5) Complete record of the activities of the committee, including financial records, attendance register at statutory meetings, complaints, litigations,

number, and titles of protocols received, reviewed, approved, rejected and pending, and the mean time from protocol submission to approval in each of the preceding 2 years.

(c) Where a registered HREC does not apply for re-registration during the life of its current registration, the HREC shall be considered de-registered and may apply anew to NHREC. No research may be conducted in the institution during this period of de-registration.

(d) Institutions may propose to have more than one HREC. In such instances, the jurisdiction of each of the HREC should be clearly defined and there should be open channels of communications between them that will allow transfer of proposals to the HREC with appropriate expertise. Researchers must not submit the same protocol simultaneously to more than one HREC within the same institution.

(e) The authority of HREC shall be limited to the boundary of the proposing institution or the activities of its permanent members of staff, unless otherwise specified by the NHREC. Where a permanent member of staff is the principal investigator of a study taking place outside the boundaries of the proposing institution, the researcher shall seek ethical oversight only from the institution in which he/she is a permanent member of staff. This provision does not preclude co-investigator(s) from seeking ethical oversight from their institution(s) where there is more than one study site.

(f) In lieu of an institution being able to constitute a health research ethics committee and where such institution desires to engage in research:

(1) Such institution shall establish a cooperative agreement with a registered HREC located within the same state of the federation as the institution.

(2) Where there is no registered HREC within the same state of the federation, agreement can be established with any HREC within the same geopolitical zone of the country as the institution.

(3) In the eventuality that there is no registered HREC within the same geopolitical zone, the institution should consult the NHREC for guidance.

(4) Where a registered HREC agrees to review proposals emanating from another institution, this arrangement shall last only for the period covered by the collaborative agreement and this cannot extend beyond the period of registration of the HREC by the NHREC.

(5) Institutions seeking to establish collaborative agreements with a registered HREC must submit an application to the NHREC.

(6) The reviewing HREC must be currently registered and must attest that it will maintain its registration status for the period covered by the proposed collaborative agreement.

(7) The applicant institution can have collaborative agreement with only one HREC at any given time, while the reviewing HREC can have multiple collaborative agreements subject to NHREC approval.

(g) Categories of HREC. The NHREC shall establish categories of HREC on the basis of the size of the committee, qualifications, training and experience of its members in research ethics and science, history of the committee (when established, past review activities, record keeping and compliance with requirements of the Code), resources available to the committee, supporting

personnel and infrastructure of both the committee and the proposing institution.

(1) NHREC shall outline from time to time detailed criteria for categorization of HREC.

(2) Categorization of HREC shall be approved during regularly scheduled meetings of the NHREC.

(3) NHREC shall outline the types of research that different categories of HREC shall review.

Section D

HREC membership

(a) The authority to establish a HREC and the procedure of selecting members is vested in the Headship of the proposing institution.

(b) Each HREC shall have at least five members and if more, then the total membership must always be an odd number.

(c) The HREC shall be sufficiently qualified through the experience, expertise and diversity of its members, including consideration of age, gender, socio-cultural backgrounds, religion and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of researchers and research participants. Members should have varying academic and professional backgrounds to promote complete and adequate review of health research conducted by the promoting institution.

(d) In addition to possessing the professional competence necessary to review specific research activities, the HREC shall be able to ascertain the acceptability of proposed research in terms of institutional regulations, applicable laws, and standards of professional conduct and practice. The HREC shall therefore include persons knowledgeable in these areas and whenever feasible, a lawyer.

(e) Each HREC shall include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in non-scientific areas.

(f) Each HREC shall include at least one member who is not affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

(g) No HREC may have a member participate in the HREC initial or continuing review of any project in which the member has a conflicting interest.

(h) If HREC wishes to review research that involves vulnerable participants, such as children, prisoners, pregnant women, physically and psychologically disabled persons, the HREC shall co-opt one or more individuals knowledgeable about and experienced in working with these participants for the review process. These individuals may not vote during the HREC meeting.

(i) Each HREC member must pledge to maintain confidentiality regarding all meetings, deliberations, applications, information on research participants and related matters that shall come to his/her knowledge during service on HREC even after leaving the HREC assignment. There is no time limit for this prohibition.

Section E

HREC functions and operations

In order to fulfil the requirements of this code, each HREC shall:

(a) Operate in accordance with the provisions of the current version of the National Code of Health Research Ethics issued by the NHREC. Additional guidance may be obtained from the Standard Operating Procedure (SOP) issued by the NHREC.

(b) Except when an expedited review procedure is used, research proposals shall be considered at regularly convened ordinary meetings of HREC at which a majority of the members are present, including at least one member whose primary concerns are in non-scientific areas.

(c) Where a member cannot physically attend a meeting, the member shall be accounted as being present if he/she can participate electronically, for example by teleconferencing for the majority of the duration of the meeting.

(d) Process for regular research approval

(1) HREC shall review prescribed application materials and have authority to approve, require modifications in (to secure approval) or disapprove all health research activities covered by this code.

(2) In order for research to be approved, the decision shall ordinarily be arrived at by discussion and consensus or it shall receive the support of a simple majority of those members present at the meeting.

(3) HREC may, at its own discretion, invite representations from the applicant(s), sponsor(s), institution(s) or any other person(s) that it may consider relevant to provide information pertinent to the research during the review process.

(4) HREC shall notify investigator(s) in writing of its decision to approve, disapprove or require modifications of the research activity.

(5) HREC shall have a maximum of 3 months from the date of receipt of a valid application to give its decision to the applicant. An application shall be considered valid only after receipt of all materials required by HREC to give a determination.

(6) Where HREC considers an application of such complexity that it cannot conclude the review, the application shall be referred to NHREC and the applicant duly informed within the stipulated 3 months.

(7) Where HREC does not conclude its review in 3 months and has not referred the case to the NHREC, the applicant shall have the right to complain to NHREC with the possibility of re-allocation of the proposal to another HREC and sanction of the concerned HREC

(8) Where HREC decides to disapprove a health research activity, it shall include in its written notification, a statement of the reason(s) for its decision and give the applicant an opportunity to respond in person or in writing within 3 months of receipt of the notification.

(9) Where HREC has received representation from the applicant in response to an existing decision, HREC may decide to uphold or modify its previous decision and shall communicate this decision to the applicant within 3 months of the representation.

(10) HREC is mandated to keep all records related to its decision(s) for a minimum of 10 years after completion of the research activity.

