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The Quest for Ethical Isometric Principles in Cross-Cultural Bioethical Research

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Preamble

It is undeniable that contemporary corpus of biomedical research continues to gather unprecedented volumetric proportions sometimes beyond the assimilative powers of many scholars even within the scientific community. We also see an increasing trend of pharmaceutical companies relocating their operational outputs and research interests in many emerging/developing countries such as India, South Africa, Ghana, Brazil and Mexico.[1] These countries have different and unique socio-linguistic dispositions that are different from those of the researchers. Since 2002, nearly 15% of clinical researches registered with the FDA have been conducted in developing countries.[2] One of the major challenges emanating from this research has been the clash between competing ethical norms during these researches. This is evident when researchers from industrial worlds find and construe certain norms in developing world as unethical. Thus an internal conflict of ethical norms poses a conundrum for the researcher. Should the researcher respect the local norms that might be seemingly at variance with his own norms? Should the researcher ignore these local norms and thus impose his own norms on the local people? In a seminal paper on this ethical phenomenon, Ezekiel Emanuel proposes certain ethical "frameworks" or "benchmarks" for investigators conducting research in developing countries.[3] He calls for greater transparency, disclosures and accountability on the part of researchers to minimize risks and avoid exploitation among others.[4]

Many scholars contend that the researcher should not impose his native norms to the local folks, as this may constitute a kind of "ethical imperialism."[5] But the researcher may also encounter certain norms that contravene international norms such as the *Declaration of Helsinki*, *Nuremberg Code* and *FDA* regulations and is under obligation to act appropriately and accordingly. For instance, a researcher may discover that in certain places, the notion of *consent* is accepted by the elder/chief of the community on behalf of the people. If the researcher decides to seek individual consent from participants devoid of the permission from the community leaders such as the chief, the chief may not trust him and this may undermine integrity of his research work. The intent of most community leaders is to protect their citizenry from perceptive predatory investigators/investors due to certain historical precedents such as colonialism and exploitation. In brief, we see genuine efforts on both parties in ensuring that both "local" and "international" ethical norms are respected in protecting participants from any form of overt or covert exploitation. But this also raises many questions. I believe that the issue of relativism and respect for universal ethical principles constitute a penumbra of ethical issue within global health research context. Consequently, this piece proposes *Ethical Isometric Principles* (EIP) that limit such ethical morass.

Scope

In an increasingly globalized world, biomedical research continues to transcend many cultures. Which ethical norm should researches follow and why? Can researchers and research participants agree on some operational ethical principles especially if there are differences? Responses to these questions will constitute the foci of this piece. The first part of this article explores the etymological and conceptual analyses of the *Ethical*

Isometric Principles. The second part will make an attempt to apply the *EIP* to cross-cultural biomedical research in contemporary times especially in developing world. This will be followed by some perspectives.

Expose on Ethical Isometric Principles

Etymologically, *isometric* is an adjective derived from the juxtaposition of two Greek words *iso* (ίσο) which is transliterated as "equal" and *metrikos* (μετρικός) which means "measure". "Isometric" implies equality of measure. Literally, *Ethical Isometric Principles* implies the mutual agreement that exists between researchers and human subjects in specific socio-cultural contexts and time.

Ethical Isometric Principles (EIP) in this piece means certain operational principles that both researcher, participants and designated regulatory entities could agree on during clinical researches such as translating the entire research protocol into local languages/dialects, leveraging formal educational and power differentials between researcher and participants, perspective assessment as a litmus test to insulate stereotypes and prejudices in cross-cultural clinical research, aligning risks-benefits quotients with local perceptions and practices among others. These principles would guarantee equal or even consensus between researchers and participants in biomedical research. In other words, international principles such as respect for autonomy of the individual, non-maleficence, dignity, justice, informed consent be adhered to especially when conducting research involving human subjects.

