

Strengthening Structures for Research Ethics in Kenya: Landscape Analysis of the Actors and Processes of Clinical Research Review

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I. Authors and Acknowledgments

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Elizabeth Bukusi, MBChB, MPH, PhD, has been working at Kenya Medical Research Institute for the last twenty years where she has been involved in many research projects related to HIV/AIDS. She has over sixteen years of experience in SRH and HIV/AIDS and earned a medical degree and Masters in Obstetrics and Gynecology degree from the University of Nairobi. She then earned an MPH and a PhD in Epidemiology from the University of Washington, working among other things on a study to examine the male factor in bacterial vaginosis. She is currently a Chief Research officer at the Kenya Medical Research Institute where she heads the Infectious Disease control program committee. She also co chairs KARSCOM, Kenya HIV and AIDS Co-ordination Mechanism (KARSCOM) at the Kenya National AIDS Control Council. In addition, she has an honorary faculty appointment in Department of Obstetrics and Gynecology at the University of Nairobi and the Aga Khan University in Nairobi; and serves as an Associate Research Professor at both the Departments of Obstetrics and Gynecology and Global Health at the University of Washington. Dr Bukusi has served on the WHO Reproductive health country development program since 2002 and WHO Department of Reproductive health Scientific and Technical Advisory group (STAG) since 2008. She is currently undertaking a postgraduate diploma in Research Ethics at the University of Cape Town. Her research interests and experience have included studies examining diaphragm use among sex workers, an acceptability trial of male microbicide use, other HIV prevention options, and the effects of HIV treatment care and transmission with STD co-morbidities.

Yasmin Halima, MPH, serves as the Director of PATH's Global Campaign for Microbicides. Prior to joining the Campaign, Yasmin worked as a Consultant in HIV, specializing in treatment access in resource-limited countries and the scientific, policy and ethical challenges of developing pre-exposure prophylaxis (PrEP). As Consultant to the AIDS Vaccine Advocacy Coalition (AVAC), Yasmin worked closely with stakeholders engaged with PrEP, including the US Centers for Disease Control and Prevention (CDC), US National Institutes for Health (NIH), the Bill & Melinda Gates Foundation, as well as academic and industry scientists and activists. Yasmin was instrumental in establishing the International AIDS Society Industry Liaison

Forum (IAS-ILF), a clinical research initiative bringing together pharmaceutical executives with developing world scientists and policy-makers. As Editorial Consultant to NAM, Yasmin took a lead in organising the NAM clinical symposia programme. Yasmin is an active advocate in HIV; a former board member of the European AIDS Treatment Group (EATG) and currently also serves as the Vice-President of the US AIDS Treatment Activist Coalition (ATAC). Yasmin completed her MPH in Global Health at Columbia University, New York, where she continues her academic affiliation by guest lecturing on global health policy.

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II. Executive Summary

To reinforce Kenya's position as a leading site for international research, the National Council of Science and Technology (NCST) seeks to develop national guidelines for research oversight in Kenya. This report provides a landscape analysis of the clinical research review process in Kenya, outlining the laws, regulations, and stakeholders governing research and laying a foundation by which key stakeholders can consider revisions to this regulatory framework.

To inform the development of national guidelines, the Kenya Medical Research Institute (KEMRI) was asked to chair a Steering Committee—including NCST, University of Nairobi and the Pharmacy and Poisons board—to develop a comprehensive understanding of policies surrounding the review of research protocols in Kenya. Dr. Elizabeth Bukusi, a Chief Research Officer at KEMRI and the team leader of the Committee, invited the Global Campaign for Microbicides to collaborate in this initial study of the ethics review process.

In order to examine the landscape for the review and approval of biomedical and health research, a team led by Dr. Bukusi and an international consultant conducted interviews with key actors (governmental and nongovernmental) during the week of 8-12 March 2010.

With the division of logistical responsibility for oversight traditionally divided between the Ministry of Higher Education, Science and Technology (parent ministry of NCST) and the newly formed Ministry of Public Health and Sanitation and Ministry of Medical Services, the ethical review process for research is fairly decentralized and not all roles are clearly defined between:

- (1) government stakeholders (between ministries; between ministries and NCST; between ministries and NGOs),
- (2) ethical review committees (many inside educational institutions), and
- (3) other organizations (relevant to the review and conduct of clinical research).

This report outlines the official and stated roles of these organizations in the review of research proposals, highlighting gaps in current understandings of the regulatory process in Kenya.

III. Introduction

The first step toward the codification and standardization of the research clearance process in Kenya occurred with the 1977 Science and Technology Act. This law established the National Council for Science and Technology (NCST) as the seat of ethical and technical review for all manner of research conducted within the country. The NCST was tasked with determining priorities for scientific research and advising the government on national science policy.

Prior to and immediately following this law, the office of the President directly issued research permits. A 1979 amendment to the Science and Technology Act called for the formation of several institutes, which were tasked with carrying out research in specific areas. For bio-medical research, the Kenya Medical Research Institute (KEMRI) was founded and mandated with the responsibility of developing health research policy and priorities for the country, consulting with higher education for training of researchers and working with other research bodies locally and internationally.

