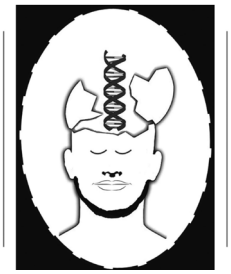

Rethinking Clinical Trials and Redefining Responsibility for Research Participants

A Focus on Africa

By
Ike Iyioke

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I dedicate this book to the Iyioke family: first, to my dear wife Ifeoma Chika Iyioke, PhD., our sons IkeNna Jr., ArinzeChukwu, IliloChi; and daughter SopuruChi. Their support has made my experience at Michigan State University a life-long lesson to cherish. It is in them that I find my anchor.

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Key to Abbreviations/Terms

Adverse Drug Reaction (ADR): A response to a drug that is noxious and unintended and occurs at doses normally used in a human for the prophylaxis, diagnosis, or therapy of disease, or for modification of physiological function. Adverse drug reactions are classified into six types (with mnemonics): dose-related (Augmented), non-dose-related (Bizarre), dose-related and time-related (Chronic), time-related (Delayed), withdrawal (End of use), and failure of therapy (Failure).

Adverse Event (AE): Any untoward medical occurrence in a patient or clinical investigation subject to whom a pharmaceutical product is administered. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether related to the medicinal (investigational) product.

All-in-one (one-in-all): A term I have used to depict the suffusion and inseparability of the individual into his or her community and environment.

Alleles: Different forms of the same gene, usually arising through mutation, that are responsible for hereditary variation.

BEC: Bio-eco-communalism just like the concept of one-in-all, refers to the inseparability of the individual within his/her community and environment. I coined it as the hallmark of my thesis.

Biome: A term from the Greek bios, meaning relation to life; used in ecology to include major life in the area, such as tundra biome, tropical rainforest biome, and grassland biome.

Biomass: The amount of matter of biological origin in a given area, for example, the living and decaying matter in the soil, as opposed to the inorganic mineral components such as sand, silt and clay.

Biosphere: (a) The zone on the earth's surface where all life exists; (b) all living organisms of the earth.

Biota: All species of plants and animals occurring in a specific area.

CRS: Corporate social responsibility is a duty or an in-built commitment by corporate bodies to uphold ethical values and ensure quality of life of the workforce, the local community, and the physical environment, while earning profits.

Ecosystem: A biological system composed of a community of organisms and the nonliving environment with which it interacts [same for Environment and Ecology].

GMM: Genetically Modified Mosquitoes, also called genetically engineered mosquitoes, transgenic mosquitoes, or living modified mosquitoes – are mosquitoes that have heritable traits derived through use of recombinant DNA technology, which alter the strain, line, or colony in a manner usually intended to result in reduction of the transmission of mosquito---borne human diseases (see Chapter 2 of this book for more details).

The Global North: Also known as the industrialized world, Western, or Euro-American -- refers to the 57 countries with high human development that have a Human Development Index above .8 as reported in the United Nations Development Program Report 2005. Most, but not all, of these countries are in the Northern Hemisphere. A few decades ago, the North could have been approximately defined as Europe along with others like Canada, the U.S., Australia, and

New Zealand, but Japan has also, clearly, been an industrialized country for many years. Several other East Asian countries, including Singapore, South Korea, and Taiwan have shifted into the North in recent decades.

Global South: The industrializing world or The Global South refers to the countries that are mostly located in the Southern Hemisphere. It includes both countries with medium human development index, HDI (88 countries with an HDI less than .8 and greater than .5) and low human development index (32 countries with an HDI of less than .5). Thus defined, the Global South is made up of some 133 countries out of a total of 197. Most of the Global South is located in South and Central America, Africa, and Asia – and boasts the greater population bloc, a.k.a., The Majority World. Together, the Global North and Global South constitute virtually the entire global population.

Holism: The interconnectivity and interdependence of all things in a given sphere.

Serious Adverse Event, SAE, or Serious Adverse Drug Reaction, SADR: Any untoward medical occurrence that at any dose results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.

Vulnerable subjects: Individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental, and nursing students, subordinate hospital and laboratory personnel, employees

of the pharmaceutical industry, members of the armed forces, and persons kept in detention. Other vulnerable subjects include patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors, pregnant women, and those incapable of giving consent.

