

**CENTRE FOR INFECTIOUS  
DISEASE  
RESEARCH IN ZAMBIA (CIDRZ)**

**REPORT  
ON**

**HUMAN INFECTION STUDIES  
REGULATORY FRAMEWORK  
IN ZAMBIA**

**BY**

**IDAHA NZALI PHIRI  
(Consultant)  
May, 2020**

**CENTRE FOR INFECTIOUS DISEASE RESEARCH IN ZAMBIA  
(CIDRZ)**

**REPORT  
On  
HUMAN INFECTION STUDIES  
REGULATORY FRAMEWORK IN ZAMBIA**

**By**

**IDAH NZALI PHIRI  
(Consultant)**

**May, 2020**

## Contents

ACKNOWLEDGEMENTS.....	3
ABBREVIATIONS.....	4
ABSTRACT.....	5
1.0. INTRODUCTION .....	6
2.0. PROBLEM STATEMENT .....	7
3.0. OBJECTIVE.....	8
4.0. METHODOLOGY .....	8
4.1. Desk Research .....	8
4.2. Fieldwork Research .....	8
4.3. Data Collection .....	9
4.4. Primary Data .....	9
4.5. Secondary Data .....	9
4.6. Data Analysis .....	9
4.7. Sampling Method .....	9
5.0. LIMITATIONS .....	10
6.0. ANALYSIS OF THE PRESENT REGULATORY FRAMEWORK.....	10
6.1. The National Health Research Act No. 2 of 2013 .....	10
a. The Principle of Respect of Persons .....	12
b. The Principle of beneficence .....	12
c. The principle of equal distribution of risks and benefits .....	13
6.1.2. International Regulations on Research Involving Humans .....	13
6.1.3. The Role of a Research Ethics Committee .....	14
6.2. The Medicines and Allied Substances Act No. 3 of 2013.....	16
6.3. The National Biosafety Act No. 10 of 2007.....	18
6.4. The Science and Technology Act No. 26 of 2007 .....	20
7.0. FINDINGS/RESULTS.....	21
8.0. RECOMMENDATIONS .....	25
REFERENCES.....	28
Annex. ....	32

## ACKNOWLEDGEMENTS

Sincere appreciation to all the Key Informants for providing their time and in-depth knowledge towards this research. These include (among others not mentioned here):

Dr. Andrew Silumesi	Director of Public Health, <b>Ministry of Health</b>
Dr. Godfrey Biemba	Director, <b>National Health Research Authority</b>
Dr. James Munthali	Former Chairperson, <b>University of Zambia Biomedical Research Ethics Committee</b>
Dr. Jean Bertin Bukasa Kabuya	Senior Scientist, <b>Tropical Disease Research Centre</b>
Dr. Soddy Mweetwa Munsaka	Chairperson, <b>University of Zambia Biomedical Research Ethics Committee</b>
Mr. Filipo Zulu	Manager, Programme Development and Implementation, <b>National Science and Technology Council</b>
Mr. Lackson Tonga	Registrar and Chief Executive Officer, <b>National Biosafety Authority</b>
Mr. Lyoko Nyambe	Assistant Director – Marketing Authorisation, <b>Zambia Medicines Regulatory Authority</b>
Mr. Moses Lupiya	Legal Manager and Board Secretary, <b>Zambia Medicines Regulatory Authority</b>
Mrs. Martha K. Tembo	Legal Counsel and Board Secretary, <b>Tropical Disease Research Centre</b>
Professor Victor Chalwe	Deputy Director – Research Promotion and Regulation, <b>National Health Research Authority</b>
Professor Victor Mukonka	Director, <b>Zambia National Public Health Institute</b>

I particularly thank **Prof. Victor Mukonka** and **Hon. Exnobert Zulu** for the massive support and assistance.



## **ABBREVIATIONS**

CIOMS	Council for International Organizations of Medical Sciences
GCP	Good Clinical Practice
GMO	Genetically Modified Organisms
HIS	Human Infection Studies
IBC	Institutional Biosafety Committee
ICH	International Conference on Harmonisation
IRB	Independent Review Boards
NBA	National Biosafety Authority
NHRA	National Health Research Authority
NSTC	National Science and Technology Council
SADC	Southern African Development Community
SOP	Standard Operation Procedures
UNZABREC	University of Zambia Biomedical Research Authority
WHO	World Health Organisation
ZAMRA	Zambia Medicines Regulatory Authority

## ABSTRACT

This research set out to collect, review and analyse applicable local and international laws, regulations and guidelines to fully substantiate requirements for the introduction of HIS in Zambia. The research methodology adopted was qualitative in nature and involved the use of desk research and field research in the form of key informant interviews. Because Zambia has not started conducting HIS, this research could not provide a participant's perspective. The research established that the overarching law on health research in Zambia is the National Health Research Act No. 2 of 2013 which allows for research on human participants and makes provision for the conduct of clinical trials. The Medicines and Allied Substances Act No. 3 of 2013 also regulates human research in Zambia and makes provision for research involving a medicine or allied substance. It is in pursuance of this Act that the Zambia Medicines Regulatory Authority (ZAMRA) developed Guidelines on Regulating the Conduct of Clinical Trials in Human Participants. The National Biosafety Act No. 10 of 2007 governs research on human participants with specific focus on research involving Genetically Modified Organisms (GMOs). The Science and Technology Act No. 26 of 2007 establishes the National Science and Technology Council whose functions are to promote science and technology so as to improve the quality of life in Zambia. The research further established that the legal requirements for research on human participants in Zambia corresponds with the requirements as provided in international instruments, regulations and guidelines such as the World Health Organisation (WHO) Guidance for Implementation Hand Book on Good Clinical Research Practice (GCP), the International Conference on Harmonisation (ICH) Guidelines for Good Clinical Practice (1995), the Nuremberg Code of Human Rights (1947), the Regulations and Guidelines on Clinical Investigator, the IRB Responsibilities (2003) Code of Federal Regulations, the World Medical Association's Declaration of Helsinki (1964-2000), the CIOMS International Guidelines for Biomedical Research involving Human Subjects (2001) and the WHO Expert Committee on Biological Standardization. The research concludes that the current legal framework on health research in Zambia does not prohibit the conduct of HIS. The legal framework is consistent with international standards and generally sufficient to process an application to approve or disapprove a proposal for HIS. The research recommends that given the sensitive and unique nature of HIS, explicit guidelines or regulations must be put in place to provide not only for the specific or exact manner of conducting HIS but also to clarify and emphasise on ethical considerations in order to guarantee safety and protect public confidence. **Key words** Human Infection Studies (HIS), health research, human participants, legal framework, clinical trials

## 1.0. INTRODUCTION

Health research is important for many reasons. It is conducted in order to establish effective ways of preventing and treating diseases. Through health research, methods to provide care are established. Research informs policy makers with evidenced based data upon which the development and implementation of health laws, policies and standard operating procedures are premised. Health research is conducted in several ways using different research subjects depending on the desired results. Humans have in the past formed and continue to form research subjects. According to Rosenbaum and Sepkowitz, “when all else fails, science looks to human beings.”<sup>1</sup> Human Infection Studies (HIS) are particularly a useful type of health research for fast tracking the development of candidate vaccines and may provide unique insight into disease pathogenesis otherwise unavailable.<sup>2</sup> For a country such as Zambia looking to develop in various sectors including the health sector, alleviate poverty, fight diseases and attain universal health coverage, HIS are an option worth exploring.

Therefore, regulation of HIS is necessary in order to ensure safe and competent practice. It sets ground rules for research as a key implementation mechanism through the setting of standards and requirements and the use of sanctions and possible incentives to exert leverage over the health system. It is thus important to understand the legal framework at the beginning of every HIS process. It is in this perspective that this research will provide a comprehensive review of the current health research laws and guidelines within the boundaries of all regulatory authorities so as to establish the legality of embarking on HIS. It will collect, review and analyse applicable local and international laws, regulations and guidelines to fully substantiate requirements for introduction of HIS in Zambia. The research argues that the prevailing legal framework is permissive to HIS provided that the Regulations detailing how the research will be conducted are prescribed, and the researcher adheres to attendant ethical clearance and the need to obtain all the relevant authorities.