(e) Process for continuing oversight of research

(1) HREC shall conduct continuing oversight of research covered by this code at intervals adjudged by HREC as being appropriate to degree of risk involved in participation in the research.

(2) HREC shall have authority to examine all aspects and documents including consent forms, questionnaires, case report forms etc. that are related to the research and necessary for the HREC to conduct its oversight function.

(3) This shall be at least once a year or at least once during the lifetime of the research where the duration of the research is less than a year.

(4) HREC shall have authority to observe or cause to be observed on its behalf, the research and its consent process to ensure compliance with the highest scientific and ethical standards.

(5) HREC may initiate process of oversight of research in the event of receipt of complaints, information or data relevant to the research from any source.

(f) Process for expedited review

(1) HREC may expedite review of research in the following circumstances:

(i) Research is found to involve no more than minimal risk – meaning that the probability and magnitude of harm is no greater than that encountered in the daily lives of all (or the great majority) persons in the population (under normal circumstances) from which research participants are to be recruited. Note that

minimal risk is applicable in non-therapeutic research only.

(ii) Research does not involve vulnerable populations such as children, prisoners, pregnant women etc.

(iii) Research does not contain serious methodological or ethical flaws

(iv) Minor changes in previously approved research during the period for which approval is authorized.

(2) Expedited review may be carried out by the HREC chairperson or his designee from among members of HREC. In reviewing the research, the reviewer(s) shall exercise all of the authorities of HREC except that the reviewer(s) may not disapprove the research.

(3) The Chairman of HREC shall bring all research reviewed expeditiously to the next meeting of HREC for notice, discussion and ratification.

(g) Process for amendment of research

(1) HREC shall require that applicants apply for permission to amend protocols in any of the following circumstances:

(i) Where there are changes in any part of the research protocol that alters the risk benefit ratio of the research.

(ii) Where there are changes in the named members of the team conducting the research.

(iii) Where there are changes in research sites.

(iv) Where there are changes in sponsorship, institutional guidelines, institutional structure, HREC requirements, national laws or exigencies that impact on the ethical conduct of research.

(2) HREC shall require that researcher submit an application for original research approval where in its opinion, the proposed amendments are substantial, such as but not limited to, change(s) in inclusion or exclusion criteria, randomization, interventions and outcome measures.

(3) Under no circumstance shall a researcher deviate from approved protocol, except such as is necessary to eliminate immediate hazard to research participants. The researcher shall notify the Chairman of HREC within 24 hours of such changes.

(4) In such circumstances as described in section (3) above, the researcher shall stop the research and the HREC shall conduct a thorough review of the research before authorizing suspension, continuation or modifications to the research.

(h) Process for exemption

(1) HREC may grant exemption from review in any of the conditions enumerated above (*vide supra*).

(2) Applicants seeking exemption shall submit the proposed research or adequate information about it to the HREC, sufficient, in HREC judgement, to make a determination.

(3) Exemptions may be granted by the HREC chairperson or his designee from among members of the HREC, in consultation with the HREC Administrative Officer – where one exists.

(4) In granting exemption, the reviewer(s) shall exercise all of the authorities of the HREC except that the reviewer(s) may not disapprove the research.

(5) Where the reviewer is uncertain and the uncertainty is unresolved after request for and provision of more information by the applicant, the proposal or summary should be referred to the HREC.

(6) The Chairman of HREC shall bring all exempted research to the next meeting of HREC for notice, discussion and ratification.

(i) Process for suspension of research

(1) HREC shall have authority to suspend research that is not being conducted:

- (i) In accordance with HREC requirements or
- (ii) In accordance with existing legislation or
- (iii) In accordance with existing institutional guidelines; or
- (iv) Where research is associated with unexpected serious harm to participants.

(2) Any suspension of research shall include a statement of the reason(s) for the HREC action and shall be reported within 2 weeks to the researcher(s), institution(s), sponsor(s) and the NHREC.

(3) Researcher(s), institution(s) or sponsor(s) shall be entitled to ask for a reconsideration of the decision of HREC to suspend research within 2 weeks of receipt of notification.

(j) Process for revision of suspension

(1) HREC may reverse its decision to suspend research if the precipitant(s) of the action is resolved to HREC satisfaction

(2) The HREC will determine the case at its next regular meeting and may require that the researcher sign an agreement with HREC on its finding(s) and agreed remedial measure(s).

(3) Where HREC allows resumption of research, an oversight review of the research shall be carried out within 6 months or at least once during the lifetime of the research if it is shorter than 6 months.

(k) Process for termination of research

(1) Where the researcher(s), sponsor(s) or institution(s) is unable to offer or the HREC is unable to ascertain or enforce satisfactory remediation of the precipitant, HREC shall terminate the research.

(2) HREC shall indicate the reason(s) for the termination of research in writing within 2 weeks to the researcher(s), institution(s), sponsor(s) and the NHREC.

(3) Researcher(s), institution(s) or sponsor(s) shall be entitled to appeal the decision of HREC to terminate research to the NHREC within 2 weeks of receipt of notification.

(l) Process for appeal of HREC decision to terminate research

(1) Upon receipt of an appeal of the decision of a HREC to terminate research, NHREC may, at its discretion, take up such an appeal.

(2) Where the appeal is sustained,

(i) NHREC may with reasons and in consultation with the institutional HREC, direct the institutional HREC to approve the research.

(ii) NHREC may with reasons and in consultation with the institutional HREC mandate modifications,

which if undertaken, can allow the research to proceed or resume as the case may be.

- (iii) Where NHREC mandates restoration of the research, the institutional HREC shall have powers of continuing oversight as outlined in relevant sections of this code

(3) NHREC may sustain the decision of the HREC and dismiss the appeal.

(m) Process for review of multi-institutional research

In the conduct of multi-institutional research, each institution is responsible for safeguarding the rights and welfare of human participants in its institution and for complying with this code.

(1) Where there are no more than 3 Nigerian research sites:

(i) The principal investigator at each research site may apply to the institutional HREC for review.

(ii) HREC may, at its own discretion, adopt the approval of research by another HREC rather than conduct a fresh review and approve the research.

(iii) Where the outcome of review is discordant (that is, some HREC approve while others disapprove the research), the applicant shall submit the comments from the different HREC to their institutional HREC for consideration and possible reconciliation.