Foreword

The practice of research ethics in Africa has been on the wrong path. The time for redress is now (or it was yesterday). Because the history of the research ethics (and the broader bioethics) field has largely been Western, it is understandable why its guiding principles are characterized by Western orientation and its application is exclusively Western-dominated; hence it is largely foreign to most African societies.

This book aims to beat a retreat on what has become common practice, and then cast a new light on the clinical trials context (and the larger bioethics project), using the African philosophical understanding of personhood. In opposition to the Western autonomy-based Principlism (the four principles of research ethics – autonomy, beneficence, non-maleficence, and justice), this project proposes an 'other-regarding' or communalist perspective which is presented here as the preferred alternative model. It is a tact that draws attention to the inadequacy of the principlist approach particularly in Indigenous African cultural settings. In essence, the approach here engenders a rethink, stimulates interest, and re-assesses the failed assumptions of universal ethical principles.

Building on some recent efforts, this attempt runs against much of the prevailing (Euro-American) intellectual mood. It is a *re-think* that strives to introduce the African viewpoint by making explicit the significance of the human person (self) in a re-contextualized arena. Viewed as such, research ethics would be guided to include as well as go beyond autonomy-based considerations for the individual with absolute right to self-determination; while embracing a more holistic-based approach that embeds the individual in his/her family, community, and the environment.

By and large, a re-conceptualized responsibility in clinical trials transcends the bare bones of Principlism to *concentrically* address the interests of all *stakeholders* in clinical studies: human subjects, family, host community, neighboring and distant communities with similar interests, the physical environment, animals, minerals, and everything else in the biota.

The content analysis will tie together related literature on the three main areas of responsibility, clinical trials, and selfhood. It is a Trinitarian thesis that demands a careful conjoining for fuller comprehension.

Ultimately, this reconceptualization move implicitly captures the comprehensive fields of bioethics and environmental ethics as one unified field of philosophical inquiry, encouraging the development of a reliable and appropriate framework of analysis of issues for the field made whole. Also, it is hoped that Africanists and native African thinkers would find reason to be more engaged in shaping the discussion and promoting traditional philosophical and multicultural values from this perspective.

"Whatever happens to the individual happens to the family or community in which he/she belongs. Likewise, the African disposition sees health

topics (wellbeing or illness) as a communal affair, sometimes to the point that family or community has a stake in becoming aware of another's health condition and having a role in the decisions regarding his/her treatment."

"We are who we are because of our roots." – Ike Iyioke.

Preface

This book is an attempt to explore the ethics of public health, specifically, ethical issues with clinical trials from an African perspective and with a focus on research ethics. It is also a reflection of the wider area and research interest forays I make in the broad field of bioethics. In it, I aim to re-conceptualize responsibility in clinical trials with the insight of the African notion of 'the self.' I strive to complement scholarly literature dealing with cross-cultural biomedical ethics and emphasize the African perspective which is rare or even non-existent in some cases.

To take on the task of this reconfiguration first, I recognize that bioethics as a field has continued to spread out from its Euro-American birthplace to numerous cultural milieus across the globe. Accompanying this spread is the challenge of how to integrate and apply its founding principles (the four principles of research ethics – autonomy, beneficence, non-maleficence, and justice – a.k.a., Principlism), and make them relevant at the local level. Faster still is the pace at which the Global South has long become the choice site for a sizeable chunk of the clinical trial enterprise from the Global North.

Of the many problems with Principlism, the one that is most directly antithetical to my thesis is its excessive individualist emphasis, focusing on individual rights, his/her autonomy, etc., to the detriment of everything else. In so doing, much is left to be desired. And that has led to its numerous revisions even in Western practice of research ethics, and a clear indication to some inbred difficulties in its application. That, in and of itself, further buoys my argument for a robust alternative -- an African perspective (a communalist approach, presented here as bio-eco-communalism or BEC, more on this later).

Further still, it is obvious that the assumptions implicit in the Western framework that makes claim to universal validity for absolute individual rights are not shared by non-Western cultures. If not reined in, the concern seems to be that the Euro-American 'individualist' approach is bound to globalize a less than global view of the world and reality. In other words, the mainstream research ethics which is grounded on Principlism is itself inherently linked to Western individualistic notions of personhood, whereas the rest of the world, particularly Africa, sees the person not as an isolated entity, but as a part of the community who is embedded in kinship, group, community, and the environment – physical and spiritual. Moreover, the totality of the African worldview in which the people's ethics is rooted, and the societal activities which center on the promotion of vitality and the regeneration of human beings, livestock, and the land on which their livelihood depends, are entirely missed by Principlism.