This paper challenges researchers to establish some kind of *linguistic isometricism* where research is *translated* and/or *interpreted* into the local languages by incorporating appropriate local jargon, conceptions and expressions that are most meaningful to the research participants.[6] This will help participants understand and assimilate the entire gamut of the research and also alley any iota of fears participants might have. For example FDA regulations (21 CFR 50.25 and 21 CFR 50.27) and the Department of Health and Human Service directives (45 CFR 46.116) and 45 CFR 46.117 unequivocally specify that *Informed Consent* should be in a language comprehensible to research participants.[7] Examples in Brazil, Kenya, Sri Lanka, many successful HIV AIDS campaign and researches and preventive campaigns were translated into various local languages for research participants.[8]

If there are conflicts of competing norms between international and local norms, researchers should look for a kind of "*Ethical Isometric Principles* (EIP). These involve active dialogue and engagement with the local people about norms that may be in tacit conflict or different with ethical principles in order to arrive at a common consensus. If possible an operational "common consensus" could be written so that both researcher and participating communities could use to leverage trust and respect for one another in ensuring that no harm is done to any one during the research. As indicated in the *Declaration of Helsinki* and affirmed by the World Health Organization (WHO), *"Every clinical trial must be registered in a publicly accessible database before recruitment of the first subject".*[9]

Another dimension of the *EIP* is that investigators should make conscious efforts to have the scope, protocol, and consent documents reviewed, and if possible approved by local IRB (if one exists) prior to approval from their home country or institutional IRBs. Both local and international IRBs should smooth out any concerns they have with the research protocol. The current practice where IRB in the investigators place of origin are accepted devoid of any scrutiny from the participant's locality without meticulous review warrants some modicum of concern and could have synergistic impact on the integrity of the research.

Furthermore, educational levels of participants should be considered. If possible, participants in developing countries should have a certain level of formal education in ensuring greater protection from exploitation. There may be some exceptions. For instance, if the biomedical research is about a pathogen or particular disease that is endemic to areas where it is difficult to find participants with some formal education, then such a research may continue. The fact is that most people without or with little formal education may be considered vulnerable populations due to the educational differentials that exist between them and researchers. For example, in the infamous *Tuskegee Syphilis Project* (TSP), many of the research subjects had no formal or little educational backgrounds and barely knew of what was going on.[10] Involving people with some modicum of formal education will leverage the playing field for research and insulate vulnerable populations from exploitation and implicitly give greater authenticity and credibility to the outcome of the research in cross-cultural contexts. This, I believe, is the quintessence of EIP.[11]

Stereotypes and prejudices are powerful and inherently cloud judgments in clinical settings even with the best of good intents from researchers. People differ due to geophysical locations, socio-cultural experiences, educational backgrounds as well as sociopolitical and economic factors. These factors, coupled with intrinsic tendencies in some people to prejudicially stereotype others, are grave issues that need to be addressed in clinical research with cross-cultural dimensions. For example, substantial stereotypic evidence about black males was found in many correspondences between investigators in the TSP that not only devalued other persons but also clouded clinical judgments.[12] We see this phenomenon also during Nazi atrocities where some people suffered egregiously due to their race and cultural background. To this effect, it is the contention of this paper that every researcher undergo a kind of *perceptive assessment* either in the participants country or in their own country of origin approved by the IRB to ascertain that there are no residues of biases or stereotypic proclivities towards the participants prior to any research. If possible participants should undergo similar assessments prior to the research. This is important because in certain cultures, participants might not readily opt out of a research and they may end up giving information that might undermine the authenticity and objectivity of researches that might be of critical pharmacological and clinical value.[13]

Researchers should carefully weigh the risk involve in research designs to align with local perceptions of risks and benefits. In addition, indices of risks and benefits should be driven by pure scientific necessity and local needs. To ensure greater protection for vulnerable populations, researchers should be in consistent communication with local health directorates and clinics in analyzing risks. A specific plan (either short or long term)

should be put in place to care for participants in the events of injury during clinical trials that involve invasive therapies, such as chemotherapy. All of these should be communicated to participants prior to enrollment into the research. For example, recently many participants in India who enrolled in clinical trials for cervical cancer died, prompting a halt to the trials and ethical inquiries.[14] Most of the victims were in the *control groups*. Initial investigation conducted by the *US Office of Human Research Protection* suggests that proper informed consent might not have been obtained from the victims. Furthermore, the level of risks involved in the research were not well disclosed to participants to the extent that such protocols will not have been approved to take place in the US or any developed country.[15]