---

<sup>1</sup> Julie Rothstein Rosenbaum and Kent A. Sepkowitz, *Infectious Disease Experimentation Involving Human Volunteers* Infectious Diseases Society of America, 2002

<sup>2</sup> Ben Bamberg et al., *Ethical Criteria for Human Challenge Studies in Infectious Diseases* Public Health Ethics Volume 9, Number 1, 2016. P. 92–103

## 2.0. PROBLEM STATEMENT

Human Infection Studies (HIS) are a type of clinical trials that involve intentionally infecting healthy volunteers with a pathogen as part of a trial design to assess efficacy of new vaccines or therapeutics.<sup>3</sup> According to Professor Chalwe, the Deputy Director of the National Health Research Authority (NHRA), HIS differ from other clinical trials in that researchers do not wait for the natural process of a participant to get infected and then challenge the infection with a drug or vaccine to ascertain its efficacy. The process is basically cut short and enables the Researcher to yield desired results or solutions to research problems timely.<sup>4</sup> The fundamental difference with other forms of clinical research is that in HIS, there is the “intentional” infection of volunteers which seems to confound the basic principle that requires physicians to “not cause any harm”.<sup>5,6</sup> There is a wealth of literature that argues that HIS have been conducted in several jurisdictions and it has been established that the scientific basis of HIS is sound as the findings are more precise in relation to how the particular drug or vaccine works.<sup>7</sup> This notwithstanding, there is no record of HIS having been conducted in Zambia. The absence of HIS in Zambia has led to lack of information and knowledge on both the local and international laws, regulations and guidelines that impede or enable HIS in Zambia. This lack of information and knowledge makes it difficult to know the legal and regulatory regime and other requirements that should govern HIS in Zambia. In order to close this gap, it is necessary to carefully review the current health research laws and guidelines within the boundaries of all regulatory authorities so as to establish the legality of embarking on these studies. Consequently, this research is aimed at collecting, reviewing and analysing applicable local and international laws, regulations and guidelines to fully substantiate requirements for introduction of HIS in Zambia.

---

<sup>3</sup> Michelo Simuyandi, Introduction to Human Infection Studies (HIS), Presentation to the Parliamentary Committee on Health, Community Development and Social Services on 3<sup>rd</sup> March, 2020

<sup>4</sup> Interview with Professor Victor Chalwe, Deputy Director – Research Promotion and Regulation, National Health Research Authority (Lusaka, 6 March, 2020)

<sup>5</sup> Michael J Selgelid and Euzebiusz Jamrozik, *Developing the Ethics of Controlled Human Infection Models in LMICs*, Indian Journal of Medical Ethics Vol III No 4 October-December 2018

<sup>6</sup> Interview with Dr. Soddy Mweetwa Munsaka, Chairperson – University of Zambia Biomedical Research Ethics Committee (Lusaka, 11 March, 2020)

<sup>7</sup> Interview with Mr. Lyoko Nyambe, Assistant Director – Marketing Authorisation, Zambia Medicines Regulatory Authority (Lusaka, 4 March, 2020)

### **3.0. OBJECTIVE**

The objective of this research was to collect, review and analyse applicable local and international laws, Regulations and guidelines to fully substantiate requirements for the conduct of HIS in Zambia.

### **4.0. METHODOLOGY**

The research employed a qualitative design which is defined as, a means by which one explores and understands the meaning that individuals or groups ascribe to a social or human problem.<sup>8</sup> The research undertaken was mainly doctrinal. The following research methodologies were used to collect and analyse data.

#### **4.1. Desk Research**

The Desk research focused on understanding the law on point. It involved the location and interpretation of relevant primary and secondary sources and synthesised the sources to form a legal position. This research method was used in order to have an in-depth understanding of the available law and literature on the subject. It provided the base line information to this research and was preferred because it enables a researcher to identify the gaps in the law and suggest ways in which the law should develop.<sup>9</sup> Desk research was conducted in various libraries and the internet to consult journals, reports, papers, statutes and law reports. The sources consulted in this regard included statutes, regulations, guidelines and policy documents that govern research and generally provide for research on human participants. Archival records, journals, reports and papers relevant to the subject were also consulted.<sup>10</sup>

#### **4.2. Fieldwork Research**

Field research was used to interrogate the understanding of researchers and regulators on the law on HIS. In this research, it was necessary to establish whether in their understanding, the law adequately allows for HIS. In this regard, consideration was made to the respondent's involvement either in research or regulation of research in human participants.

---

<sup>8</sup> John W. Cresswell, *Research Design: Qualitative, Quantitative, and Mixed Methods Approaches*, 3<sup>rd</sup> Ed., (SAGE Publication, Inc. London, 2009) p. 4.

<sup>9</sup> Lynne Taylor, *From Legal Writing: A Complete Guide for a Career in Law* (LexisNexis, 2014), [www.google scholar.com/learnlawlife.co.nz](http://www.google scholar.com/learnlawlife.co.nz) as at 22:59 on the 12<sup>th</sup> December, 2019

<sup>10</sup> Robert K. Yin, *Case Study Research: Design and Methods*, 4<sup>th</sup> Ed. (SAGE Publication, Inc. London, 2009), 99

#### **4.3. Data Collection**

Both primary and secondary data was collected to add knowledge to the present subject. The sources of primary data included local statutes and regulations, international regulations and guidelines and structured & unstructured interviews conducted with some key informants. This data was resorted to both for its originality, and for purposes of triangulation. Secondary data was obtained through evaluation of metadata which include other researched documents on the subject matter.

#### **4.4. Primary Data**

Primary data was obtained from statutes, and purposively sampled key informants. The data from key informants was secured through questionnaires and attendant responses. The selection of key informants was informed by the need to collect rich data from those directly involved in the health research, and the attendant regulators. All ethical considerations were adhered to.

#### **4.5. Secondary Data**

Secondary data was mainly accessed through journals, published and unpublished articles, papers, reports and other researched materials on the subject matter.

#### **4.6. Data Analysis**

The research used thematic and content analysis. This involved the identification, collection, evaluation and critique of relevant contending and consistent sources of data.

#### **4.7. Sampling Method**

The purposive method was employed to identify the key informants. The research targeted particular informants based on their experience and profound knowledge in the subject matter. Purposive sampling was preferred to achieve the objectives of this research since most respondents were either researchers or regulators in the within field. From the sample identified, the sampling procedure consisted of simple random sampling from among the targeted institutions.

## **5.0. LIMITATIONS**

Due to the fact that Zambia has not begun HIS, the research was unable to get the views of the participant so as to have an understanding of the situation from the participant's perspective. Although a study was conducted with potential participants in which it was found that they were willing to take part in a HIS should one be done,<sup>11</sup> it is not possible to determine what their perspective would be after it is done.

## **6.0. ANALYSIS OF THE PRESENT REGULATORY FRAMEWORK**

### **6.1. The National Health Research Act No. 2 of 2013**

The National Health Research Act No. 2 of 2013 is the overarching law for health research in Zambia. It is important to note from the onset that in the year 2009, the Government of the Republic of Zambia banned all research on living human beings because there was no legal framework for conducting research involving human beings.<sup>12</sup> The law on health research involving human beings, at the time, was the Human Tissue Act Chapter 306 of the Laws of Zambia which only allowed research to be conducted on dead bodies. Chanda-Tembo explains that the Ministry of Health began addressing the outstanding ethical issues surrounding the conduct of health research in Zambia in 2007 when it was realized that most of the research was being conducted in the country without ethical approval thereby directly compromising the protection of human participants.<sup>13</sup> In the absence of the legal framework, the Ministry of Health considered halting research involving human beings on the Government's directive that a law be put in place to provide the framework upon which research could be conducted on living human beings. This ban was not lifted until February 2011 when Zambia's draft National Health Research Bill was finally developed and thereafter, the National Health Research Act No. 2 of 2013 came into place.<sup>14</sup>

In 2014 the National Health Research Act through the Ministry of Health (MOH) established the National Health Research Authority (NHRA), a regulatory body that was charged with the mandate to provide a regulatory framework for the development, regulation, financing and

---

<sup>11</sup> Ng'andu et al, <https://www.researchsquare.com/article/re-17568/v1>

<sup>12</sup> Interview with Dr. Godfrey Biemba, Director, National Health Research Authority (Lusaka, 5 March, 2020)

<sup>13</sup> Pascalina Chanda-Kapata et al., Health Research Policy and Systems, 2012

<http://www.health-policy-systems.com/content/10/1/17>

<sup>14</sup> Interview with Dr. Godfrey Biemba



coordination of health research in order to ensure the development of consistent health research standards and guidelines for ethically sound health research in Zambia.<sup>15</sup> The mission of the Authority is to promote, regulate, and coordinate ethical conduct of quality health research and facilitate translation of all research products into evidence-based policies and programs that improve the health of the people of Zambia and beyond.<sup>16</sup> The functions of the NHRA are set out in Section 5 of the Act and these include: research promotion, research regulation, research coordination, research capacity building, and, research dissemination and knowledge translation.