In the face of this, I urge for a reappraisal of the place of responsibility for human subjects in research. More specifically, as many clinical trials are off shored abroad (away from the West), this book project provides an opportunity to weigh in on the Western emphasis on individualism and to acknowledge the cultural systems of other peoples, for instance, communitarianism (or communalism). While opposing individualism (a Euro-American mantra), the African perspective stresses communitarianism. By definition, the communitarian philosophical viewpoint instantly recognizes that ethical issues with biomedical studies are far more broad-based than just focusing on the individual study subject or participant.

Therefore, responsibility in clinical trials must in tandem, be broad-based. There is no debate that research studies do impact the individual research participant, but that impact extends in ***varying degrees*** to everyone and everything else around him/her – family, neighborhood, community and even the physical/non-physical

environments. Put otherwise, responsibility in research enterprises particularly those dealing with human subjects, must be seen to extend beyond the individual person and to encompass the community and the physical/spiritual environment within which the individual resides. Because the African notion of selfhood is communalist and broad-based, it is adequately structured to address the shortcomings in the mainstream individualist perspective. As such, responsibility for (and by) the individual can only make sense through the community he/she relates with or is domiciled. Consequently, I urge that the current understanding of responsibility be rejigged. When this is done, responsibility for human subjects in research (particularly in adequately suited cultural environments), will henceforth mean responsibility for the individual rights, plus, those of his family, community, and the ecosystem.

Chapter One: Introduction

Clinical trials of our time

The many progresses in biomedical research serve as signposts to the dizzying height modern biomedical science has attained. These quintessential feats, thanks to clinical trials, represent the unleashing of the human brain power in making dreams a reality by improving mankind's physical, emotional, and material conditions.

However, scientific research has sometimes become more a search for material gains, absolute control, and power, and less in quest of the truth, even if inconvenient. When science fashions a project to serve such agendas, the avowed purpose of dominating nature can easily turn into the domination of the human person,[1] and ethical problems of enormous proportions often do arise; problems to which science has no clue, much less an answer. Hence, the very essence of humanity stands the risk of being compromised, sometimes irreversibly (Okere, 2005).

Clinical trials refer to protocols which serve as foundation for study planning, conduct, reporting, and appraisal (Chan, et al., 2013). More broadly, the U.S. National Institutes of Health (USNIH), describes it as "a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other controls) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes," (NIH Grants and Funding). The protocol is a carefully defined process,

[1] Person, man/woman, self, individual, human being/person, and to a lesser extent, identity; have been used interchangeably in this book to mean the same thing (in line with existing literary corpus). However, there are places where exceptions are made.

for instance, participants are sometimes picked in a pre-determined manner but more often are randomly selected individually or in clusters depending on the intended outcome.

> A "health-related biomedical or behavioral outcome" is defined as the pre-specified goal(s) or condition(s) that reflect the effect of one or more interventions on human subjects' biomedical or behavioral status or quality of life. Examples include: positive or negative changes to physiological or biological parameters (e.g., improvement of lung capacity, gene expression); positive or negative changes to psychological or neurodevelopmental parameters (e.g., mood management intervention for smokers; readingcomprehension and/or information retention); positive or negative changes to disease processes; positive or negative changes to health-related behaviors; and, positive or negative changes to quality of life (NIH Grants and Funding, https://grants.nih.gov/policy/clinical-trials/definition.htm).

Clinical trial results can be used to generate data on safety, efficacy, and/or effectiveness of treatments, devices, biologics, etc. Research studies usually phased over a period, start out with pre-specified hypotheses or assumptions which are put to test in a trial process that includes a pre-specified number of research participants needed to detect the proposed treatment difference. "These studies can investigate associations between specific patient characteristics, disease characteristics, treatments, and outcomes" (Minneci and Deans, 2018, p. 332).

Running through the entire gamut of the process – from conception to production – is a set of ethics guidelines that binds researchers and administrators to a set of prescribed expectations on research conduct, in particular, appropriate treatment of research participants.