In 1984, the NCST issued guidelines for research clearance, which laid out those who may conduct research in Kenya and under what circumstances. Private institutions based in Kenya could apply to the NCST for standing approval—provided that they followed their own specified standard operating procedures—but any non-Kenyan groups were required to seek affiliation with one of these institutions. Individual Kenyan individuals or institutions not preapproved could seek clearance directly from the Office of the President. Even after the establishment of the NCST, the process for seeking and granting research permits remained unclear. The original Science and Technology Act and subsequent amendments do not address the role of the ethical review process for studies involving human subjects.

In 2000, the World Health Organization (WHO) issued guidelines to establish an international standard for the make-up and standard operating procedures of ethical review committees.¹ To implement these international guidelines, WHO brought together a wide range of stakeholders to build capacity for the establishment of ethical review. Through meetings and workshops in various African countries (Kenya, Uganda, Zambia, and Malawi), it was noted that the existing ethics committees often did not adhere adequately to international guidelines in terms of process and membership. Out of these guidelines, WHO participants established Kenya's second ethical review process through the combined efforts of the University of Nairobi and Kenyatta National Hospital. In 2001, Kenya signed on to an Africa-wide agreement to use the Council for International Organizations of Medical Sciences (CIOMS) guidelines as the minimum requirement for research with human subjects. These International Ethical Guidelines for Biomedical Research, originally published in 1993, provide guidance for the national application of the international ethical principles of the Helsinki Declaration.

To address gaps in the rules pertaining specifically to human research, the NCST issued guidelines in 2004 to establish the processes by which institutions must grant permission to conduct research with

¹ WHO Operational Guidelines for Ethics Committees that review Biomedical Research. 2000.

human subjects.² Buttressed by additional requirements for HIV vaccine research, these NCST Guidelines for Ethical Conduct of Biomedical Research Involving Human Subjects in Kenya outlined how an ethical committee should be constituted and should operate in reviewing research. However, with the practice of ethical review highlighting gaps in the 2004 NCST Guidelines, the Steering Committee plans to hold a December 2010 stakeholder workshop to initiate discussions on the revision of national guidelines and to provide a framework for improved governance and management of health research in Kenya. This report informs that larger NCST discussion.

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² Guidelines for Ethical Conduct of Biomedical Research Involving Human Subjects in Kenya. 2004.

IV. Methods

This landscape analysis employs process tracing to examine the actors and processes involved in the review of clinical research. The specific steps of this method involved:

- Identification of key actors involved in the review or conduct of clinical research in Kenya;
- Gathering information from identified key informants through semi-structured interviews conducted at host sites;
- Collection and review of corresponding documentation, including legislation and regulation, scope of practice guidelines, correspondence among stakeholders, newsletters or other communication vehicles and organizational position papers.

Careful content analysis of interviews and ancillary documents allowed for the construction of a landscape model for clinical research review and the identification of institutional dynamics in the protocol review process.

This review was based on sixteen (16) semi-structured qualitative interviews with informants from governmental agencies, research institutions, and nongovernmental organizations. (To assure that no key actor or evidence was inadvertently overlooked, interviewees were asked to identify other participants in the clinical research review process who could provide additional perspectives.) The semi-structured, confidential interviews covered a variety of subjects and issues, focusing on the:

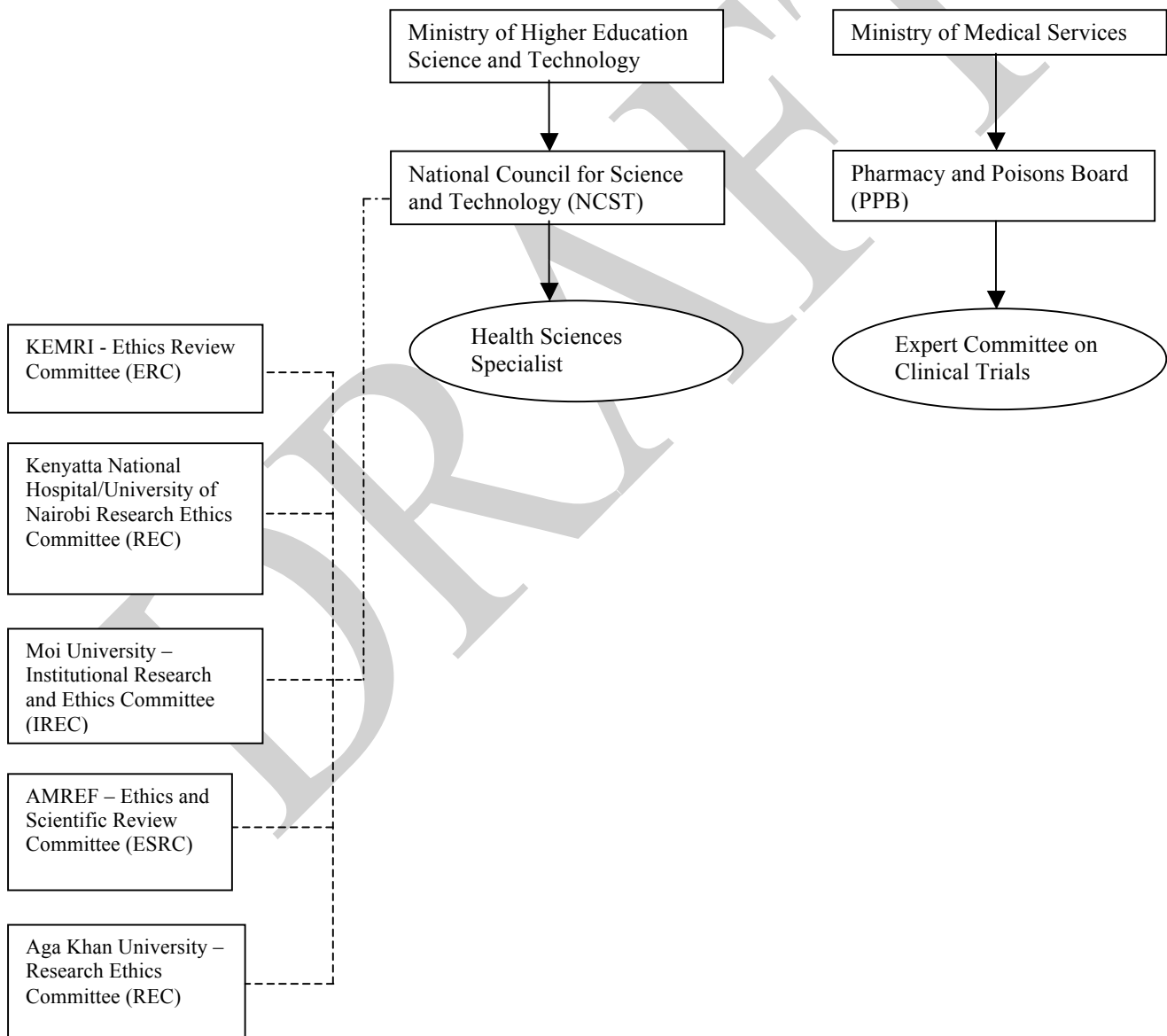
- Role of the informant in the research review process;
- Challenges encountered in the review of research; and
- Gaps in national policy.

Based upon notes and recordings from these interviews, and careful reading of supporting documents, a narrative description of the research review process was drafted and themes were identified for analysis. At the conclusion, several key informants were asked to review specific sections of the resulting landscape analysis in draft form to identify any factual errors and to comment on any conclusions drawn in this analysis.

V. Ethical Review Process

All biomedical and health research projects are required to receive approval from an authorized ethical review committee, with clinical trials subsequently requiring scientific and ethical approval from the Pharmacy and Poisons Board in order to import an investigational product or pharmaceutical. Subsequent to this two-step approval process, as depicted diagrammatically in the figure below, these institutions are required to keep the NCST apprised of the investigators and the current status of all research projects in Kenya.

Figure 1. The Kenya Research Review Process



With periodic reporting to these organizations required throughout the course of the study—culminating in yearly renewals—each study concludes with a final study report and a close-out letter to both the ethical review committee and the Pharmacy and Poisons Board.

A. Ethical Review Committees

No clinical research is permitted in Kenya without the approval of an authorized ethical review committee (ERC), as these committees are responsible for providing ethical research clearance before the start of any research study. With different formats and processes, which may lead to imprecise substantive standards for ethical review, the following five research institutions are authorized by NCST to approve research protocols through their respective ethical review committees:

1. The Kenya Medical Research Institute

Established by the Science and Technology Act of 1979, KEMRI is the main conduit for medical research in Kenya, exercising largely independent authority to conduct research in biomedical sciences. With its own Ethics Review Committee (ERC), comprised primarily of members who are not affiliated with the institute and its own guidelines for ethical consideration, KEMRI is responsible for carrying out health research through research sites countrywide, strengthening research partnerships with domestic and international research organizations and disseminating and translating research findings for policy formulation and implementation. Institutionally situated under the Ministry of Public Health and Sanitation, KEMRI has detailed standard operating procedures (SOPs)³ for research in general, a special SOP for the ERC specifically, and a Client Service Charter outlining what external clients can expect from the process.

The review process at KEMRI has three steps. For internal proposals—originating in one of KEMRI’s 10 research centres in Nairobi, Kisumu, Busia and Kilifi—the proposal first is reviewed by the scientific team within the centre carrying out the research to examine the quality of the proposal – with emphasis on the potential for capacity building, scientific and ethical soundness and appropriateness of research personnel. (As KEMRI also provides approval for foreign researchers without local partnership, this first step is bypassed for external research.) If the research proposal is passed, it is forwarded to KEMRI’s Scientific Steering Committee (SSC), where review is delegated to two experts in the field, who then present the proposal to the full SSC (made up of the Directors of each of the 10 KEMRI centres, the Head of Scientific Programmes, and Assistant Directors). If the SSC reaches consensus to approve the research, the proposal is transmitted to the Ethics Review Committee (ERC), where three members are appointed as the primary reviewers, who then present the proposal and their comments as lead discussants at the ERC’s monthly meeting.

In the ERC’s review, committee members consider the provisions for subject safety and the rights and well-being of research study participants by reviewing, approving and providing continuing review of

³ KEMRI. Standard Operating Procedures for Research and Related Activities. 2010.