The Authority is governed by a Council whose core function, among others, is to set, review and enforce ethical standards and human research ethical guidelines, including ethical standards and guidelines for clinical trials. Section 13 further establishes the National Health Research Ethics Board which regulates ethics on human research and oversees and ensures adherence to health research ethics as provided in the regulatory framework and ethics guidelines. It is also the mandate of this Board to give ethical approval for all clinical trials involving medicines, vaccines or other biological products, new therapeutic regimes, as well as invasive diagnostic procedures in addition, among others, to giving ethical approvals for health research proposals that meet the health research ethics guidelines. It is in this perspective that Section 17 provides that all proposals for health research must be reviewed by the Board (or any other accredited Health Research Ethics Committee as may be prescribed), and approved by the Board. Therefore, Section 18 mandates research institutions and health establishments conducting research to constitute Health Research Ethics Committees and to have them registered with, and accredited by the Board or any other accredited Health Research Ethics Committee.

Part V of the Act specifically makes provision for Health Research on, or experimentation with human participants. It provides that health research or experiments on a human participant shall be conducted in the prescribed manner consistent with the Act and with the written consent of the person, after the person has been informed of the objectives of the research or experimentation and any possible potential risks or benefits on that person's health.<sup>17</sup> Further requirements of conducting research on human participants are that the research must not

---

<sup>15</sup> National Health Research Authority website <https://www.nhra.org.zm/>

<sup>16</sup> *ibid*

<sup>17</sup> Part V, National Health Research Act



threaten national security, violate social and cultural norms and must be done with ethical approval by the Board or an accredited Health Research Ethics Committee.<sup>18</sup> It is in this regard that Section 45 Subsection 2, highlights the three basic pillars of health research ethics to be embraced in research involving human participants. These include the respect of persons (autonomy); benefit to the research participants (beneficence); and equal distribution of risks and benefits (justice).<sup>19</sup>

#### **a. The Principle of Respect of Persons**

The principle of respect of persons or autonomy states that every human being is an autonomous individual and has the right to decide what should and should not happen to them.<sup>20</sup> Dr. Biemba explains that the principle enjoins the recognition of a person as an autonomous, unique, and free individual with the right and capacity to make his or her own decisions. This means that a health researcher is required to explain all the implications of the study to the participant through an informed consent process. The Researcher must then, not only ensure but also document that the participant understands what he or she (researcher) intends to do and thereupon signs for it. A signed consent attests that the participant understands what the research is about, the implications of the study and what is expected of him (or her) and that he agrees to participate in the study freely and voluntarily. He contends that as long as the participant understands and agrees, the research is ethically correct and allowed to this extent.<sup>21</sup>

#### **b. The Principle of beneficence**

The principle of beneficence, also known as non-maleficence states that whatever the study is, “do good and do no harm”.<sup>22</sup> Dr. Biemba augments that the researcher must demonstrate in the protocol that they have done a risk benefit analysis in that they have identified all risks either known or anticipated based on what is known. These risks must be documented and described in detail. The researcher must also describe the benefits of the study in all respects, that is, to the participant, to public health or to the

---

<sup>18</sup> ibid

<sup>19</sup> Section 45, National Health Research Act

<sup>20</sup> <https://www.fhi360.org/sites/default/files/webpages/RETC-CR/en/RH/Training/trainmat/ethicscurr/RETCCREn/pr/Contents/SectionIV/b4sl34.htm> last accessed on 10 March, 2020

<sup>21</sup> Interview with Dr. Godfrey Biemba, Director, National Health Research Authority (Lusaka, 5 March, 2020)

<sup>22</sup> <https://www.ncbi.nlm.nih.gov/books/NBK459281/> last accessed on 10 March, 2020

community and to science generally as a positive contribution to the existing body of knowledge. The Researcher must then weigh the benefits against the risks. In order for the study to be ethically correct and allowed, the benefits should outweigh the risks.<sup>23</sup>

### **c. The principle of equal distribution of risks and benefits**

The principle of equal distribution of risks and benefits, also known as the principle of justice, in this context means fair play. It suggests that regardless of caste, creed and social status, every individual should be treated equally.<sup>24</sup> It relates to fair procedures and outcomes used to select research participants, and ensuring that there is a fair distribution of benefits and burdens to populations who participate in research.<sup>25</sup>

Having highlighted the three basic pillars of health research ethics as provided for by the law on health research, it must be noted with emphasis that every protocol for research on human participants must satisfy these three principles in order to be ethically correct and allowed.<sup>26</sup>

### **6.1.2. International Regulations on Research Involving Humans**

One must hasten to note that the basic pillars of health research underlined in the Health Research Act No. 2 of 2013 are derived from internationally recognized principles which are a standard for the ethics review of any research involving human participants. The International Ethical Guidelines for Health-related Research Involving Humans for example emphasises on these principles.<sup>27</sup> Guideline 1 relates to the principle of respect of persons whereas guidelines 3 and 4 provide for the principle of equitable distribution of benefits and burdens in the selection of individuals and groups of participants and the principle of potential individual benefits and risks respectively.<sup>28</sup> These principles are also espoused in the World Medical Association's Declaration of Helsinki (1964-2000) in which the key highlight is emphasis on informed consent. This principle was comprehensively broken down into Principles of Respect of Persons (Autonomy), Beneficence (Maleficence) and Equal Distribution of Risks and Benefits (Justice) in the Belmont Report (1979) and the CIOMS International Guidelines for

---

<sup>23</sup> Interview with Dr. Godfrey Biemba

<sup>24</sup> <https://cehe.instructure.com/courses/21871/pages/irb-unit-5-training> last accessed on 10 March, 2020

<sup>25</sup> Interview with Dr. Godfrey Biemba

<sup>26</sup> *ibid*

<sup>27</sup> Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO), 2016

<sup>28</sup> *ibid*

Biomedical Research involving Human Subjects (2001). Further, the WHO Expert Committee on Biological Standardization considered the regulatory and ethical considerations for HIS (also known as Human Challenge Trials) for Vaccine Development. This committee equally relied on informed consent as a fundamental ethical requirement with the underlying principle of minimising risks and maximising benefits to both the individual subjects and the community (or society).<sup>29</sup>

The National Health Research Act No. 2 of 2013 generally reflects these guidelines with the ultimate insistence that the interest of science must never supersede safety. The replication of these principles in the Zambian Legal Framework means that Zambia is in fact in compliance with these instruments. In addition, the requirements adopted in the National Health Research Act No. 2 of 2013 in terms of institution of Health Research Ethics Committees (Independent Review Boards or Independent Ethics Committees), review of research proposals and attendant procedures way through to the conclusion of research are derived from the World Health Organisation (WHO) Guidance for Implementation Hand Book on Good Clinical Research Practice (GCP)<sup>30</sup> and the International Conference on Harmonisation (ICH) Guidelines for Good Clinical Practice (1995). Worth noting is that the principles embraced in the Health Research Act are also, to a large extent, derived from the Nuremberg Code of Human Rights (1947) as well as the Regulations and Guidelines on Clinical Investigator and IRB Responsibilities (2003) Code of Federal Regulations. Upon reading these instruments, one concludes that the National Health Research Act generally borrows from them and is written in accordance with the stipulated international principles or standards being the internationally accepted minimum requirements for one to conduct health research on human beings.