With the lessons of history, e.g., Tuskegee experiment (https://www.cdc.gov/tuskegee/timeline.htm), guidelines have been codified to grant study participants supreme considerations for their rights and wellbeing.

While science cannot advance without experimentation, pursuit of narrow scientific goals and populist economic motives have sometimes led to troubling behaviors by some scientists which undermine research ethics guidelines and principles. And as Western[2] research arenas continue to tighten their regulatory noose, coupled with the rapidly drying pool of volunteer enrollees (Petryner, 2009; and *U.S National Institutes of Health*, 2020 "Trends, Charts, and Maps"), some researchers are either compelled to seek out soft targets or are attracted elsewhere, including Africa; after all, water always follows the path of least resistance.

As the Global South has become the choice site for a sizeable chunk of the clinical trials enterprise, in this book I urge for a reappraisal of sorts, and for a harder scrutiny about the place of responsibility for participants in clinical trials. My thesis is to reformulate the concept of responsibility by replacing the notion of personhood via Principlism lenses with the concept of personhood from a communalist perspective. Question: should science be left to push its empiricist/materialist agenda unchecked? More specifically, as clinical trials continue to settle at new locales across the world including the Global South, it seems about time to halt the Western extreme emphasis on individualism and the tendency to fuse, at all costs, knowledge and might, and truly acknowledge other philosophical and cultural perspectives and systems.

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[2] Western, Euro-American, the Global North, the industrialized world, all mean the same thing in this book. On the other hand, the Global South, the industrializing world (including Africa), are used interchangeably to mean the same thing.

To reiterate, the four principles (a.k.a., Principlism) for mainstream bioethics are: respect for autonomy (a norm of respecting the decision-making capacities of autonomous persons); non-maleficence (a norm of avoiding the causation of harm); beneficence (a group of norms for providing benefits and balancing benefits against risks and costs); and justice (a group of norms for distributing benefits, risks, and costs fairly). My central argument is that we must recalibrate responsibility around the following questions: Is the autonomy based Principlism still relevant in research ethics as compared to the communalist perspective (for whose benefit and at whose expense)? How relevant is Principlism to Africa or in an African context?

It is apparent that the assumption implicit in the framework that makes claim to universal validity for Principlism is not shared by non-Western cultures (Onuoha, 2007). The false assumption in question is that research ethics principles are equally applicable to *everybody everywhere*. If this assumption is not reined in, the concern seems to be that the approach according to Widdows (2007), is bound to "globalize a less than global view of the world and reality." The related point of seeing African matters through Western lenses also led to Okere's (2005) concern in his allusion earlier. For instance, the mainstream research ethics purports to adhere to the principlist quartet, which is inherently linked to Western individualistic notions of personhood, whereas much of the rest of the world, for instance Africa, sees the person not as an isolated power drunk individual, but as a part of the community who is embedded in the immediate family, kinship, group, clan, and the environment.

As I shall soon explicate in detail, while the African concept of a person is unitary, the Euro-American concept is essentially split between persons and non-persons within the human species. For instance, fetuses, human infants, young children, people with mental disorder, and patients in persistent vegetative state may be technically

considered as non-persons because they 'do not possess any moral standing' in the secular moral community. Tristram Engelhardt (1996), makes this strident point in *The Foundations of Bioethics*, a polemic publication that has significantly shaped today's mainstream bioethical practice.

But a slew of other considerations is entirely missed by this assumption. They include the holism of the African worldview in which the people's ethics is rooted; and the societal activities which center on the promotion of vitality and fertility of human beings, livestock, and the land on which their livelihood depends. In essence, African philosophical concepts are never considered as individuated concepts, rather they are holistic. Hence, it is common to see how a simple ethical discussion can morph into and encompass spiritual/ religious, metaphysical, ontological, social, or cultural spheres.

This book presents a tripartite thesis: (1) responsibility (2) clinical trials, and (3) personhood (specifically, the African notion of personhood). The aim is to harmoniously blend these seemingly disparate themes (which ordinarily are full-fledge concepts in their own rights), to justify why it makes sense to achieve my purpose.