(1) study protocols, (2) any amendments issued to the approved study protocol and (3) methods and tools to be used in obtaining and documenting informed consent of study participants. The ethical aspects of the proposed research study include, among other things, study eligibility criteria, recruitment plans, risk/benefit balance, plans for data oversight, statistical analysis, compensation and costs for study participants, provisions for confidentiality, sample repository and analysis plans. With processes that are seen as structured, predictable and transparent, KEMRI has developed informal mechanisms for sharing knowledge and lessons learned with other ethics committees.

2. Kenyatta National Hospital/University of Nairobi

The Kenyatta National Hospital (KNH) and University of Nairobi (UoN) have been authorized by NCST to conduct ethical review and approval through a joint Research Ethics Committee (REC). Its fifteen volunteer members—including social scientists and lay members—are appointed by the Director of KNH to conduct simultaneous ethical and scientific review of research proposals. Reviewing studies only from researchers collaborating with KNH or UoN investigators, funding for the REC comes from the KNH budget and application processing fees (with a sliding fee scale for internally and externally-sponsored research). As an all-volunteer body, the REC faces challenges related to both human and physical resources such as limited office space and computers. While there exists no prescribed training for new or existing members, new members are inducted by existing members and periodically supported to attend trainings through foreign ethics grants. With SOPs and a format for submission of research protocols for review, the REC meets monthly (or as necessary) to review protocols.

Upon receipt of an application, two REC members (one with expertise in the subject matter) present the study to an ad hoc sub-group, which reviews the application and can approve a proposal without tabling it to the full REC if the proposal meets the set ethics criteria or presents the study at the full REC meeting. The committee has no standing checklist for its scientific or ethical approval, but it seeks to review applications objectively, excluding personal and religious considerations and operating in general accordance with relevant national and international guidelines (CIOMS, Belmont Report, Declaration of Helsinki). Decisions are generally reached by consensus, with rare decisions made on the basis of a majority vote. With very few research proposals rejected for ethical violations or scientific flaws, the REC sees its role as providing guidance to investigators on research requirements (inviting these investigators to REC meetings when necessary), examining safety reports where adverse events have occurred and reviewing annual progress reports.

In this review process, the REC examines applications based upon: the design and conduct of the study, recruitment methods for participation, care and protection measures for research participants, confidentiality, informed consent processes, community considerations and local participation. This consideration of the extent of local participation is unique to ethical review through the KNH/UoN REC. Examining the roles, responsibilities and degree of involvement of KNH/UoN researchers, the REC notes that it advocates for strong local collaboration, arguing that local investigators “must be active actors in the research process, from design to execution, and not simply ‘sample suppliers’.” Viewing its ethical review as part of capacity building and technology transfer in Kenya, the REC reviews research budgets and propriety rights under intellectual property agreements and scrutinizes the

export of biological and other samples outside the country (often proposing instead that foreign researchers import any equipment necessary for sample processing and analysis in Kenya). Through this process of ethical review, the REC seeks to assure that the local researchers and local populations benefit from the study.

3. Moi University

Located in Eldoret, the Moi University College of Health Sciences (MU/CHS) and Moi Teaching and Referral Hospital created an Institutional Research and Ethics Committee (IREC) to serve as the regulatory body for the evaluation of scientific and ethical merits of research proposals. The IREC at MU/CHS was created in 1993 and authorized by the NCST in 2003 to conduct research reviews and provide ethical clearance for research protocols. With approval for research review, MU/CHS signed a memorandum of understanding with the University of Indiana, School of Medicine to further collaborative research participation between the two institutions.

Overseeing research and upholding ethics in research proposals, the IREC is comprised of seventeen members from various disciplines within and outside the Hospital (e.g., biomedicine, clinical and social sciences, biostatistics, and law). With members appointed to three-year terms by the Director of MU/CHS, the IREC's standard operating procedures (SOPs) require that these members meet a minimum of once every two months and require a quorum of half of the membership of the board.⁴ In reviewing proposals, there are detailed and standardized processes for submitting a proposal, with forms available on the IREC website. Although the guidelines do not go into detail about the evaluation criteria for ethical review, MU/CHS monitors and evaluates all approved research studies at a frequency deemed necessary – but no greater than once yearly for all active proposals.

4. AMREF

With the African Medical and Research Foundation's (AMREF's) strategic plan for 2007-2011 calling Health Systems Research one of its three main objectives, AMREF received NCST approval for its Ethics and Scientific Review Committee (ESRC) in November 2008. The ESRC was constituted so that all AMREF research involving human subjects takes the necessary ethical considerations and precautions, assuring that all research and evaluation conducted by AMREF staff and its partners conforms to the highest ethical and scientific standards. By February 2009, the ESRC membership was trained and in place to handle ethical issues arising from increased research undertakings by the foundation.