### **6.1.3. The Role of a Research Ethics Committee**

As noted above, the National Health Research Act No. 2 of 2013 compels all research institutions and health establishments conducting research to constitute Health Research Ethics Committees<sup>31</sup> and generally provides standards for research ethics. These committees play a critical role in ethical regulation of research on human participants as every researcher intending to conduct health research on human participants first submits a research proposal to

---

<sup>29</sup> WHO Expert Committee on Biological Standardization: Human Challenge Trials for Vaccine Development: regulatory considerations, 2016

<sup>30</sup> 2002

<sup>31</sup> Section 18 of Act No. 2 of 2013

the Ethics Committee for approval.<sup>32</sup> The basic expectations in terms of the role of Research Ethics Committees could be understood from the University of Zambia Biomedical Research Ethics Committee (UNZABREC) Standard Operating Procedures (SOPs).<sup>33</sup>

In terms of the UNZABREC SOPs, the role of a Research Ethics Committee is to review all types of research proposals involving human participants to safeguard the dignity, rights, safety and well-being of all actual and potential research participants. Much emphasis is placed on the fact that the goals of research, however important, must never be permitted to override the health, well-being and care of research participants. The Research Ethics Committee must therefore take care to ensure that all the cardinal principles of research ethics as highlighted in Section 45 of the National Health Research Act, namely, Autonomy, Beneficence, Non-maleficence and Justice, are taken care of in the planning, conduct and reporting of the proposed research. In this respect, the Research Ethics Committee ought to consider the aspects of the informed consent process, risk/benefit ratio, distribution of burdens and benefits and provisions for appropriate compensation wherever required.<sup>34</sup>

The UNZABREC SOPs further aver that the Research Ethics Committees review and approve proposals before the start of the study as well as monitor the research throughout the study until and after completion of the study through appropriate well-documented procedures, for example progress reports, final reports, and site visits. The Committee also examines compliance with all regulatory requirements, applicable guidelines and laws.<sup>35</sup>

It must be noted that the role of a Research Ethics Committee as highlighted in the UNZABREC SOPs is, as a mark of prudence, consistent with the provisions of the National Health Research Act aforesaid. One therefore argues that the current legal framework provides a quality and consistent ethical review mechanism for Health and Biomedical Research that is consistent with international ethical guidelines for biomedical research on human participants.

---

<sup>32</sup> Interview with Mrs. Martha K. Tembo, Board Secretary, Tropical Disease Research Centre (Lusaka, 27 February, 2020)

<sup>33</sup> University of Zambia Biomedical Research Ethics Committee (UNZABREC) Standard Operating Procedures (SOPs) [https://healthresearchweb.org/en/zambia/ethics\\_2128](https://healthresearchweb.org/en/zambia/ethics_2128)

<sup>34</sup> University of Zambia Biomedical Research Ethics Committee (UNZABREC) Standard Operating Procedures (SOPs) [https://healthresearchweb.org/en/zambia/ethics\\_2128](https://healthresearchweb.org/en/zambia/ethics_2128)

<sup>35</sup> *ibid*

## **6.2. The Medicines and Allied Substances Act No. 3 of 2013**

To start with, it must be noted that while the National Health Research Act No. 2 of 2013 remains the overarching law on health research in Zambia, every health research conducted on human beings which involves a medicine or allied substances must be approved by the Zambia Medicines Regulatory Authority (ZAMRA). This mandatory requirement is provided for in Section 54 Subsection 3 of the National Health Research Act. The said provision states that

A medicine to be used in a clinical trial shall be approved by the Zambia Medicines and Regulatory Authority as prescribed under the Medicines and Allied Substances Act, 2013.

It follows therefore that the Medicines and Allied Substances Act No. 3 of 2013 is another important piece of legislation in terms of regulation of clinical trials in Zambia. This Act creates the Zambia Medicines and Regulatory Authority (ZAMRA) and sets out its functions which include the registration and regulation of medicines and allied substances; the regulation of the manufacture, importation, exportation, possession, storage, distribution, supply, promotion, advertising, sale and use of medicines and allied substances and the regulation and control of clinical trials.<sup>36</sup>

Section 7 of the Act provides for the constitution of the Board of the Authority. The Board is charged with the responsibility of establishing and issuing guidelines and standards in order to effectively operationalise this Act. The Board is further mandated to constitute and does have an Expert Advisory Committee consisting of experts in human medicine, and allied substances. The functions of this committee include, among others, advising the Board on monitoring the conduct of clinical trials; providing technical and scientific advice on any aspect of medicines and allied substances and reviewing risk assessment and risk management measures relating to medicines and allied substances.

Part VI of the Act provides for Regulation of Clinical Trials. Section 49(1) prohibits conducting a clinical trial involving a medicine or allied substance without a clinical trial certificate. Breach of this provision amounts to a criminal offence which attracts a fine not exceeding three million penalty units or imprisonment for a period not exceeding five years, or to both.

---

<sup>36</sup> Zambia Medicines Regulatory Authority Website <https://www.zamra.co.zm/>

Although the Act confers powers on the Minister to issue Regulations by way of Statutory Instrument to operationalise the provisions in the Act for effective regulation of clinical trials, no Regulations on the conduct of clinical trials are currently effective. As of writing, the Regulations on the conduct of clinical trials await signing by the Minister of Health.<sup>37</sup> This notwithstanding, the process of application is being done administratively based on the principal Act as the fees are already prescribed in the Medicines and Allied Substances (Fees) Regulations.<sup>3839</sup> As such, there is no prejudice. Much reliance is placed on the guidelines made pursuant to Section 68(1) of the Act which guidelines are binding on all persons regulated under this Act. Important to note is that these guidelines although made pursuant to the Pharmaceutical Act (No. 14) of 2004 continue to apply by virtue of the continued existence of the Pharmaceutical Regulatory Authority and mere re-naming of it as the Zambia Medicines Regulatory Authority.<sup>40</sup>

The objective of these guidelines is to ensure that Clinical trials conducted in Zambia meet acceptable standards of Good Clinical Practice (GCP). In this regard, the guidelines outline the information required by the Regulatory Authority from sponsors and applicants wishing to conduct clinical trials and also define the evaluation process for the conduct of clinical trials. The guidelines further indicate the order of the material to be submitted and the minimum requirements for conducting clinical trials. Imperative to note is that these guidelines were prepared in accordance with the WHO/SADC Guidelines, therefore abiding by international standards. It must be mentioned however that as of writing, these guidelines are being reviewed. Worth noting in this regard is that the proposed revisions, made pursuant to Section 49 to 53 of the Act<sup>41</sup> in order to define the general norms and scientific principles and to set applicable standards for the conduct, performance and control of clinical trials in humans in Zambia, have specific language that relates to HIS. For example, the Draft Guidelines for Authorisation of Clinical Trials of Medicines, Nutritional Supplements, Vaccines and Medical Devices in Zambia,<sup>42</sup> in laying out the categories of products that require an application for approval to conduct a clinical trial provide that

---

<sup>37</sup> Interview with Mr. Lyoko Nyambe

<sup>38</sup> Statutory Instrument No. 38 of 2016

<sup>39</sup> Interview with Mr. Moses Lupiya, Legal Manager and Board Secretary, Zambia Medicines Regulatory Authority (Lusaka, 4 March, 2020)

<sup>40</sup> Preamble of Act No. 3 of 2013

<sup>41</sup> Medicines and Allied Substances Act, No. 3 of 2013

<sup>42</sup> Document No. DRAFT 3.1, 20-DEC-2019



“Challenge agents in Human Infectious Studies shall be regulated in the same manner as vaccines, and are expected to be studied with authorisation in accordance with clinical trial regulations, whether or not an investigational vaccine is to be used in the same clinical investigation protocol.”

The draft guidelines, which refer to HIS as Infectious Human Challenge Trial, have therefore defined HIS as

“A trial that involve the deliberate exposure of human volunteers to infectious agents. Trial participants are intentionally challenged (whether or not they have been vaccinated) with an infectious disease organism. This challenge organism may be close to wild-type and pathogenic, adapted and/or attenuated from wild-type with less or no pathogenicity, or genetically modified in some manner.”

This definition has also been included in the Draft Guidelines for Good Clinical Practice in Zambia.<sup>43</sup>

### **6.3. The National Biosafety Act No. 10 of 2007**

The National Biosafety Act No. 10 of 2007 is also an important piece of legislation in health research. This Act is very specific about research in Genetically Modified Organisms (GMOs). It creates the National Biosafety Authority (NBA) whose mandate is to regulate the import, export, development, research, contained use and release or placing on the market of any GMO whether the activity involves intentional or unintentional release of GMOs into the environment as a pharmaceutical product, food, feed, processing or product of a GMO.<sup>44</sup> It follows therefore that every health research conducted on human beings which involves a GMO must also be approved by the NBA in addition to any other approvals required in other pieces of legislation. Although this premise is not expressly provided for in the National Health Research Act No. 2 of 2013, it is implied from Section 10 of the National Biosafety Act which provides that

---

<sup>43</sup> The Zambia Medicines Regulatory Authority Draft Guidelines on Good Clinical Practice in Zambia Version No. Draft 3.1, 20-DEC-2019

<sup>44</sup> The National Biosafety Authority website <https://www.nbazambia.org.zm/>

A person shall not research on, develop, produce, import, export, transit, carry out any contained use, release or place on the market any genetically modified organism or any product of a genetically modified organism or deal in any manner with any genetically modified organism or a product of a genetically modified organism without the prior approval of the Authority.