(iv) Where the outcome of review by different institutional HREC is favourable but different modifications are requested, the applicant shall submit the comments their institutional HREC for reconciliation.

(v) HREC shall, as much as possible, consult with each other in order to resolve discordant reviews and

generate consistent single response to multi-site research.

(2) Where there are more than 3 Nigerian research sites:

(i) Applicant(s) may follow the steps outlined above or

(ii) Applicant(s) may apply to NHREC directly.

(3) In international collaborative research

(i) Only applicant(s) with qualification(s) and background sufficient to serve as principal investigator(s) and based in a registered institution in Nigeria that is capable of carrying out the proposed research shall apply for review of research.

(ii) HREC may adopt the approval of another HREC or that of any other local or international ethics review committee (to the degree that such approvals comply with the requirements of the code and take account of local circumstances) and approve the research.

(iii) Where the outcome of review is discordant, the applicant shall submit the comments from the different HREC or ethics committees their institutional HREC for consideration and possible reconciliation.

(iv) Where the outcome of review is favourable but different modifications are requested, the applicant shall submit the comments from the different HREC or ethics committees their institutional HREC for consideration and possible reconciliation.

(v) HREC and ethics committees shall, as much as possible, consult with each other in order to resolve discordant reviews and generate consistent single response to multi-site research.

(n) Materials Transfer Agreement

Transfer of samples and biological materials such as animals, herbs and plants out of Nigeria shall require a Materials Transfer Agreement (MTA) detailing the type of materials, anticipated use, location of storage outside Nigeria, duration of such storage, limitations on use, transfer and termination of use of such materials subject to any law, regulations and enactment in Nigeria.

The purpose of MTA is to protect the interests of local researchers and Nigeria's human and natural resources in all its biodiversity as well as how they can be legitimately used. It ensures that the interests of all relevant parties, human and community participants in research and the Nigerian nation are protected from exploitation and egregious harm.

(1) The MTA shall be signed by all parties involved in the research including local and international principal investigators, heads of local institutions, research sponsors and other relevant parties.

(2) HREC shall review the MTA to ensure consistency with the stated objectives of the research, the contents of the informed consent documents and the principles enumerated above. The HREC shall grant provisional approval pending the submission of MTA to NHREC and receipt of acknowledgement from the NHREC.

(3) The applicant for research review shall file a copy of the MTA and provisional approval by the institutional HREC with the NHREC for record purposes only.

(4) NHREC shall acknowledge receipt of the MTA to the applicant who shall inform the institutional HREC.

(5) Institutional HREC shall grant final approval to research involving international transfer of Nigerian samples

after all other criteria stated in this code for approval of research has been met and upon receipt of acknowledgement of MTA.

(6) The MTA does not vitiate the right of research participants or communities to request that their samples be withdrawn from research according to the terms of the informed consent process.

(7) Where there is any change in the MTA, a request for amendment of protocol shall be submitted to HREC and HREC shall consider this in the usual manner used for amendment of protocol.

(8) Where there is verifiable proof that the applicant has sent a copy of the MTA to the NHREC and has not received an acknowledgement in 2 weeks, the applicant shall file evidence of this with the institutional HREC who shall proceed to issue the final approval for the research.

(o) Clinical Trial Agreement (CTA)

Where there is contractual agreement between a Sponsor and a Principal Investigator conducting a clinical trial, such contractual agreement requires approval by the Head of the Institution in which the trial is being conducted or designee thereof appointed for this purpose. Approval by the director of the institution, as mentioned above, is also required for any contract between a Sponsor or representative thereof and a Principal Investigator or any other Investigator who is taking part in and affiliated (as defined above) with the clinical trial.

The agreement shall include, inter alia, the following details:

(1) Names of all the parties signing the agreement, including the Principal Investigator, the Sponsor and/or representative thereof and the Head of the Institution where research is to be conducted.

(2) The clinical trial protocol, number and date of the protocol, and dates of any protocol amendments.

(3) Statement of commitment by the Principal Investigator to conduct the clinical trial in compliance with the National Code for Health Research Ethics, the ICH-GCP (and/or ISO 14155 for trials of medical devices), relevant oversight and regulatory agencies, institutional guidelines and the requirements of the Federal Ministry of Health.

(4) Approximate number of participants, budget of the clinical trial and payment dates.

(5) Statement of commitment by the Sponsor of the clinical trial to take out the appropriate medical insurance, including insurance against third-party claims resulting from the clinical trial.

(6) Statement of commitment by the Principal Investigator and the Institution to cooperate fairly and appropriately with the Sponsor in the event of a legal claim relating to the conduct of the trial.

(7) Statement of commitment by the Sponsor not to refer directly and/or indirectly in commercial publications to the name of the institution conducting the clinical trial and/or to the name of any employee of the institution conducting the clinical trial and/or to the trial results, and not to use their names as recommendations for the quality of the investigational product and/or medical device.

(8) The Director of the medical institution must ensure that there is no conflict of interest in conducting the trial at the medical institution between the commercial company and the Investigator, employee of the medical institution.

(9) In clinical trials where the Sponsor is a Sponsor-Investigator, he/she must present to the Head of the Institution or designee appointed for this purpose, an estimate of the cost of the trial and information regarding the sources of finance, and must ensure adequate arrangements for protection of trial participants and the study staff involved in the clinical trial.

(p) Communication with other regulatory agencies

HREC(s) shall have the authority to communicate with other ethics regulatory agencies and institutions about matters relevant to review of research. In such instances, HREC shall notify researcher(s), sponsor(s) and institution(s) about the communication(s).

(q) Process for NHREC review of research

(1) The NHREC may review research where:

(i) The research is nation-wide in coverage or

(ii) The research involves more than 3 sites in Nigeria or

(iii) The research was referred to NHREC by HREC(s) or

(iv) There is no HREC in an institution and the institution does not have a HREC cooperative agreement or

(v) The researcher considers the research of such complexity that there may be inadequate expertise in any one local institution or

(vi) At its discretion.

(2) The NHREC may review research by:

(i) Mandating review by any HREC in the country to act as a "HREC of record" and review the research on its behalf.

(ii) Constituting itself into a review committee and exercising all the powers applicable therein as outlined for HREC in this code.

(iii) Constituting an *ad hoc* HREC at its discretion.

(3) Where NHREC utilizes any of these methods, it shall assign continuing oversight of research to institutional HREC.