The 12-member ESRC is chaired by the Deputy Country Director of AMREF in Kenya and has so far reviewed 10 research proposals. In doing so, the AMREF application process is standardized and clearly laid out, with the appropriate forms available electronically. The SOPs clearly state that "Ethical clearance must be obtained for all approved research proposals, involving observations, questioning, examination, specimen collection or intervention with human subjects." This document goes on to

⁴ Institutional Research and Ethics Committee. Standard Operating Procedures. 2008. Available at: <http://www.mtrh.or.ke/IREC/Home2.html>.

explicitly mandate the composition and SOPs of the ESRC, which include a gender balance requirement and representation from the community and civil society. Members are appointed for two-year terms, with the larger committee meeting at least once every two months. While members are not paid for their involvement, they are eligible to receive a stipend of around \$12 US for each meeting attended.

5. Aga Khan University

The Aga Khan University Hospital has recently been granted authority to provide ethical research clearance through its Research Ethics Committee. With NCST's July 2009 approval, this nine-member committee—appointed by the University, with a minimum of two members trained in bioethics and five members from outside Aga Khan University—receives and reviews applications submitted by its medical school faculty and students. Much like KEMRI, the review process is reviewed by a scientific committee prior to ethical review, with approvals required by the Research Committee and then the Research Ethics Committee before the proposal is sent to the Board for full approval. Although policy documents state that the Research Ethics Committee shall meet monthly, limited workload has necessitated meetings only every other month.

Research Ethics Committee policies are being developed using international standards and Aga Khan International guidelines, with this process overseen by the Dean of Research at Aga Khan University in Pakistan. These standards for review have been codified in the Terms of Reference of the Research Ethics Committee, which provides a comparatively extensive website detailing committee SOPs and review criteria, with these criteria based on internationally recognized standards (WHO's International Ethical Guidelines for Biomedical Research Involving Human Subjects and NIH's IRB Guidebook).⁵ The Research Ethics Committee is able to stay apprised and review both the scientific and ethical aspects of the research through these detailed SOPs, which include board makeup, application procedure (with standardized application form) and on-going follow up.⁶ To maintain the capacity for this ethical review, the Research Ethics Committee has collaborated with KEMRI to train committee members, with further information sharing programs planned among the Aga Khan universities in East Africa.

B. Pharmacy and Poisons Board

Authorized as Kenya's drug regulating authority under the 1957 Pharmacy and Poisons Act and now situated within the Ministry of Medical Services, the Pharmacy and Poisons Board (PPB) derives its authority over the clinical trials process through a 2002 authorization to regulate the importation and distribution of pharmaceutical and medical products to be used in clinical trials. Within the PPB's Department of Pharmacovigilance, the Expert Committee on Clinical Trials (ECCT) was established in 2006 to review applications and protocols for investigational products and medical devices to be used

⁵ Aga Khan University Faculty of Health Science, Research Ethics Committee Terms of Reference and Standard Operating Procedures. 2008. Available at: <http://www.aku.edu/res-office/res-erc.shtml>

⁶ Ongoing research is difficult to monitor due to lack of capacity, although researchers are required to submit a progress form and report to the committee Administrator every six months.

in clinical trials and to approve all imports once a study has received approval by an ethical review committee.⁷

ECCT membership is made up of clinical research experts from outside the PPB, who are elected during the annual PPB meeting and meet monthly to review protocols and reports of ongoing research. Explicit training for ECCT members, especially the ECCT Secretariat, is sporadic, but members receive other training through their external appointments. In the PPB review process, the study protocol is submitted to the ECCT (electronically and in hard copy) along with an insert for the studied drug, the investigator's brochure (on the product manufacturing process, quality control, stability, and previous studies), trial site details, ethical review committee approval and a processing fee. Where necessary, the ECCT can request that the investigators present directly to the committee to clarify their proposal in-person. Once approved—allowing for a drug import permit—the ECCT requires safety reports from the investigators quarterly, or immediately in the case of an adverse event, with these reports reviewed as necessary. Although the ECCT provides communication with the investigators undertaking the clinical research, the ECCT does not have any independent communication with the ethical review committees responsible for the study.

In its review, the ECCT does not seek to reevaluate the ethical considerations of a protocol in detail, since it is understood that the study has already been given ethical approval by an NCST-authorized ethical review committee, with the ECCT serving instead to promote the search for new, better, more effective and safe drugs and medical devices. In doing so, the ECCT reviews the drug in question, the dosage, pharmacokinetics, previous studies/research in animals and adverse drug reactions before their use in clinical trials. During these reviews, the ECCT ensures that all necessary ethical considerations have been put in place and participant safety has been ensured. Although the PPB is in the final process of developing guidelines to expedite this review process, it has already begun to allow for parallel/simultaneous submission of a clinical trial protocol for ethics and regulatory review, allowing clinical trials to commence as soon as ethical clearance is granted.

C. National Council for Science and Technology

Responsible for all research in Kenya, NCST was created by and derives its authority from the 1977 Science and Technology Act, which gives it the mandate to advise the government on issues of science and technology and to review and approve all scientific research in the country.⁸ Where once ad hoc approval for research was given directly by the Office of the President, NCST's authorization was thought to provide a measure of stability and transparency to the research review process. Operating as a quasi-independent agency under the Ministry of Higher Education Science and Technology (MoHEST), NCST sets standards for ethical compliance, approves research clearances/permits, reviews applications for research grants and advises the government on how to implement the results of research.