Mr. Tonga, the Registrar and Chief Executive Officer of the NBA augmented that in terms of clinical trials involving the use of GMOs, the Authority makes assessments and follows through the entire process. The Authority conducts risk assessments as well as cost-benefit analysis and once safety is ascertained, approval is given.<sup>45</sup> He noted that guidelines in this regard are underway but the process is being done administratively based on the principal Act.<sup>46</sup>

The Act therefore compels every institution that is involved in the import, development, research, transit, export, handling, contained use, release or placing on the market of any GMO or product of a GMO to establish an Institutional Biosafety Committee (IBC) to institute and control safety mechanisms and approval procedures at institutional level. It is in this regard that the General Guidelines for Institutional Biosafety Committees for Research and Development Uses were developed. These guidelines describe the composition and roles of IBCs. They provide information for compliance requirements by IBCs and processes to be followed while dealing with GMOs or materials or products derived from DNA recombinant technologies. The guidelines thus provide for responsibilities of the NBA in field research in which regard the Authority has the direct responsibility for evaluating and approving proposals for work on GMOs and microorganisms. The supervising IBCs are thus mandated to follow closely all the affairs through the initial proceedings and thereafter throughout the conduct of research. The NBA reserves the right to inspect field work and contained laboratory trial at any time, without prior notice.

Section 46 of the National Biosafety Act clothes the Minister with power to make Regulations by Statutory Instrument necessary for carrying out or giving effect to the provisions of this Act. In exercise of this authority, the Biosafety (Genetically Modified Organisms for Food, Feed and Processing) Regulations, 2010 were made mainly to provide for importation of GMOs as

---

<sup>45</sup> Interview with Mr. Lackson Tonga, Registrar and Chief Executive Officer, National Biosafety Authority (Lusaka, 17 March, 2020)

<sup>46</sup> Interview with Mr. Lackson Tonga



well as labelling and traceability of the same. These Regulations provide detailed guideline for health research or clinical trials in particular that involve importation of GMOs and are further operationalised through the General Guidelines for Public Consultation on Importation of Genetically Modified Organisms (GMOs) into Zambia. Worth noting is that Section B of these guidelines specifically relates to research and development. It follows that by the nature of HIS, it is certain that challenge agents will in one way or another be genetically tampered with. Thus, the National Biosafety Act, Regulations and attendant guidelines are key to accommodating HIS.

#### **6.4. The Science and Technology Act No. 26 of 2007**

The Science and Technology Act No. 26 of 2007 is equally an important piece of legislation in respect of health research. This Act establishes the National Science and Technology Council (NSTC) whose functions are to promote science and technology so as to improve the quality of life in Zambia. The Council regulates research in science and technology in Zambia. The Act also provides for the establishment of research and development support centres. Section 9 makes it mandatory for every centre or institute to apply to the Council for registration as a centre or institute in the prescribed form stating the name of the private centre or institute; the principal place of business; the names and qualifications of its research and development staff and the areas of research and development in which the private centre or the institute is involved.

Science and Technology in Zambia is guided by the National Policy on Science and Technology<sup>47</sup> which policy inspired the enactment of the Science and Technology Act. The goal of this policy in terms of research is to enhance linkages between technology research institutes, the private as well as the public sector in order to encourage demand driven research and development. The objective in terms of research and development and specific to health research include ensuring that research priorities are geared to generating information intended to solve health and nutritional problems; ensuring that research capabilities and capacities of institutions carrying out health research are strengthened; relating the research programmes to the priority problems in the health sector; establishing effective linkages between research

---

<sup>47</sup> National Policy on Science and Technology, 1996 <http://www.nstc.org.zm/>

institutions on one hand, and users on the other and establishing an effective health data bank for research results and mechanisms for their utilization.

In light of the aforesaid, the NSTC is clothed with authority to provide oversight on centres or institutes involved in research in science and technology. This conclusively includes institutes or centres involved in health research on human participants or subjects.<sup>48</sup>

## **7.0. FINDINGS/RESULTS**

Having reviewed and analysed the local and international legal framework on health research, the following are the findings:

- 7.1.** The National Health Research Act No. 2 of 2013 is the principal or overarching piece of legislation on health research in the country. It expressly provides for research or experimentation on human participants and sets out general procedures for ethical authorisation. Undoubtedly, there is no provision in this Act which expressly speaks to HIS. In other words, the term HIS is not defined or even mentioned in this Act. What is there is the term clinical trial which means a systematic study, involving human participants or animal subjects, that serves to answer specific questions about the safety or efficacy of a medicine, vaccine or method of prevention or treatment.<sup>49</sup> Given that HIS are simply a type of clinical trial conducted equally for purposes of answering specific questions about the safety or efficacy of a medicine, vaccine or method of prevention or treatment,<sup>50</sup> one would argue in agreement with Dr. Munsaka's assertion that they (HIS) are covered or incorporated in the definition of clinical trial provided for by the Act.<sup>51</sup>

It is in this regard that one is inclined to agree with Professor Chalwe that given the evolving nature of clinical trials and science generally, it is not excepted or even conscionable that an Act of parliament would provide comprehensively for

<sup>48</sup> Interview with Mr. Filipo Zulu, Manager – Programme Development and Implementation, National Science and Technology Council (Lusaka, 18 March, 2020)

<sup>49</sup> Section 2 of Act No. 2 of 2013

<sup>50</sup> Michelo Simuyandi, Introduction to Human Infection Studies (HIS), Presentation to the Parliamentary Committee on Health, Community Development and Social Services on 3rd March, 2020

<sup>51</sup> Interview with Dr. Sody Mweetwa Munsaka

each and every type of clinical trials.<sup>52</sup> It is therefore imperative at this point for one to consider the purposive intention of the legislators or drafters of the National Health Research Act, No. 2 of 2013 which expressly allows for experimentation or research on human participants in a general or broad sense. The basic position is that what the law does not specifically, expressly or impliedly outlaw or prohibit is legal. It could thus be concluded that the purpose of the National Health Research Act No. 2 of 2013 was to provide for all types of clinical trials in a progressive fashion. It follows that any desired guidelines regarding the specific or exact manner of conducting different types of clinical trials could, if necessary, be provided for merely as guidelines or indeed by way of Regulations in Statutory Instruments.

This position is true for the Medicines and Allied Substances Act No. 3 of 2013 and the National Biosafety Act No. 10 of 2007 which also regulate health research in human participants. In the case of the Medicines and Allied Substances Act No. 3 of 2013, the underlying principle is whether the health research being conducted on human beings involves a medicine or allied substances. A detailed analysis of the provisions of this Act points to the fact that the Act does not seem to speak to any specific type of clinical trial. Equally, the National Biosafety Act places much emphasis on a researcher obtaining prior approval of the Authority in order to research on, develop, produce, import, export, transit, carry out any contained use, release or place on the market any genetically modified organism or any product of a genetically modified organism or deal in any manner with any genetically modified organism or a product of a genetically modified organism. This Act also does not speak to any specific type of clinical trial.

This research therefore holds that the position espoused by Prof. Biemba that there is nothing in the current legal framework on health research that prohibits the conduct of HIS is correct. He contends that given the current legal framework on health research, anyone can conduct any type of study on human

---

<sup>52</sup> Interview with Professor Victor Chalwe, Deputy Director – Research Promotion and Regulation, National Health Research Authority (Lusaka, 6 March, 2020)

participants as long as he can demonstrate in the protocol that all the ethical requirements discussed above have sufficiently been satisfied. Simply put, the onus rests on the researcher intending to conduct HIS to demonstrate in the protocol that the basic pillars of health research ethics and all other elements required to be fulfilled have been adhered to.<sup>53</sup> Beyond ethical requirements, one further agrees with Professor Chalwe that the current legal framework adequately allows for HIS in that there are provisions in the existing pieces of legislation on storage,<sup>54</sup> importation or movement of biological samples or materials,<sup>55</sup> general guidelines on the conduct of clinical trials and in addition, the laws are in conformity with international standards.<sup>56</sup>

This said, one notes that the mention or inclusion of HIS in the ZAMRA draft guidelines discussed above strongly demonstrates an understanding or appreciation not only by ZAMRA as a regulatory institution but also all stakeholders that contributed to these guidelines that the legal framework in its current form does accommodate HIS. This is premised on the fact that ZAMRA would not accommodate that which is proscribed in the National Health Research Act being the overarching law on health research in Zambia. ZAMRA can still process an application for HIS that involves a medicine or an allied substance with the existing guidelines in the same way as any other clinical trial even before the draft guidelines come into effect.