(4) Where NHREC assigns continuing oversight functions to institutional HREC, the institutional HREC shall have all the authority of oversight function as outlined in relevant sections of this code

(r) Fees

HREC may charge fees for any or all of its activities, at its discretion and in consultation with the principal officers of the institution.

(1) Fees may vary depending on the size, complexity, duration, status of researcher and sponsor of the researcher.

(2) Fees must be commensurate with anticipated expenses required for adequate oversight of research.

(s) Protection of participants in research

(1) HREC shall protect research participants

(i) All consent processes shall include explicit information about the researchers, their qualifications, their institutional affiliation, detailed contact information including telephone numbers and e-mail address, and all other necessary information that will allow the research participant, HREC, NHREC and institutional officials to contact the researchers as may be indicated.

(ii) The consent process shall contain the name, address, telephone number and e-mail address of the chairman of the HREC that approved the research, that of the institutional ombudsman or similar official(s) and all other individuals that research participants may need to contact in order to increase their knowledge about research or to complain about specific aspects of the research.

(iii) Where appropriate, as determined by HREC, researchers and research sponsors shall provide complete medical care and commensurate compensation for all research related injuries that participant may suffer.

(iv) Where appropriate, as determined by HREC, researchers and research sponsors may be required to provide evidence of insurance coverage of the research to provide adequate compensation for research related injuries, their care and compensation.

(v) Under no circumstances may research participants be asked to waive their legal rights, including the right to legal redress of research related injuries and compensations

(vi) Participants may complain directly to researchers or their associates, the HREC, institutional officials or the NHREC about any conduct that may have occurred in relation to their participation which breached ethical and scientific standards.

(vii) All complaints must be investigated by HREC and a report of the investigation as well as the decision of HREC about the complaint must be communicated to the researchers, research sponsors, institutional officials and NHREC within 3 months of the lodgement of the complaint.

(viii) The NHREC shall determine the action to be taken in all such circumstances based on the advice from the HREC

(2) HREC shall protect the right of researcher(s) to publish their research.

(i) In certain situations, this will require the submission of an agreement between sponsor(s), institution(s) and researcher(s) allowing researcher(s) to use the outcome of research in manner consistent with current practice within the research community.

(ii) HREC shall evaluate whether such agreement is necessary when the research is being reviewed and if found necessary, request same before approval is given.

(3) HREC shall protect researchers from exploitation.

(i) In certain situations, this will require the submission of an agreement between sponsor(s), institution(s) and researcher(s) indicating rights to, ownership of and rights of access to data, resources, intellectual property and infrastructure generated in the course of the research.

(ii) HREC should evaluate whether such agreement is necessary when the research is being reviewed and if found necessary, request same before approval is given.

(4) HREC shall protect communities participating in research from exploitation.

(i) In certain situations, this will require the submission of an agreement between sponsor(s), institution(s), researcher(s) and the community indicating adequate community consultation and agreement with the proposed research.

(ii) HREC should evaluate whether such agreement is necessary when the research is being reviewed and if found necessary, request same before approval is given. This implies that the HREC has ordinarily found the study approvable but requires that the community should be engaged and their assent sought before research is allowed to proceed. In this circumstance, the HREC cannot change its decision on the approval status of the research once the community engagement process has commenced.

(iii) Where applicable, such community assent or engagement efforts shall be documented and evidence of same submitted to HREC during the research review process.

(iv) The definition of community shall vary with research and shall be based on application of the best scientific principles.

(5) HREC must protect researcher(s) from undue pressure from sponsor(s), institution(s), participant(s) or any other source by ensuring that no researcher enters into an agreement or is subjected to circumstances that limits his/her legal rights, freedoms and obligations under Nigerian law to pursue his/her research activities.

(6) Responsibilities of researchers, sponsors and institutions where research is conducted

The investigator is responsible for the overall conduct and supervision of the research. Specifically:

(i) The investigator must sign the protocol and is responsible for ensuring that it is strictly followed. The investigator may not make any changes in the protocol without the prior approval of the HREC, except when necessary to eliminate an apparent immediate hazard or danger to a research participant or participants. Any change must be in the form of a protocol amendment,

appended to the original protocol and signed by the investigator, the sponsor, and the appropriate HREC.

(ii) The investigator, must promptly investigate all serious adverse events, take appropriate measures to ensure the safety of all research participants, and reports these and any other information that is likely to affect the safety of the participants or the conduct of the research events, to the Sponsor, HREC, NHREC and for any drugs/ devices testing research, to the NAFDAC.

(iii) The investigator must provide adequate and safe medical or dental care, where appropriate, to participants during the research, within the expertise of the investigator, and must ensure that appropriate medical care and follow-up procedures are maintained after the research for a period of time that is dependent upon the nature of the disease, the research, and the intervention(s).

(iv) The investigator must provide assurances that reasonable efforts shall be made to ensure that the benefits of research is made available to the community where the research was conducted. Details of any arrangement to ensure this shall be worked out by the researchers, sponsors, HREC, community leaders and Community Advisory Committees

(v) In the event of early termination of the research, except as ordered by the data safety and monitoring committee, HREC, NHREC, NAFDAC or any other oversight body or agency, the investigator must advise the HREC about this and the reason for the premature termination of the research.

(vi) In interventional studies, the investigator must provide evidence of adequate provision to cover claims for injuries, disabilities, or death of a research participant resulting from participation in research.

(vii) The investigator is responsible for the documentation of all steps in data management to allow step-by-step retrospective assessment of the quality of the data and the performance of the research.

(viii) The investigator shall ensure appropriate and timely feedback on the research process and findings.

The sponsor is responsible for providing all the necessary financial support for initiation and completion of the research study. Specifically:

(ix) The sponsor is responsible for the preparation and appropriate approval of a comprehensive final study report that is suitable for regulatory purposes, whether or not the research has been completed.

(x) The sponsor is responsible for the provision of special forms for the reporting of any adverse events that occur during the course of the research, and monitor the investigation and management of adverse events until resolution or stabilization.

(xi) The sponsor is responsible for providing compensation or indemnity in the event of research-related injuries, disability, or death.

For research involving investigational new drug/product, the sponsor:

(xii) Must ensure that the investigational product and any comparator products are of appropriate quality and are subject to quality assurance procedures. This information must be accurate and adequate to justify the nature, scale, and duration of the clinical trial.

(xiii) Must promptly provide to the investigator with any relevant new information that arises during the course of the trial, including information relating to product safety.