Perspectives and Conclusion

The debate between cultural relativism and universal ethical principles during research continue to pose ethical, policy and legal quagmires. Relativism is a serious ethical principle that holds the view that ethics or morality varies from person to person or culture to culture. On the other hand some ethicists have suggested universal ethical principles such as respect for autonomy, justice benevolence, non-maleficence that seem transcends all cultures be followed during biomedical researches. In conducting clinical research, we see these notions generating certain ethical tensions. These issues become even more complex as significant clinical researches take place in many developing countries that may have unique ethical systems. Sometimes, some of these local or cultures may easily accept westernized clinical protocols. In some instances the local ethical system may be seemingly and diametrically opposed to general principles of informed consent, autonomy, justice. This piece acknowledges these challenges. This paper has contended and suggests *Ethical Isometric Principles* as a solution to some of these challenges especially as applicable to the global/cross-cultural nature of conducting clinical researches in developing countries. Simply put, when divergent ethical principles occur among the researcher and the local people, it is possible to reach a common consensus that respects both parties and at the same time ensuring that no harm occur to any human subject. As a prominent ethicist poignantly noted:

> … an ethical framework for research in developing countries must provide more than broad principles. This framework of principles and benchmarks is complex, because ethical evaluation of clinical research is complex. A single ethical principle is rarely absolute; most situations implicate multiple principles. Consequently, the various principles and benchmarks will compete and must be balanced against each other—a process that inevitably requires judgment.[16]

In brief, clinical research/trials are important in general health care for the global community. Recruiting participants in developing countries should be carefully aligned with the coefficient of protection for vulnerable human subjects. The contention of this piece is that every effort should be harnessed to ensure that even if there are doubts about the applicability of international ethical norms to specific local situations, some kind of "*ethical isotopy"* is reached at least by both researchers and participants prior to commencing a clinical research. After all as the aphorism goes *medio tutissimus ibis*-it is

better to go in the middle of things. Or put succinctly, *in medio stat virtus*-virtue or ethics lies in the middle of two extremes.[17] Arriving at such an *Ethical Isometric Principles* will continue to involve open, honest, transparent dialogues for researchers, participants, designated regulatory and neutral agencies involve in biomedical research.

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[1] Glickman, Seth et al. "Ethical and Scientific Implications of the Globalization of Clinical Research." *New England Journal of Medicine* 360, no. 8 (2009): 816-23. See also, Arun Bhatt "*Quality of Clinical Trials: A moving Target* in *Perspectives" Clinical* Research. Vol 2, no 4 (2011 Oct-Dec):124–128

[2] Ibid

[3] Ezekiel Emanuel et al. "What Makes Clinical Research in Developing Countries Ethical? The Benchmarks of Ethical Research" *Journal of Infectious Diseases* Vol 189, no5 (March 1, 2004):930-937

[4] Ibid. See also Ezekiel Emanuel *et al* "What makes Clinical Research Ethical?" *JAMA* Vol 283 no 20 (2000):2701-2711

[5] Angell, Marcia. "Ethical Imperialism? Ethics in International Collaborative Research" *New England Journal of Medicine* Vol 319, no (1988)

[6] http://www.ispor.org/workpaper/research practices/PROTranslation_Adaptation.pdf

[7]Wade, Mark "Translation plays a critical role in global clinical trials" *Future Pharmaceuticals,* Vol 2, (2006):16-19 and Alicia Bolaños-Medina. "The Key Role of the Translation of Clinical Trial Protocols in the University training of Medical Translators" *Journal of Specialized Translations* Vol 17, (2012)

[8] Ibid

[9] Article 19 of the *Declaration of Helsinki*

[10] Jones J *Bad Blood: The Tuskegee Syphilis Experiment*. 2nd ed. (Free Press: New York, 1993)

[11]Jennifer Hawkins et al. *Exploitation and Developing Countries: The Ethics of Clinical Research.* (Princeton University Press, NJ 2008)

[12] Jones J. *Bad Blood* Ibid

[13] Ezekiel Emanuel et al *Clinical Research Ethics* (Oxford University Press; London, 2011). See also Angus Dawson et al. *Ethics, Prevention and Public Health* (Oxford University Press; London 2009) see also Ankier SI *Dishonesty, misconduct and fraud in clinical research: an international problem* in Journal of International Med. Res. (2002 Jul-Aug) 30(4):357-65

[14] Agomoni M. Ganguli Care And Consent: The Fraught Ethics Of International Clinical Trials in The Conversation (October 2013)

[15] Ibid

[16] Ezekiel Emanuel. *What Makes Clinical Research in Developing Countries Ethical? The Benchmarks of Ethical Research* (2004):930

[17] Aquinas is purported to have translated it from Aristotle