In light of the aforesaid, the research concludes in agreeing with Mr. Nyambe that the current legal framework is sufficient to process an application to approve or disapprove a proposal for HIS and adds that what matters is the merits in the proposal based on the principle that the interest of science must never supersede safety.<sup>57</sup>

---

<sup>53</sup>Interview with Dr. Godfrey Biemba, Director, National Health Research Authority (Lusaka, 5 March, 2020)

<sup>54</sup>Section 49 of the National Health Research Act, No. 2 of 2013 - Also see the Environmental Management Act, No. 12 of 2011 and the Health Professionals Act, No. 24 of 2009

<sup>55</sup> The National Health Research (Material Transfer) Regulations, Statutory Instrument No. 92 of 2018 and The Guidelines for Transfer of Biological Materials for Research and Quality Assurance Purposes in Zambia

<sup>56</sup> Interview with Professor Victor Chalwe, Deputy Director – Research Promotion and Regulation, National Health Research Authority (Lusaka, 6 March, 2020)

<sup>57</sup> Interview with Mr. Lyoko Nyambe, Assistant Director – Marketing Authorisation, Zambia Medicines Regulatory Authority (Lusaka, 4 March, 2020)

It must be noted at this point that a review of international instruments on research on humans equally points to the fact that no instrument makes provision for specific regulations for HIS. As is the case with the local legal framework, the reviewed international instruments make general provisions for research or experimentation on human participants and set minimum ethical standards to be met. One further notes in this regard that the WHO Expert Committee on Biological Standardization in considering the regulatory considerations for HIS (or Human Challenge Trials) for Vaccine Development recognised that regulation of HIS needs to be (well) defined by respective national regulatory authorities.<sup>58</sup> This committee acknowledged that in some countries, these studies are expected to be studied with authorisation in compliance with clinical trial regulations. The committee observed that

“In cases when challenge should be studied in compliance with clinical trial regulations, there is greater clarity about regulatory expectations, including the quality of the challenge stock to be used, because the clinical trial regulations or requirements would apply.”<sup>59</sup>

It follows therefore that there are no gaps in the Zambian legal framework per se that require to be closed in order to conform with international standards for purposes of introducing or implementing HIS.

**7.2.** As demonstrated above, the current legal framework (local) on health research on human participants is on all fours with international standards.

In sum and for avoidance of doubt, this research takes the view that the present laws on research are permissive to HIS provided that the manner in which HIS will be undertaken is prescribed, the necessary authorities discussed above are obtained, and attendant regulations and ethical considerations adhered. At present, save for the said provision in the ZAMRA draft regulations, there appears to be no regulations that explicitly prescribe the extent and manner in which HIS will be conducted.

---

<sup>58</sup> WHO Expert Committee on Biological Standardization: Human Challenge Trials for Vaccine Development: regulatory considerations, 2016

<sup>59</sup> *ibid*

## 8.0. RECOMMENDATIONS

- 8.1. Having held that the legal framework in Zambia is sufficient for the introduction of HIS, it is recommended, given the unique and sensitive nature of these studies and in order to secure public confidence, that explicit guidelines or regulations be put in place to provide not only for the specific or exact manner of conducting HIS but also to clarify and emphasize on ethical considerations. Simply put, the legal framework in Zambia does allow for clinical trials in a general sense and undoubtedly, HIS are adequately covered or incorporated therein. However, as rightly argued by Selgelid and Jamrozik and the majority of the interviewees in this research (76.9%), HIS are ethically sensitive.<sup>60</sup> Most (76.9%) interviewees agreed with the argument of Selgelid and Jamrozik that HIS, among other issues,

“raise complex questions concerning (i) the acceptable limit of risks to which healthy volunteers may be exposed, (ii) appropriate financial payment/compensation of participants, (iii) the potential need for special review procedures (e.g dedicated committees and/or the involvement of infectious disease experts), (iv) the need for protection of third-parties from infection (transmitted by participants), and (v) appropriate criteria and processes for participant selection/exclusion.”<sup>61</sup>

It is in this perspective that Ben Bambery et al averred that

“... challenge studies may only be ethical if they are limited to study designs in which: (i) they may generate important scientific knowledge; (ii) there are no satisfactory alternative methods; (iii) well informed competent adult volunteers consent freely to infection; (iv) they are subject to appraisal by an ethics review committee; (v) there is acceptable balance of benefits and harms; and (vi) there is equitable selection of study participants. However, above and beyond these common standards (which should apply to all clinical trials), we argue that human challenge studies

<sup>60</sup> Ben Bambery et al., Ethical Criteria for Human Challenge Studies in Infectious Diseases, Public Health Ethics Volume 9, Number 1, 2016. P. 92–103

<sup>61</sup> Michael J Selgelid and Euzebiusz Jamrozik, *Developing the Ethics of Controlled Human Infection Models in LMICs*, Indian Journal of Medical Ethics Vol III No 4 October-December 2018



should also include (vii) independent expert reviews, including systematic reviews; (vii) a publicly available rationale for the research, to protect public confidence; (ix) implementation of measures to protect the public from spread of infection beyond the research setting; and (x) a new system for compensation for harm.”<sup>62</sup>

Drawing from the aforesaid, one is of the view that it is necessary for regulations to make provision for HIS to be reviewed and approved by at least two independent experts in infectious diseases in addition to the already existing requirement for review and approval by an independent ethics committee as well as the NHRA. It is also important for regulations to include a requirement for researchers to make available a publicly accessible rationale for the study, explaining the benefits and risks, the inadequacy of alternatives and adequacy of measures to protect participants and the community from harm. The regulations must also speak to issues of public protection in terms of risks to those who may come into contact with the volunteer, communication of such risks, whether and how these risks will be managed and whether there are measures in place to protect the community from spread outside the research setting. Further, regulations should provide clear guidance in terms of whether there are measures in place to compensate volunteers in the event of research-related injury.<sup>63</sup>

Interesting to note is that this recommendation could not have come at a better time than now when the ZAMRA Regulations on the conduct of clinical trials are in draft form and the NHRA Regulations still await signing.

- 8.2.** Flowing from the need to protect the public and to safeguard public confidence; and further in light of the principle of respect for persons or individual autonomy is the indisputable fact that one who has the right to consent reserves the right to withdraw that consent at any time. Absent the discretion to withdraw consent would degenerate the agreement into servitude. Since the person subject of the experiment may withdraw consent at any time including at a point when such a person is a carrier of an infectious diseases, such withdraw and consequent re-integration into society might pose a danger

---

<sup>62</sup> Ben Bambery et al., *Ethical Criteria for Human Challenge Studies in Infectious Diseases*, Public Health Ethics Volume 9, Number 1, 2016. P. 92–103

<sup>63</sup> Ben Bambery et al., *Ethical Criteria for Human Challenge Studies in Infectious Diseases*

to un-consenting third parties. This might put the researcher under the risk of vicarious liability. To avert this risk, it is recommended that the Regulations in the Public Health Act regulating infectious diseases in general be extended to the National Health Research Authority in so far as they relate to carriers of infectious diseases that have withdrawn consent.<sup>64</sup> The researcher should be empowered to detain that person for a specific period necessarily to report the matter to the Medical Director and moving that carrier to a designated quarantine. Important to note however is that at the time of writing, the Public Health Act is undergoing review.<sup>65</sup>

---

<sup>64</sup> The Public Health (Infectious Disease) Regulations

<sup>65</sup>Interview with Professor Victor Mukonka, Director, Zambia National Public Health Institute (Lusaka, 21 February, 2020)



## REFERENCES

### Acts of Parliament

The Human Tissue Act Chapter 306 of the Laws of Zambia

The Medicines and Allied Substances Act No. 3 of 2013

The National Biosafety Act No. 10 of 2007

The National Health Research Act No. 2 of 2013

The Public Health Act Chapter 295 of the Laws of Zambia

The Science and Technology Act No. 26 of 1997

The Environmental Management Act No. 12 of 2011

The Health Professionals Act No. 24 of 2009

### Statutory Instruments

The Biosafety (Genetically Modified Organisms for Food, Feed and Processing) Regulations, Statutory Instrument No. 42 of 2010

The Medicines and Allied Substances (Fees) Regulations, Statutory Instrument No. 38 of 2016

The National Health Research (Material Transfer) Regulations, Statutory Instrument No. 92 of 2018

The Public Health (Infectious Diseases) Regulations, Statutory Instrument No.