(xiv) Is responsible for the proper packaging and labelling of the investigational product(s) or medical device. The investigational and comparator products must be labelled in conformity with the protocol and the labelling must state that the product is for investigational purposes only.

(xv) Must retain sufficient samples of each batch of the investigational products under study and a record of analyses and characteristics so that, if necessary, an independent laboratory may check the product for quality control or bio-equivalence.

Host institution

The institution must work closely with, and monitor research activities of the investigator(s) at their institution. Specifically, host institutions should:

(xvi) Establish, and/or designate a functional Health Research Ethics Committee to review their research protocols in accordance with the provisions of this code.

(xvii) Ensure that they have qualified and competent investigators to carry out the research studies at their institution.

(xviii) Facilitate the smooth implementation of research studies conducted at their institution.

(xix) Take appropriate disciplinary action against investigators for non-compliance with these guidelines.

(xx) Implement disciplinary action against researchers, HREC members or the HREC as may be stated by the NHREC

Section F

Ethical Principles and Guidelines for HREC approval of research

In order to approve research covered by this code the HREC, shall determine a balance between the various principles guiding the ethical conduct of research, some of which are outlined below. Since some of these will inevitably conflict, judgement and consensus are essential in determining whether a research should be conducted.

(a) Research must have **social or scientific value** to either participants, the population they represent, the local community, the host country or the world, in order to justify the use of finite resources and risk exposure of some participants to harm. Research should evaluate issues that lead to improvements in health and contribute to meaningful knowledge. Such knowledge should be disseminated to all relevant stakeholders during and after the conduct of research. In certain instances, for example in some international collaborative studies, research should be integrated with comprehensive capacity building, technology transfer and health care delivery strategies that address significant local health problems and add value to local participants of research, including researchers, institutions, communities and the country.

(b) For research to be ethical, it must be have **scientific validity**. Research lacking clear scientific objective(s); using invalid methodology; that is underpowered; lacking equipoise (for clinical studies); whose operationalizing plans are inadequate within the context of the environment where research would be conducted; lacks plausible data analysis plan (including a specific role for a Data and Safety Monitoring Board [DSMB] in clinical trials) and research with biased measurement(s) of outcome(s) is unethical.

(c) Ethical research must ensure **fair selection of participants based on the scientific objective(s) of the research** while minimizing risk. This requirement refers to both who is included

and who is excluded from recruitment and the strategies employed for participants' recruitment (including choice of research sites and communities). Regardless of this requirement, participants who are at excessively increased risk of harm should be excluded. Children, pregnant women, socially, culturally, economically, politically, educationally, physically and psychologically disadvantaged groups, groups with constrained autonomy and other vulnerable populations should not be excluded from research without explicit reasons for doing so; particularly from studies that can advance their health and well being. However specific safeguards should be included to protect the vulnerable, appropriate to degree of risk. Groups, communities, participants and researchers who bear the burden of research should share in the benefits.

(d) All research involve risks; to be ethical therefore, there must be **valid attempts to minimize risks and maximize health related benefits** (as distinguished from risks and benefits of therapies that participants would be exposed to even if they were not participating in research or incidental risks or benefits) to participants in order to engender favourable risk benefit ratio within the context of where the research is being conducted.

(1) Where the risks outweigh the benefits to the participants, other criteria outlined in this code must justify such risks.

(2) Risks and benefits should be considered at the level of individual research participants and at the community, whenever appropriate.

(3) Comprehensive delineation of risks and benefits should be done for participants during the research, the population hosting the research and for both participants and population after completion of research

(4) Therapeutic procedures must fulfil requirements of clinical equipoise – there must be genuine uncertainty, among at least a significant minority of unbiased acknowledged experts who are not associated with the study under consideration, about preferred treatment.

(5) The risks associated with non-therapeutic procedures must be minimized by:

- (i) Procedures consistent with sound research designs
- (ii) Procedures that do not expose participants to undue risk
- (iii) Using procedures already being performed on participants for diagnostic or therapeutic purposes, whenever appropriate
- (iv) Applying risk-knowledge calculus to ensure that risks are reasonable compared to the knowledge to be gained from the study.

(e) For research to be ethical, it must undergo **independent review**. Research participants, researcher(s), sponsor(s) and institution(s) have multiple and overlapping interests which can generate conflicts and distort judgements. Independent review, through a system of ethical review and oversight of such systems assures society that reasonable attempts have been made to minimize the potential impacts of these conflicting interests and ensure balanced judgements.

(f) **Informed consent** is a *sine qua non* for ethical conduct of research. In order for consent to be valid, it must have the following components

(1) Adequate information must be provided at the educational level no higher than that of individuals with at most 9 years of education in Nigeria.

(2) The design of the consent process must be appropriate for the type of research, expected participants, risks anticipated and the research context.

(3) Consent forms shall not be longer than 8 pages in order to ensure comprehensibility and enhance recall of pertinent information. Unnecessary verbiage, legalisms, jargons and truth-dumping are to be avoided. The recommended format for each page of the consent form is as follows:

- (i) Paper size – A4
- (ii) Font – Times New Roman or similar
- (iii) Font Size – 12
- (iv) Spacing – 1.5
- (v) Margins – 2.5 cm, no gutter

(4) Where indicated, additional information can be provided on supplementary information sheets.

(5) The informed consent document shall contain the following aspects:

- (i) Title of the research
- (ii) Name(s) and affiliation(s) of researcher(s) of applicant(s)
- (iii) Sponsor(s) of research
- (iv) Purpose(s) of research
- (v) Procedure of the research, what shall be required of each participant and approximate total number of participants that would be involved in the research.
- (vi) Expected duration of research and of participant(s)' involvement.
- (vii) Risk(s)
- (viii) Costs to the participants, if any, of joining the research
- (ix) Benefit(s)
- (x) Confidentiality
- (xi) Voluntariness

- (xii) Alternatives to participation
- (xiii) Incentive (inducement) to participants
- (xiv) Consequences of participants' decision to withdraw from research and procedure for orderly termination of participation.
- (xv) Modality of providing treatments and action(s) to be taken in case of injury or adverse event(s).
- (xvi) What happens to research participants and communities when the research is over?
- (xvii) Statement about sharing of benefits among researchers and whether this includes or exclude research participants.
- (xviii) Any apparent or potential conflict of interest.
- (xix) Detailed contact information including contact address, telephone, fax, e-mail and any other contact information of researcher(s), institutional HREC and head of the institution.