On another front, it is easy to misconstrue my reference to 'African notion of personhood,' as essentializing. As I shall prove, particularly in Chapter Four, that I am not overgeneralizing. In fact, beneath the apparent diversity of African philosophical expressions of the self, there is a fundamental and undisputed uniformity in understanding the concept, thus setting the stage for a clear-cut cultural relativity (ethical particularism, nay cultural autonomy). As with many other African concepts, something that Egbeke Aja's 2006 work attests to, values seem to vary from one region of the continent to another, but if put under scrutiny, "in terms of their functions and interrelationships, some general principles emerge." There is abundant literature that

backs up the fact that this trend is most prevalent in Black Africa, and similarities abound in much of North ('Arab') Africa as well. For illustration, I give one example among many from each of the sub-region. The popular Southern African (Zulu) *Ubuntu* philosophical concept that means "I am because we are," – to be explored later, is replicated at all sub-regions of the African continent. Among the Swahili people in East Africa, it is "Utu" or "Tu-wa-moja." The same concept is expressed as "Anyi b'ofụ" among the Igbo ethnicity in Nigeria, West Africa. And in much of North Africa where the belief systems are homocentric; God is the origin of "man" and provides for man's needs: immortality, rejuvenation, food, knowledge. This understanding describes the human existence as being predicated on multiple aspects of relationships between the individual, the community, and the environment (physical and spiritual).

Chapters Two and Three discuss respective sides (each in contra-opposition) of clinical trials that are germane to my exegesis. The 'clinical trials' theme – both as the fulcrum of research ethics and as a concept – has endured since the dawn of experimentation, presenting a platform for analyses on a wide range of issues. That platform is pivotal (if not more so) today than it has ever been. After some preliminaries, Chapter Two looks at the historical trends that foreshadowed modern biomedical research and ends with the 1996 Nigeria-Pfizer *Trovan* case study. The big pharma drug testing in Nigeria stands as a forefront warning that bad practices have been breaking loose on a neo-colonial model. That experimentation episode that resulted from severe meningitis and cholera outbreaks in Kano, a northern Nigerian city involving huge ethical issues with the American pharmaceutical company, provide both the catalyst and a test case for this book.

Chapter Three reviews relevant aspects of the WHO-sponsored *Guidance Framework for Testing of Genetically Modified Mosquitoes*, by

highlighting the excellent and easily replicable examples it has set for clinical trial protocols. In sum, it prescribes remedies that could be used to address the glaring deficiencies attributable to a case like the Pfizer's *Trovan*.

Chapter Four deliberates on the age-old concept of responsibility. Ordinarily, 'responsibility' is a conceptual theme some theorists claim to have long teased apart and reduced to minute analyzable pieces for easy understanding. In this book, I don't have to reinvent the wheel, but I make bold to present what could pass as an unorthodox but valid perspective of the concept.

Chapter Five examines personhood from an African perspective and hones in on my conclusions. Personhood is introduced as a third panel to the equilibrium (others being 'responsibility' and 'clinical trials') by bringing to bear its African philosophical dimension. I wish to use the notion of personhood in African thought to provide a perspective of what responsibility can mean in an African context and then apply it to biomedical clinical trials with human subjects. Ultimately, the African philosophical notion of selfhood will put in perspective my argument to reconstruct the understanding of responsibility in clinical trials. More specifically, while opposing individualism (a Euro-American mantra), the African perspective stresses communalism/communitarianism. As such, responsibility for, and by the individual can only make sense through the community in which he/she is rooted. Ultimately, the triangular themes of responsibility, clinical trials, and the African concept of personhood, consummate to make a geometric sense.

Chapter Six is forward looking. First, it proposes that ethics guidelines should shift focus towards the development of collaborative partnerships with local scientists, community engagement, post-trial obligations to research participants and communities, and standards of care. To facilitate that shift, bioethics must focus on research that

promotes equity and develops local capacity. It stresses the urgent need to modify the currently accepted standards for research ethics. Next, while the three principles outlined in the Belmont Report – respect for persons, beneficence, and justice (US Office for Human Research Protections) – remain central to research ethics and to the protection of research subjects, the understanding of what makes research ethical has expanded to include greater emphasis on the scientific and social value of the research itself, and to recognition of the potential complexity of the relationship between researchers and communities. Finally, it notes that the expansion of biomedical research in Africa demands an increase in the capacity for research ethics oversight. "Capacity" is not just a matter of numbers or of assuring compliance with existing frameworks. Capacity also implies strengthening the ability of academic and research institutions to provide bioethics education that is culturally sensitive and relevant to community needs and research sites.