⁷ Pharmacy and Poisons Board. Clinical Trials. 2010. Available at: <http://www.pharmacyboardkenya.org/index.php?id=21>.

⁸ National Council for Science and Technology. Available at: <http://www.ncst.go.ke/index.htm>.

In authorizing research, NCST's main role is to grant direct approval for research proposals it funds and to grant clearance authority to other organizations' ethical review committees. Since its inception, NCST has delegated its research review powers through the authorization of the five ethical review committees – KEMRI, UoN/KNH, Moi University, AMREF and Aga Khan University. Organizations seeking authorization to empanel an ethical review committee can apply to the NCST Health Science Specialist Committee in writing, following the set guidelines. Even where the NCST has granted these organizations the authority to approve research proposals, it reserves the right to summarily decommission any ethical review committee or summarily terminate any research taking place in Kenya.

Overseeing this process, NCST has a presence on KEMRI's board of directors and in the KEMRI Scientific Programs Committee, which reviews all research activity at KEMRI (representing the majority of research in Kenya). In addition, each institution is expected to submit annual reports to NCST on its research activity – including the number of proposals reviewed, number of proposals rejected, cases of serious adverse reactions, memberships of committees and trainings conducted or attended. Although the larger institutions (KEMRI, UoN) comply with this reporting requirement, the voluntary nature of this reporting process can lead NCST to be unaware of all the research conducted in Kenya.

To specify the substantive criteria for ethical review, NCST issued research guidelines in 1984, but these early guidelines did not specifically address ethical treatment of human subjects. Partially in response to Kenya's burden of HIV cases, NCST issued new 2004 guidelines specific to the ethical treatment of human subjects, "Guidelines for Ethical Conduct of Biomedical Research Involving Human Subjects in Kenya," using internationally recognized reference materials to outline the development and implementation of ethical review committee functions. These guidelines heavily informed the development of specific HIV vaccine research guidelines.⁹ To assure that researchers are aware of these regulations, NCST has advertised them in local newspapers and on its website.

⁹ Kenya National Guidelines for Research and Development of HIV/AIDS Vaccines. 2005.

VI. Non-Ethics Institutions Relevant to the Review & Conduct of Clinical Research

Outside of formal review mechanisms, many institutions take part in the research review process, largely by virtue of their roles in the conduct of research.

A. Ministry of Medical Services

The Ministry of Health was formerly the official government “parent” body designated to oversee health policy, HIV/AIDS programs, and ethical issues and dilemmas raised during biomedical research.¹⁰ As of May 2008, the Ministry of Health was split into two ministries – the Ministry of Public Health and Sanitation and the Ministry of Medical Services.¹¹

Under this new organizational structure, the Ministry of Medical Services (MoMS) holds responsibility for medical service policy formulation and implementation – providing preventive, promotive, curative, and rehabilitative health services: creating standards and regulations; and monitoring and evaluating health care service provisions. Within the MMS, the Director of Medical Services hosts the Department of Standards and Regulatory Services, which has “research and development” under its purview. Despite authorization for the Department of Standards and Regulatory Services to participate in the NCST ethical committee, this does not occur.

Thus, while MoMS engages professional regulatory bodies and medical training institutions, its formal role in the ethical review process is unclear. In practice, the MoMS has no official role in the ethical review process and does not have an ethical review board. Applications that are occasionally received by MoMS for research approval—for research to be conducted by MoMS or within MoMS facilities—are forwarded on to the ethical review boards at KEMRI or UoN/KNH. These concerns about MoMS roles and responsibilities in health research has led the Permanent Secretary to seek to establish national guidelines to regulate research review.

B. Ministry of Public Health and Sanitation

The Ministry of Public Health and Sanitation’s (MoPHS’s) main role in the clinical research process is to serve as the parent ministry to KEMRI. In the recent division of the Ministry of Health, KEMRI’s status as a ‘parastatal’ organization was upheld, but administrative responsibility for KEMRI fell to the newly formed MoPHS. Given this new allocation of research authority within the former Ministry of Health,

¹⁰ <http://www.statehousekenya.go.ke/government/health.htm>.

¹¹ <http://www.msh.org/news-bureau/leadership-perspectives-from-kenya-kiambati-aswa-25-05-2009.cfm>. Under this new system, The Ministry of Medical Services (MMS) provides treatment, care, and services to levels 4-6 of the health care facilities in Kenya, while the Ministry of Public Health and Sanitation (MoPHS) work from Levels 1-3 (dispensary to health centers).

KEMRI represents MoPHS at the NSCT and coordinates planning between MoMS and MoPHS. Nevertheless, MoPHS has a stated mandate under its Strategic National Plan to conduct operational research that informs policy, which is coordinated through MoPHS's Technical Planning and Performance Monitoring department and carried out by relevant departments within the Ministry. As such, the MoPHS plays an oversight role in public health matters relating to, among other things, water sanitation, disease control (AIDS and STI control), and international health relations.¹² While not currently engaged in any clinical research activities, the MoPHS is actively seeking collaborators through an Interagency Coordination Committee (ICC), and plans are in place to establish an ICC forum for the joint review of proposals (although the department which handled this under the former Ministry of Health is now situated under MoMS).