(6) Research participants are entitled to retain a copy of the consent form.

(7) Where appropriate, researcher(s) may be required to undertake a re-consenting process during the course of research as determined by the HREC.

(8) Where, in ordinary circumstances, participant(s) are unable to provide written consent, researcher(s) must propose a process of consent that adequately records participants' informed decision such as witnessed thumb-printing or witnessed audio recording. The process proposed must be approved by the HREC before the research commences.

(9) HREC may require that all or some types of consent process be witnessed.

(10) Researcher(s) must keep all copies of consent form and make them available for examination by participant(s), sponsor(s), institution(s), HREC and NHREC.

(11) Where appropriate, HREC may require researchers to provide translations of consent processes appropriate to the socio-cultural characteristics of the population to be studied.

(12) All consent activities must be documented.

(13) Consent in other situations, including research involving children, persons with diminished autonomy, vulnerable populations and other extraordinary situations, including waiver of consent, are described in other guidance documents issued by NHREC.

(g) For research to be ethical there must be **respect for potential and enrolled participants**. This implies that potential participants be treated with respect from the moment that they are approached to the conclusion of the research should they choose to participate. Their right to privacy may not be needlessly compromised. Participants must know that their involvement is voluntary and that they can withdraw at any time without penalties. However, data, samples, etc. already contributed to the research up to that point may not needlessly be withdrawn as this may jeopardise the scientific validity of the research, unjust to those who remain in the study and all or part of their sample or data may have been used or modified into different form(s), including presentation at meetings or publications by the researchers.

Respect entails that participants must be treated as partners in the research enterprise with every opportunity taken to inform them of the progress of the research and any new finding that may have potential impact on their health and well being, and on their continued participation in the research. It also entails protection of the welfare of research participants. This means that the process of research must be carefully monitored to ensure that participants are not exposed to excessive risk and all adverse events are examined in detail and promptly. Such adverse events must also be reported to HREC

and efforts made to prevent future occurrences. Full medical care must be provided to participants who have suffered such adverse events and where warranted compensations paid.

The requirement to respect both enrolled and potential participants means that researchers should engage with communities where research is being conducted whenever this is appropriate. In certain instances, community consultation or assent may have to precede research activities in order to engender community buy-in and to respect the socio-cultural values of the community and its institutions. It may also be necessary to inform the community from time to time about the progress of the research, pertinent findings that may influence their health and well being, and the outcome of the research.

(h) For research to be ethical, nothing must be done to undermine the **trust relationship** that is at the heart of the researcher(s)-participant(s) relationships. This requires that there is transparency in all matters relating to the research enterprise including clear description of goals, risks, benefits, alternatives to participation and voluntariness. It is also necessary to determine the social value of the research and engage in creative approaches for effective representations and involvement of researchers and communities in the entire enterprise. Strategies for dynamic and reciprocal collaboration that leads to transformation of essential relationships based on reciprocity are also essential. This trust principle encourages the engagement of individual participants and communities, respects local socio-cultural values and encourages the provision of relevant and timely feedback to communities.

(i) For research to be ethical, **the interest of participants, researchers, sponsors and communities must be protected.** This will ensure that the research has lasting impact, transfers technology where appropriate, contributes to capacity building and demonstrates respect for socio-cultural and other differences. Risks, benefits and responsibilities of research must be shared during the development, planning, conduct, dissemination of results. Intellectual property, indigenous knowledge and contributions of all parties must be taken into consideration, adequately protected and compensated

particularly where research leads to tangible or intangible benefits. Satisfactory parameter(s) that shall determine sharing of commercial and other benefits should be clearly articulated and where indicated, benefit sharing agreements, materials transfer agreements, patent rights, intellectual property and royalties' distribution agreements should be signed before initiation of research.

(j) For research to be ethical, it must be conducted in accordance with the principles of **good clinical and laboratory practices**. These are international standards for designing, conducting, and reporting clinical trials that involve human participants. Compliance with these standards is additional assurance that the rights, safety and well-being of trial participants are protected in a manner that is consistent with the highest ethical and scientific standards.

Any clinical trial, including the planning, approval, conduct, recording, and reporting thereof shall be carried out in due compliance with the principles outlined in this code, the relevant laws, the provisions of the Federal Ministry of Health's guidelines, the provisions of the current **Harmonized Tripartite Guideline for Good Clinical Practice (ICH-GCP E6)** and the provisions of the current ISO 14155-1, 14155-2 (2003): **Clinical Investigation of Medical Devices for Human Subjects**, as well as regulations and guidelines published periodically by the Federal Ministry of Health.

Section G

HREC Education and Training Responsibility

(a) HREC shall organise, cause to be organized on its behalf, sponsor, support or associate with training and educational programs for biomedical, social and behavioural sciences' researchers.

(b) In order for such programs to be accepted for purposes of membership of HREC and as evidence of satisfactory training of biomedical researchers for purposes of research review, the curriculum must be certified by NHREC.

(c) Suitable educational programs must contain modules on national code of health research ethics, principles of research ethics, functions of HREC, research integrity and misconduct. Additional training in research methodology and administration may also be provided.

Section H

Independent Educational and Training Activities in Research Ethics

(a) Suitably qualified individuals and organizations shall have the right to provide training programs in research ethics for biomedical, social and behavioural sciences' researchers.

(b) For such programs to be acceptable for the purposes of membership of HREC and considered adequate training of biomedical researchers applying for review of research, the curriculum must be certified by the NHREC.

(c) Suitable educational programs must contain modules on national code of health research ethics, principles of research ethics, functions of HREC, research integrity and misconduct. Additional training in research methodology and administration may also be provided.

Section I

HREC Research Ethics Consultation and Clinics

(a) HREC may conduct ethics' clinics and consultations, at its own discretion, and upon payment of fees, as it may determine, for the purposes of providing advice to researchers during the development of research protocols or during the conduct of research.

(b) Such clinics and consultations shall be rigidly separated from the process of ethical review of research and shall not have any effect on HREC review or oversight functions.

Section J

Independent Research Ethics Consultation and Clinics

(a) Suitably qualified individuals or organizations may conduct ethics consultations and clinics, for fees, during the course of protocol development or during the conduct of research.

(b) All independent ethics consultations and clinical services must be certified by NHREC according to guidelines that it may release from time to time

Section K

HREC Records and Reports

HREC shall prepare and maintain adequate documentation of all its activities, including the following:

(a) All materials pertinent to research review such as:

(1) Copies of all research proposals reviewed.