Section 1

Chapter Two: Who Is Responsible For Human Subjects (When Experiments Travel)?

2.1 Introduction

The question that this chapter seeks to answer is not new. In fact, it is so old it is now trite and rhetorical – I apologize but don't be disappointed. However, the upshot is that it needs to be re-contextualized, and then answered. I shall address it in the context of a new world order – a globalized clinical trials dispensation.

In the current 'globalized' world, it is daunting to keep track of the quantum number of clinical trial projects that are ongoing at any given time. As such, a few of the questions that dogged humanity in the wake of landmark clinical trial abuses including the ones by the Nazi doctors in concentration camps have both lingered on as well as become more complicated. The atrocities led to the Nuremberg code of 1947, a direct result of Nuremberg War Crime Trials after WWII. It set standards for judging physicians and scientists who conduct biomedical experiments to guarantee that research involving human subjects are carried out in an ethically accepted manner. As I will shortly review, other codes and guidelines that have emerged include the Helsinki Declaration (of 1964, but which has witnessed multiple revisions sine then); the 1974 U.S. Code of Federal Regulations (45 CFR Part 46); and the 1979 Belmont Report of the U.S. National Commission, to name just three. All these outline ethical principles and guidelines for the protection of human subjects in biomedical, social, and behavioral research. The challenge continues to be how to discourage abusive research and promote quality ones that protect research subjects everywhere. Hence, the following questions remain

pertinent: How should human research subjects be protected? Who should protect them? In our increasingly interconnected world, how can we ensure compliance, guideline consistency, and checks and balances across borders? These questions remain relevant particularly because even as most clinical studies today are initiated and registered in the Global North (predominantly in the U.S.), the actual trials are sometimes outsourced and offshored often to the Global South (Petryna, 2009; and *U.S National Institutes of Health*, 2020 "Trends, Charts, and Maps").

On paper, the 2001 Presidential Ethics Advisory Board Report suggests two principal approaches that could improve the protection of human participants in international clinical trials, thus:

1. relying on reviews by U.S. IRBs and assurance processes to supplement and enhance local measures or determining that a host country or host country institution has a system of protections at least equivalent to that of the U.S., and,

2. helping host countries build the capacity to independently conduct clinical trials and to carry out their own scientific and ethical review.

But sadly enough, these idealities or moral epistemological assumptions have not always been matched by actions in real life. In practice, real world ethical problems take place within non-ideal circumstances. Translation: the above approaches are easier said than done.

Coupled with the changing geography is the fact that private sector research by, for example pharmaceutical companies, have led the way since the 1980s. And foremost on their mind is speed and profitability (Petryna, 2009; Llamas, 2021). That approach is a concern

that triggers further questions: If the multinational companies are so disposed, is it likely that responsibility for study subjects would feature conspicuously in their deliberations? Even so, would they additionally be bound by the local systems (socio-cultural, political, and legal systems where available) and/or would they abide only by international codes of research conduct as though they were in their home turfs (where enforcements are strict)? It has forcefully been argued that the financial interest and overwhelming corporate influence in test results by companies, unduly influence the drug testing system (for e.g., Llamas, 2021). It is therefore the in-built bias, outside pressure, and other motives that sometimes distort the accuracy and acceptability of drug research (Shapiro, 1978; Santoro, M. and Gorrie, T., 2005; Edwards, 2017).

The core questions of, how should human research subjects be protected; who should protect them; and how can we ensure compliance and guideline consistency across borders, directly link up with the overarching position in this book for the need to re-conceive responsibility in clinical trials by redefining responsibility for research subjects. As I will make apparent, it is by rethinking 'responsibility' that we rejig our understanding in the context of an increasingly globalized world, including complexities associated with cultural, social, and political realities. The burden of my argument will be to demonstrate that this recommendation is a crying urgency if we must truly reflect the meaning of our moral condition in the fields of biomedical and social science research (given present day cross-disciplinary and inter/transdisciplinary approaches).

This chapter is divided into four main parts. I will start by sketching out an overview of the historical background to human experimentation in biomedicine. Next, I will review some of the U.S. and international research ethics guidelines which resulted