### Guidelines/Policies

The General Guidelines for Institutional Biosafety Committees for Research and Development Uses

The Guidelines for Transfer of Biological Materials for Research and Quality Assurance Purposes in Zambia

The National Health Research Committee Guidelines

The National Policy on Science and Technology, 1996

The University of Zambia Biomedical Research Ethics Committee (UNZABREC) Standard Operating Procedures (SOPs)

The Zambia Medicines Regulatory Authority Draft Guidelines for Authorisation of Clinical Trials of Medicines, Nutritional Supplements, Vaccines and Medical Devices in Zambia Document No. DRAFT 3.1, 20-DEC-2019

The Zambia Medicines Regulatory Authority Guidelines Regulating the Conduct of Clinical Trials in Human Participants

### **International Instruments**

International Ethical Guidelines for Health-related Research Involving Humans (2016) - Prepared by the Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO)

The Belmont Report (1979)

The CIOMS International Guidelines for Biomedical Research involving Human Subjects (2001)

The Nuremberg Code of Human Rights (1947)

The Regulations and Guidelines on Clinical Investigator & IRB Responsibilities (2003) code of federal Regulations.

The WHO and the ICH Guidelines for Good Clinical Practice (1995)

The World Medical Association's Declaration of Helsinki (1964-2000)

The WHO Expert Committee on Biological Standardization: Human Challenge Trials for Vaccine Development: regulatory considerations, 2016

### **Books**

John W. Cresswell, *Research Design: Qualitative, Quantitative, and Mixed Methods Approaches*, 3<sup>rd</sup> Ed., (SAGE Publication, Inc. London, 2009) p. 4.

Lynne Taylor, *From Legal Writing: A Complete Guide for a Career in Law* (LexisNexis, 2014) [www.google scholar.com/learnlawlife.co.nz](http://www.google scholar.com/learnlawlife.co.nz) as at 22:59 on the 12<sup>th</sup> December, 2019

Robert K. Yin, *Case Study Research: Design and Methods*, 4<sup>th</sup> Ed. (SAGE Publication, Inc. London, 2009), 99

### **Journals/Articles**

Ben Bamberly et al., *Ethical Criteria for Human Challenge Studies in Infectious Diseases* Public Health Ethics Volume 9, Number 1, 2016. P. 92–103

Julie Rothstein Rosenbaum and Kent A. Sepkowitz, *Infectious Disease Experimentation Involving Human Volunteers*, Infectious Diseases Society of America, 2002

Michael J Selgelid and Euzebiusz Jamrozik, *Developing the Ethics of Controlled Human Infection Models in LMICs*, Indian Journal of Medical Ethics Vol III No 4 October-December 2018

## **Presentations/Meetings**

Michelo Simuyandi, Introduction to Human Infection Studies (HIS), Presentation to the Parliamentary Committee on Health, Community Development and Social Services on 3rd March, 2020

ZAMRA Clinical Trials Guidelines Stakeholders Meeting, Mulungushi International Conference, 4th – 5th March, 2020

## **Interviews**

Interview with Dr. Andrew Silumesi, Director of Public Health, Ministry of Health (Lusaka, 27 February, 2020)

Interview with Dr. Godfrey Biemba, Director, National Health Research Authority (Lusaka, 5 March, 2020)

Interview with Dr. James Munthali, Former Chairperson – University of Zambia Biomedical Research Ethics Committee (Lusaka, 13 March, 2020)

Interview with Dr. Kabuya, Tropical Disease Research Centre (Lusaka, 6 March, 2020)

Interview with Dr. Soddy Mweetwa Munsaka, Chairperson – University of Zambia Biomedical Research Ethics Committee (Lusaka, 11 March, 2020)

Interview with Mr. Filipo Zulu, Manager – Programme Development and Implementation, National Science and Technology Council (Lusaka, 18 March, 2020)

Interview with Mr. Lackson Tonga, Registrar and Chief Executive Officer, National Biosafety Authority (Lusaka, 17 March, 2020)

Interview with Mr. Lyoko Nyambe, Assistant Director – Marketing Authorisation, Zambia Medicines Regulatory Authority (Lusaka, 4 March, 2020)

Interview with Mr. Moses Lupiya, Legal Manager and Board Secretary, Zambia Medicines Regulatory Authority (Lusaka, 4 March, 2020)

Interview with Mrs. Martha K. Tembo, Legal Counsel and Board Secretary, Tropical Disease Research Centre (Lusaka, 27 February, 2020)

Interview with Professor Victor Chalwe, Deputy Director – Research Promotion and Regulation, National Health Research Authority (Lusaka, 6 March, 2020)

Interview with Professor Victor Mukonka, Director, Zambia National Public Health Institute (Lusaka, 21 February, 2020)

## **Websites**

<https://cehe.instructure.com/courses/21871/pages/irb-unit-5-training> (last accessed on 10 March, 2020)

<https://www.fhi360.org/sites/default/files/webpages/RETC-CR/en/RH/Training/trainmat/ethicscurr/RETCCREn/pr/Contents/SectionIV/b4sl34.htm> (last accessed on 10 March, 2020)

<https://www.ncbi.nlm.nih.gov/books/NBK459281/> (last accessed on 10 March, 2020)

National Health Research Authority website <https://www.nhra.org.zm/> (last accessed on 10 March, 2020)

Ng'andu et al <https://www.researchsquare.com/article/re-17568/v1> (last accessed on 12 April, 2020)

Pascalina Chanda-Kapata et al., Health Research Policy and Systems, 2012 - <http://www.health-policy-systems.com/content/10/1/17> (last accessed on 10 March, 2020)

The National Science and Technology Council Website (<http://www.nstc.org.zm/>)

Zambia Medicines Regulatory Authority Website <https://www.zamra.co.zm/> (last accessed on 10 March, 2020)

## Annex.

### Summary of Findings and Recommendations



#### Abstract

✚ This research set out to analyze the Legal Framework on Human Infection Studies (HIS) in Zambia. The overarching law on health research in Zambia is the National Health Research Act No. 2 of 2013 which allows for research on human participants and further makes provisions on the conduct of clinical trials. The Medicines and Allied Substances Act No. 3 of 2013 also regulates human research in Zambia and makes provision for research involving a medicine or allied substance. It is in pursuance of this Act that the Zambia Medicines Regulatory Authority (ZAMRA) developed Guidelines on Regulating the Conduct of Clinical Trials in Human Participants. The National Biosafety Act No. 10 of 2007 governs research on human participants with specific focus on research involving Genetically Modified Organisms (GMOs). The conclusion points to the fact that the current Legal Framework is consistent with international standards on health research involving human participants and generally sufficient to process an application to approve or disapprove a proposal for HIS. However, given the sensitive and unique nature of these studies, it has been recommended that explicit guidelines or regulations be put in place to provide not only for the specific or exact manner of conducting HIS but also to clarify and emphasize on ethical considerations in order to guarantee safety and protect public confidence.

#### Methodology

✚ **Desk Research-** Review of existing legal framework on health related research so as to get an understanding of the law, identify gaps and suggest ways of filling up the gap. To this end, Statutes, Regulations, Policies and all relevant documents were reviewed.