(2) All reviews that accompany the proposals.

(3) Copies of approved consent documents, including forms, adverts etc.

(4) All progress reports submitted by researcher(s), institution(s) and sponsor(s).

(5) All reports of injuries to participants and adverse events.

(6) Attendance at meetings.

(7) Date proposals submitted and date approval given.

(8) Financial records.

(b) Minutes of HREC meetings which shall be in sufficient detail to show:

(1) Attendance at the meetings.

(2) Actions taken by the HREC.

(3) The vote on these actions including the number of members voting for, against, and abstaining.

(4) The basis for requiring changes in or disapproving research.

(5) A written summary of the discussion of controversial issues and their resolution.

(c) Records of continuing oversight activities.

(d) Copies of all correspondence between the HREC and applicants, researchers, sponsors, and any other agent consulted by HREC in the discharge of its duties.

(e) Statements of complaints or information/data used to determine decision(s) on research.

(f) The applicant applying for ethics review must submit the following:

(1) Copy of the research proposal.

(2) Copy of all materials to be used for the consent process such as consent forms and advertisements, including but not limited to promotional materials, advertisements, notices in newspapers, trade publications, audio, video and web advertisements.

(3) Copy of brief curriculum vitae (2 – 3 pages) of the principal investigator(s) sufficient to judge ability to carry out the proposed research.

(4) Copy of letter(s) of support from co-investigator(s), laboratories and sources of required resources.

(5) Where applicable, letter of sponsorship.

(6) One page plain language summary of the research.

(7) Copies of all questionnaires and instruments to be used for the study.

(8) Other ethics committee(s)' review of the study and their decisions, where applicable.

(9) Evidence of NHREC certified informed consent training by applicant and co-investigator(s) undertaken within 2 years of the date of submission of a valid application to HREC.

(10) Copies of all agreements such as the MTA etc. where indicated.

(g) Investigator(s) must submit an annual report on their research to HREC within 3 months of expiry of their current research approval.

(1) This report shall contain brief summary statistics about the research – number of participants recruited and their breakdown, number of adverse events, complaints and their resolution, any ongoing investigation or review and copies of any publications, reports or abstracts arising from the research.

(2) Failure to submit annual report within the stipulated period shall lead to termination of research by HREC. HREC may issue letters of notification advising researchers of the need to submit annual reports.

(h) HREC shall determine the form and number of copies of materials to be submitted by applicants for research review.

(i) All HREC records shall be accessible for inspection and copying by NHREC and through NHREC by other agencies at the discretion of NHREC and in a reasonable manner.

Section L

NHREC oversight of HREC functions

NHREC shall exercise oversight of HREC functions in order to promote the health and well being of research participants.

(a) NHREC shall review annual reports of HREC functions including:

(1) Record of attendance at HREC meetings to ensure that forums are formed, membership is diverse, outsiders are co-opted as indicated etc.

(2) Record of all materials pertinent to approval of research and their determinations.

(b) NHREC shall review materials from HREC to ensure that registration status is maintained.

(c) NHREC shall review the commitment of institution(s) to provide resources for proper functioning of HREC.

(d) NHREC shall, at its own discretion, conduct oversight visits to HREC.

(e) NHREC may institute disciplinary action including suspension of registration, debarment from review of all or certain categories of research or any such action as it may deem fit against HREC that is found to be in violation of this code.

(f) Any dispute arising from any quarters, including research participants, researchers, sponsors, institutional officials or any other source, about the appropriate interpretations or intentions of any section of this code, other than matters of legality, shall be referred to NHREC for clarification and elaboration.

(f) NHREC shall conduct any other activities in the exercise of its functions as enumerated in the relevant laws and guidelines.

Section M

Relationship with other regulatory agencies and oversight bodies

The Federal Government of Nigeria acting through any of its organs and establishments has the overall duty of protecting the welfare of the citizens of Nigeria. It may therefore exercise all the powers of protecting citizens according to the law, including citizens participating in research.

In addition, some agencies of state in discharge of their duties according to law may also exercise regulatory functions within the research environment.

(a) **Oversight of Clinical Trials by National Agency for Food and Drug Administration and Control (NAFDAC).** NAFDAC is the agency responsible for registration of new finished products for sale or use as food or drugs in Nigeria. NAFDAC therefore exercises regulatory functions in the conduct of clinical trials to test efficacy and safety of such products. NHREC is responsible for ensuring that all research including clinical trials are conducted according to the highest ethical and scientific standard. Clinical trials involving new finished products in Nigeria therefore require the permission of NAFDAC and compliance with both the clinical trials guidelines issued by NAFDAC and the National Code for Health Research Ethics.

(b) **Oversight by institutions.** Institutions where research is conducted may elaborate guidelines for the conduct of research in accordance with their enabling law and consistent with the need for maintenance of the highest ethical and scientific standard as outlined in this code.

Oversight by other committees such as data safety monitoring boards, biosafety committees, scientific committees, community advisory committees etc.

(c) **Oversight by Community Advisory Committees**

(1) **Oversight by Community Advisory Committees (CAC)** CAC are established by the study investigators depending on the nature of the proposed research, the research site, the study base or on the recommendation of either the institution research is based or the HREC supervising the research.

(2) They are important forums for facilitating dialogue between community members, research participants and researchers. CAC members should be identified from communities where research is to be undertaken through a stakeholder consultative process.

(3) The CAC role and expectations should be clearly stated in their terms of reference. Members of the CAC may include the following:

- (i) Persons with understanding of local laws, cultural values and gender issues
- (ii) Peer leaders
- (iii) Religious leaders
- (iv) Representative of the study population
- (v) Professionals who understand research or science issues
- (vi) Community leaders
- (vii) Representatives of the research team who should form no more than 20% of the membership of the CAC

(4) The primary role of a CAC is to assist investigators understand and incorporate community concerns into their research activities. This happens through different ways like relaying community concerns and problems to the community leaders, research team, institutional officials or the HREC; advising on; issues central to the informed consent process, achieving successful participants' recruitment and retention, among others.