C. National AIDS Control Council

The National AIDS Control Council (NACC) was established by the State Corporations Act by Presidential Order in Legal Notice No. 170 of September 26, 1999 as a means "to provide policy and strategic framework for mobilizing and coordinating resources for prevention of HIV transmission and provision of care and support to the infected and the affected in Kenya."¹³ Its mission is:

1. To reduce the number of new HIV infections in both vulnerable groups and the general population,
2. To improve treatment and care, protection of rights and access to effective services for infected and affected people, and
3. To adopt existing programmes and develop innovative responses to reduce the impact of the epidemic on communities, social services, and economic productivity.

While the NACC does not carry out research, it has a coordinating function in determining priority areas for HIV related research.¹⁴ Operating with its public and private partners through the Kenya HIV and AIDS Research Co-ordination Mechanism (KARSCOM), NACC seeks to determine priority areas for HIV research through elaborate stakeholder consultations with civil society, NGOs, Community-Based Organizations (CBOs), and Faith-Based Organization (FBOs). In funding HIV research priorities, established through a JPR (Joint Programme Review), NACC has does not conduct ethical review but ensures that investigators undertaking research under the auspices of NACC (or those who have received NACC funds) have ethics approval from either KEMRI, KNH-University of Nairobi, or a group identified and constituted by NCST. To evaluate its research strategy under its strategic plan for HIV, NACC conducts joint annual program review of its four-year strategic plan and its two-year plan of

¹² http://www.information.go.ke/index.php?option=com_content&task=view&id=262&Itemid=388

¹³ http://www.nacc.or.ke/2007/default2.php?active_page_id=319; http://www.nacc.or.ke/2007/default2.php?active_page_id=125; http://www.youth-policy.com/policies/Kenya_National_HIV_AIDS_Strategic_Plan.pdf (This organization is not directly related to the research protocol, but has an interest in HIV/AIDS.)

¹⁴ NACC does not seek to dictate policy for HIV prevention research, which has been delegated principally to KAVI and IAVI.

operations (sub-activities from the strategic plan) to assess and modify Kenya’s goals for addressing HIV/AIDS.

D. Pharmaceutical Industry

The major transnational pharmaceutical corporations have been conducting clinical research in Kenya long before an ethical review process was established and have worked closely with the ethical review committees and PPB as they have taken shape to assure that industry studies continue to receive approval. To facilitate study approval, pharmaceutical corporations carry out research through principal investigators associated with one of the major ethical review committees. Working with local investigators, the corporations will often address the major regulatory hurdles and protocol submissions for the investigator, assisting investigators with protocol design/development/feasibility, informed consent forms, scientific rationales, and committee-specific formatting requirements. If any issues/queries are raised by the review committees (scientific or ethical)—e.g., attesting to budgetary sustainability, handling of biological samples (particularly if transported outside Kenya), or simplifying and translating consent processes—the corporation allocates staff to work with the investigators in addressing the issues or providing additional information.

E. Consortium for National Health Research

The Consortium for National Health Research (CNHR) was established in 2007 by a grant from the UK Department for International Development (DFID) and the Wellcome Trust to “improve the quality of health in the country through promotion of quality research, encourage the practice of evidence-based health policy formulation to improve health care and its delivery, build the research capacity of Kenya’s talented youth and the creation of functional strategic partnerships.” Within the CNHR, the Council of Founder Members establishes policies to foster and fund additional research in Kenya through the cooperative and collaborative efforts of governmental, nongovernmental, and academic research institutions. To institutionalize multidisciplinary health research in Kenya through a national health research policy that promotes production, analysis, storage, archiving, synthesis, packaging, sharing, and use of relevant high quality health research and technology, CNHR seeks specifically to work with other institutions to “strengthen the legislative framework under which health research is conducted.”

The CNHR is in the process of establishing a memorandum of understanding with the NCST for a division of labor in coordinating research across Kenya, seeking specifically

1. To establish a centralized national repository of all health research being conducted in Kenya¹⁵ and

¹⁵ As discussed earlier, no institution is currently compiling information on research conducted in Kenya, although CNHR held a conference in August 2009 to discuss the possibility of such a repository.

2. To convene stakeholders periodically for capacity building and continuing education in different areas of research development, review, and implementation.

As a means to bring institutions together collaboratively for the advancement of research ethics, coordinating research funding efforts while avoiding duplication, CNHR sees itself as a nongovernmental means to assure the harmonization of review processes and standards for research ethics.

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VII. Gaps in the Ethical Review Process

Based upon this landscape analysis, this study has identified the following gaps in the ethical review process for clinical research in Kenya.

A. NCST Authority

NCST's role in research clearance and authorization in the current landscape for ethical review of clinical trials needs to be more clearly publicized so that a variety of stakeholders involved or interested in health research are aware of its role in review processes. It is important for the NCST to provide this information in formats that can be accessed not only locally but also internationally since most health research taking place in Kenya involves international collaborators. While NCST is legally responsible for granting permission to other institutions to form and operate ethical review committees and has de jure oversight over all research in Kenya, the NCST needs to ensure standardized application of all review and oversight procedures nationally. Establishing a clear and transparent mechanism for approval and accountability will assure that clinical trials can be efficiently and effectively undertaken in Kenya.