	<p>✚ <b>Field Work</b>– Used to interrogate researchers and regulator in a bid to get their understanding of the law on HIS. Respondents were purposefully sampled based on their vast knowledge and experience in the within field. Respondents provided a wealth of knowledge that significantly informed the study.</p> <p>✚ <b>Data Analysis</b>- Thematic and content analysis was used. It involved the identification, collection, evaluation and critique of relevant contending and consistent sources of data.</p> <p>✚ <b>Limitation</b> – Due to non-availability of participants, the research was unable to get the views of subjects so as have an understanding of HIS from the participant’s perspective.</p>
Statement of the Problem	<p>✚ Human Infection Studies (HIS) are a type of clinical trials that involve intentionally infecting healthy volunteers with a pathogen as part of a trial design to assess efficacy of new vaccines or therapeutics. There is a wealth of literature that argues that HIS have been conducted in several jurisdictions and it has been established that the scientific basis of HIS is sound as the findings are more precise in relation to how the particular drug or vaccine works. This notwithstanding, there is no record of HIS having been conducted in Zambia. The absence of HIS in Zambia has led to lack of information and knowledge on both the local and international laws, regulations and guidelines that impede or enable HIS in Zambia. This makes it difficult to know the legal and regulatory regime and other requirements that should govern HIS in Zambia. In order to close this gap, it is necessary to carefully review the current health research laws and guidelines within the boundaries of all regulatory authorities so as to establish the legality of embarking on these studies. Consequently, this research is aimed at collecting, reviewing and analysing applicable local and international laws,</p>

	regulations and guidelines to fully substantiate requirements for introduction of HIS in Zambia.
Objective	 To collect, review and analyse applicable local and international laws, regulations and guidelines to fully substantiate the requirements for the introduction of Human Infection Studies in Zambia.
Analysis	 <b>The National Health Research Act No. 2 of 2013</b> is Act is permissive to HIS. Although it does not specifically mention HIS, Section 5 of the Act spells out the functions of the National Health Research Authority (NHRA) to include promoting research, coordinating research, regulating research, research related capacity building, research dissemination and knowledge transmission. <p>Attendant to regulation, the Act established the Council as the governing body of the authority and vested it with authority to set, review and enforce ethical standards and Human research guidelines clinical trials, among others. Section 13 of the Act creates the Ethics Board whose functions include enforcement of the attendant ethics and guidelines.</p> <p>Section 17 makes it mandatory for the said Board to review all research proposals. The proposal can also be reviewed by any other delegated/accredited research Ethics Committee. The Research Ethics Committees are created and accredited pursuant to section 18 of the Act. Imperative to state is the fact that the duty to avail the proposal to the committee on board rests with the researcher, or the institution intending to undertake the research.</p> <p>Part V of the Act makes provision for experimentation on human participants. It however imposes an obligation to prescribe the manner in which such experiments shall be conducted. The wording of the Act on point is couched in mandatory terms therefore leaving</p>

no room for discretion. Section 45 (2) enjoins the researcher to adhere to the three pillars of research namely; respect for individual autonomy, adherence to the principle of beneficence, and the equal distribution of risk and benefit. The within principles have been discussed above.

#### **The Medicines and Allied Substances Act o. 3 of 20**

Creates the Zambia Medicines Regulatory Authority (ZAMRA). Section 54 (3) of the Act vests ZAMRA with the jurisdiction to approve all medicines to be used in clinical trials. It follows therefore that any researcher engaged in HIS involving medicines and allied substances must of necessity obtain approval for the use of the medicines or allied substances from ZAMRA. The said section is couched in mandatory terms thus the researcher has no discretion to waive such approval. Approval of such medicines and allied substances is evidenced by issuance of a clinical trial certificate. Section 49 of the Act makes it an offence to conduct clinical trials with unapproved medicines or allied substances.

The Regulations intended to operationalize certain provisions of this Act to ensure effective and efficient conduct of clinical trials are yet to be prescribed. In other words, there are no Regulations attendant to this Act.


#### **The National Biosafety Act No. 10 of 2007**

This Act regulates research on Genetically Modified Organisms (GMO). It creates the National Biosafety Authority (NBA) and gives it mandate to regulate the import, export, development, research, contained use and release of GMOs into the environment as pharmaceutical products, food, feed, processing of a product of GMOs. Thus any GMOs that are to



be use in HIS must be approved by the NBA. Concomitantly, any HIS research that alter or involve the genetic modification of the human participant, or that use challenge agents that have the attendant effect on human participants must be approved by the NBA. Section 10 of the Act which provides for approvals is couched in mandatory term thus granting no discretion to the researcher or institution conducting research on point to ignore it. The onus is on the researcher to obtain such authority. The Act also mandates institutions involved in GMOs research to establish an Institutional Biosafety Committee in accordance to the prescribed composition. The committee is mandated to institute and control safety mechanisms and approval procedures at institutional level.

Section 46 of the Act vests in the Minister, authority to promulgate Regulations through Statutory Instruments. The regulations are in place and provide detailed guidelines on health research or clinical trials. Imperative to note, for purposes of HIS, is section B of the guidelines that relate to research and development.

 **The Science and Technology Act No. 26 of 2007**– creates the National Science and Technology Centre (NSCT) and mandates it to promote science and technology so as to improve the quality of life in Zambia. Section 9 makes it mandatory for any institution that intends to set up a research centre to seek NSCT’s approval and registration.

 **International Regulations on Research Involving Human**

The ethical considerations provided for in the National Health Research Act No. 2 of 2013 in terms of the basic pillars of health research, elements to be adhered to, institution of Health Research Ethics Committees (Independent Review Boards or Independent Ethics Committees), review of research proposals and attendant

procedures way through to the conclusion of research are derived from internationally recognized principles which are a standard for the ethics review of any research involving human participants. The replication of these principles in the Zambian Legal Framework means that Zambia is in fact in compliance with international requirements.

✚ Those consulted include:

1. The Nuremberg Code of Human Rights (1947)
2. The World Medical Association's Declaration of Helsinki (1964-2000)
3. The Belmont Report (1979)
4. The International Conference on Harmonisation (ICH) Guidelines for Good Clinical Practice (1995)
5. The CIOMS International Guidelines for Biomedical Research involving Human Subjects (2001)
6. World Health Organisation (WHO) Guidance for Implementation Hand Book on Good Clinical Research Practice (GCP) (2002)
7. The Regulations and Guidelines on Clinical Investigator and IRB Responsibilities (2003) Code of Federal Regulations.
8. The International Ethical Guidelines for Health-related Research Involving Humans (2016)

✚ Further, the WHO Expert Committee on Biological Standardization (2016) considered the regulatory and ethical considerations for HIS for Vaccine Development. This committee recognised that regulation of HIS needs to be (well) defined by respective national regulatory authorities. This committee acknowledged that in some countries, these studies are expected to be studied with authorisation in compliance with clinical trial regulations.

✚ The committee observed that "In cases when challenges should be studied in compliance with clinical tr

	<p><u>regulations, there is greater clarity about regulatory expectations, including the quality of the challenge stock to be used, because the clinical trial regulations or requirements would apply.”</u></p>
Findings	<ul style="list-style-type: none"> <li>✚ The prevailing legal framework is permissive to HIS provided that the Regulations detailing how the research will be conducted are prescribed, and the researcher adheres to attendant ethical clearance and the need to obtain all the relevant authorities.</li> <li>✚ The National Health Research Act Regulations still awaits Ministerial assent as at date of research.</li> <li>✚ The ZAMRA Regulations are undergoing review as at date of research and are still in draft form.</li> <li>✚ There are no Regulations that specifically prescribe the manner in which HIS is to be conducted in Zambia.</li> <li>✚ The law regulating health research squarely adheres to the minimum international standards governing research involving human participants.</li> </ul>
Recommendations	<ul style="list-style-type: none"> <li>✚ Need to prescribe specific regulations for HIS in Zambia</li> <li>✚ In order to protect public confidence, it is necessary for regulations to make provision, among all other requirements, for <ul style="list-style-type: none"> <li>○ HIS to be reviewed and approved by at least two independent experts in infectious diseases in addition to the already existing requirement for review and approval by an independent ethics committee as well as the NHRA.</li> <li>○ a requirement for researchers to make available a publicly accessible rationale for the study, explaining the benefits and risks, the inadequacy of alternatives and adequacy of measures to protect participants and the community from harm.</li> </ul> </li> </ul>

- issues of public protection in terms of risks to those who may come into contact with the volunteer, communication of such risks, whether and how these risks will be managed and whether there are measures in place to protect the community from spread outside the research setting.
- clear guidance in terms of whether there are measures in place to compensate volunteers in the event of research-related injury.

✚ To avoid risk to third parties when an infected human participant withdraws consent during the experiment, there is need to amend the NHRA Act to empower a researcher to detain the participant for a minimum duration necessary to report the matter to the Medical Director pursuant to the Public Health Act Chapter 295 of the law of Zambia so that such a participant could be quarantined.