(5) The responsibilities and terms of reference for CAC may vary according to the study location, size, etc, but generally, they are to:

- (i) provide information on traditional beliefs and needs of the study population and their concerns regarding research;
- (ii) where appropriate, CAC may provide input into the design of the protocol as appropriate including the informed consent process;
- (iii) advise on effective methods for disseminating information about the research and its outcomes;
- (iv) provide advice and support regarding recruitment and retention of participants in the research including gender equity
- (v) resolving ethical problems that may arise during the conduct of research and after the research is over

(d) Institutional Biosafety Committees (IBC)

Institutional Biosafety Committees (IBC) are established by institutions that undertake research on classified hazardous substances of physical or biological nature.

(1) Any institution involved in or planning to conduct research in the classified hazardous substance is required to set up or designate a competent IBC.

(2) Each IBC once formed shall consist of a biosafety officer and at least three other officers with appropriate expertise.

(3) The IBC shall comply with regulations and guidelines contained in the sub-code regarding research on hazardous substances issued by the NHREC.

(4) The IBC shall be registered with the NHREC.

(5) It is the responsibility of researchers to notify and provide to the IBC, the research proposal involving classified hazardous substances of physical or biological nature.

(6) The IBC shall minimize potential human and environmental risks associated with research on or with classified hazardous substances such as pathogens, radioactive material and applications of biotechnology especially recombinant DNA techniques and processes. In order to do this, the IBC shall:

- (i) Notify the NHREC of any research with hazardous substances in their Institutions
- (ii) Conduct biosafety review of research proposals on hazardous substances
- (iii) Ensure the provision of suitable and safe storage and disposal facilities for all materials involved in work with hazardous substances
- (iv) Ensure that all appropriate technical personnel of the institution have adequate training in biosafety
- (v) Institute a health-monitoring programme for all high-risk personnel involved in application, use and production of restricted categories of classified substances.

(e) Data and Safety Monitoring Boards

A Data and Safety Monitoring Board (DSMB) is an independent group of experts established by the study sponsors to review safety data during a clinical trial.

(1) DSMB ensures that the study is conducted and the data are handled in accordance with the provisions of the protocol and monitors adverse events and safety data.

(2) Where appropriate, DSMB should be established before the commencement of the clinical trial and its membership submitted to the HREC for their record.

(3) All interventional studies including drug efficacy trials, and all clinical trials should have a safety monitoring plan which will be implemented through the DSMB.

(4) The membership of the DSMB should include:

(i) Individuals with appropriately training and scientific knowledge in all aspects of research

(ii) People with adequate medical, pharmaceutical, scientific, biostatistical and/or ethics qualifications and clinical trial experience. The qualifications most appropriate for a specific DSMB will depend on the nature of the clinical trial and of the product under investigation

(iii) At least three individuals including a clinician with competence in the research field of the trial and a statistician

(iv) Individuals who are independent of the clinical trial and the sponsor.

(5) The functions and responsibilities of DSMB include:

(i) Ensure safety of study participants

(ii) Preserve the integrity and credibility of the trial

(iii) Ensure availability of definitive and reliable results in a timely manner

(iv) Make decisions related to the safety of the study, based on the submitted results and adverse event reports on whether the study should continue or not

(6) The DSMB must report to the sponsor(s) of the trial, HREC and institutional officials any:

- (i) Concerns over differences in serious adverse events between study arms
 - (ii) Serious social harms
 - (iii) Concerns about the conduct of the trial
 - (iv) Concerns about data integrity
 - (v) Whether the study should be terminated or continued based on safety and interim data
- (7) The DSMB should determine before the commencement of the study, the following:
- (i) Mode and time frame for receiving adverse events reports
 - (ii) Frequency of receiving data
 - (iii) Frequency of meetings to review the data and adverse event reports at hand. (Where there may be any element of concern, the DSMB may chose to review the data more frequently)
 - (iv) Channels of communication with the Principal Investigator, IRC and sponsor where necessary on decisions reached by the DSMB

Section N

HREC Compliance and Disciplinary Powers

HREC shall have the power to recommend to NHREC that disciplinary action is taken against researcher(s) who violates the norms, standards and guidelines set out in this code, institutional guidelines, rules and regulations and the law.

(a) Such recommendations shall be made after exhaustion of all steps outlined in this code for resolution of problems identified in research.

(b) Such recommendations shall be made after the matter is discussed at a regularly convened ordinary meeting of the HREC.

(c) All records pertinent to the matter shall be forwarded to the NHREC within 2 weeks of the HREC meeting at which the decision is taken to recommend the matter to NHREC and a formal notice shall be issued to the researcher(s), institution(s) or sponsors(s) by the HREC.

(d) Such recommendation shall not preclude the HREC from reporting acts that are clear violations of civil and criminal law such as fraud, assault and battery to constituted authorities or clear violations of institutional rules and guidelines to the institution where the researcher is based.

Section O

NHREC Compliance and Disciplinary Powers

(a) NHREC may advertise all cases of research misconduct reported to it, its plan of action and the resolution of cases to the public.

(b) NHREC shall take or cause to be taken disciplinary action against researcher(s), sponsors, or institutions that breach the tenets of this code.

(c) NHREC shall report all cases of fraud, deception, infamous conduct, plagiarism, fabrication, falsification to the appropriate regulatory, the police and other relevant authorities.

(d) NHREC shall bar researchers from conducting research for variable periods of time depending on the severity of findings of misconduct.

(e) NHREC shall cause researchers to make restitution appropriate to the case under consideration to research participants, collaborators, institutions, sponsors or any other persons as may be required by the facts of the case.

(f) In international collaborative research, NHREC shall report its findings of misconduct against researchers, sponsors and collaborators to the national ethics regulatory agency of the country of origin of the researcher. This does not preclude the institution of appropriate legal action, where indicated, against such researchers, his/her representatives, collaborators or agents in Nigeria.

Section P

Continuing Review of the National Code of Health Research Ethics and sub-codes

The NHREC shall regularly update, revise, edit and modify the National Code of Health Research Ethics in accordance with new developments in international research ethics, local laws and enactments and at its discretion.

The most recent version shall always be posted on the index page of the web site of the NHREC (<http://www.nhrec.net>) and shall be dated. The existence of a code with a more recent date invalidates all the previous codes and their provisions. The new code shall be enforced from the date indicated on it. Its provisions shall however not be retroactive.

Sub-codes provide additional guidelines and where their provisions appear to conflict with that of the National Code of Health Research Ethics, the latter shall be the superior authority.

The National Code of Health Research Ethics shall be available in different Nigerian languages but the English version shall be the only correct interpretation of the provisions of the code.