In addition to authority for approval, NCST requires transparent abilities to sanction those who run afoul of research ethics. While the NCST has authority to inspect research sites at any time or even raise any queries, NCST needs to clearly outline situations that would lead to termination of studies that have received ethical approval from the ERCs, receiving adequate resources to discharge its research oversight functions. To begin to address these challenges, NCST is currently advancing a draft bill through Parliament to provide it with financial, human, and technical resources independent of the Ministry of Education, Science and Technology, allowing NCST to formalize its mandate to streamline the structures of application, review, and approval of research proposals. Should these additional authorities be granted, it will be important for the NCST to publicize this to a broad range of research stakeholders.

B. Ethical Review Harmonization

Among the six institutions that have authorized ethical review boards, there is no formal mechanism to standardize processes, procedures, and substantive standards of ethical review. Having uniform processes and standards across different organizations is important for the research landscape in Kenya for a number of reasons. Most importantly, an unscrupulous investigator could engage in 'forum shopping' – applying to the review board that is perceived to be the weakest or applying to more than one institution simultaneously. (To alleviate forum shopping, KEMRI has an MOU with UoN/KNH, which spells out a non-compete arrangement in the event that proposals are simultaneously submitted to both organizations.) Secondly, in the absence of any concrete ethical guidance in decision-making, many ethical review committees focus on the scientific basis of the proposal and the content of the informed consent forms. And finally, international investigators are more likely seek

partnerships with local institutions if they are assured that research they are engaging in will follow the letter and spirit of the local law.

As the oldest and largest research institution in Kenya, KEMRI has relationships with most of the other ethics boards and has conducted informal training and capacity building activities with them. Beyond these mechanisms, there is no national-level body coordinating the harmonization of processes in the various ethics review committees. At the national level, NCST has held several meetings in the past to bring ethical review committee members together in a forum to share experiences and raise the issue of harmonization; at the international level, ethical review committee members in the East African region interact and exchange experiences, mostly through regional bioethics training workshops or ethics meetings.

Nevertheless, informants remained concerned that there are no standard practices enforced across ethical review committees, and NCST has yet to establish and standardize best practices for these committees. For example, the ethical review committees examined in this report all take their standards and operating procedures from recognized international guidelines (CIOMS, Belmont Report, Declaration of Helsinki), but there is no mechanism to assure the application of these standards by the ethical review committees. Although NCST issued guidelines on ethical conduct of human research in 2004, these have not been routinely incorporated in the policies of ethical review boards, and there is no mechanism in place for NCST to verify that ethical review boards meet these standards.

C. Capacity Building

Although there is widespread agreement that ethical review boards need “initial and continued education regarding the ethics and science of biomedical research”—a WHO consensus replicated in NCST’s Guidelines for Ethical Conduct of Biomedical Research Involving Human Subjects in Kenya—this recognized importance of ethics education needs to be strengthened in the policies and practices of ethical review boards.

While the SOPs for ethical review boards all specify the qualifications and makeup of their respective boards, none require any previous knowledge or training on ethical matters. Where membership in these boards is usually based primarily on clinical, legal, or community engagement experience and expertise, it is imperative that all members are trained in ethics at the onset so that ethical review can be grounded on a framework guided by internationally accepted ethical standards.

With current regulations prescribing no level of training in ethics for ethical review committee membership, informants often found that standards for the capacity of members are vague and unenforceable. Some ethical review boards have conducted training sessions for their members, largely through work with international research institutions, but it will be necessary to develop a sustainable national effort to engage ethical capacity building, to train members in bioethics if they are to strengthen ethical review.

D. Clinical Research Documentation

One of the conditions under which organizations are allowed to grant ethical clearance is that they must submit annual reports on the outcomes and progress of research that is approved; however, this requirement is largely overlooked and unenforced.

Aside from depriving NCST of important information for oversight, this also means in practice that there is no central repository of up to date information on current research in Kenya. Several informants stated that they were unable to easily find out who else was doing similar research in Kenya and thereby to benefit from their experiences. This is especially important for the ethical review process, as issues or problems that have come up in the past could be used to inform current decision-making.

In August 2009, CNHR held a conference to solicit ideas about the establishment of a resource database of approved studies in Kenya and the results of these studies (similar to the United States database clinicaltrials.gov). If NCST could enforce the current requirements that the investigators provide information for ongoing studies, it would be possible for an organization like CNHR to assist NCST with the technical support necessary to create such a database.

Conclusion

Internationally sponsored research is moving toward a model by which studies will be conducted only in countries in which there are clear regulatory and ethical frameworks. To assure the benefits of this research, Kenya will need to ensure that approval processes for biomedical and social scientific research are (1) clear, (2) simple, and (3) transparent.

To assure the future of Kenyan research systems—for the benefit of the health of the Kenyan people—it will be necessary to consider the development of national guidelines for health research. As such, this report recommends a meeting of key stakeholders to clarify and coordinate the different authorities and institutions in this ethical review process. It is expected that this report will serve to support such a stakeholder meeting, allowing stakeholders to clarify the institutional processes and standards necessary for health research governance in Kenya.

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