NATIONAL BIOSAFETY AUTHORITY

GUIDELINES FOR DETERMINING THE REGULATORY PROCESS OF GENOME EDITED ORGANISMS AND PRODUCTS IN KENYA

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TABLE OF CONTENTS

FOREWORD

Genome editing technology has been identified as a potential new option to augment existing interventions in pursuance of achieving the African Union Agenda 2063 and it is expected that proposed applications for genome editing technology for basic research, conservation, agriculture, public health and other purposes will likely continue to expand as genome editing tools become more refined.

Genome editing has broad applications in plant and animal improvement, as well as in the medical field. For example Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) has been used to edit the genome of rice resulting to improvements in yield-related traits, such as dense and upright panicles and reduced plant height; development of late flowering soybean, resulting in increased vegetative size; development of citrus plants resistant to citrus canker; generation of animals suitable for human disease modelling such as CRISPR-edited cynomolgus monkeys for brain disorders that cannot be fully studied in mice; studies for the treatment of Human Immunodeficiency Virus (HIV) among other applications.

In responding to the continuous advancement in genome editing technology, the Authority has developed a guideline document for determining the regulatory process of genome editing techniques through broad stakeholder consultations and review of regulatory mechanisms in other countries where such technology has been deployed.

The document incorporates the aspects of implementation, as well as essential testing pathways and implementation strategies in the country, taking into consideration all the possible socio-cultural and ethical issues. This document is not meant to detail how risk assessment and risk management of genome edited products will be conducted.

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ABBREVIATIONS

CPB - Cartagena Protocol on Biosafety

DNA - Deoxyribonucleic acid

GE - Genetically engineered

GM - Genetically modified

GMO - Genetically modified organisms

ODM - Oligonucleotide-Directed Mutagenesis

r-DNA - Recombinant-DNA

RNA - Ribonucleic acid

SDN - Site –Directed Nucleases

TALENs - Transcriptional Activator Like Effector Nucleases

ZFNs - Zinc Finger Nucleases

DEFINITION OF TERMS

Applicant: means a person submitting an application to the Authority in pursuant to the provisions of the Biosafety Act, 2009 or those who wish to determine whether the genome edited products or processes are regulated by NBA.

Authority: means the National Biosafety Authority established under section 5 of the Biosafety Act, 2009;

Biosafety: means the avoidance of risk to human or animal health and safety, or the conservation of the environment;

Contained use: means any activity undertaken within a facility, installation or other physical structure which involves genetically modified organisms that are controlled by specific measures;

Conventional counterpart: means a closely related organism, its components and/or products for which there is experience of established safety based on common use.

Environment: includes the physical factors of the surroundings of humans and animals, including land, water, atmosphere, soil, vegetation, climate, sound, odour, aesthetics, fish and wildlife;

Foreign Genetic material: Refers to novel combination of genetic material from sexually non-compatible species through the use of modern biotechnology techniques;

Genetically modified organism: means any organism that possesses a novel combination of genetic material obtained through the use of modern biotechnology techniques;

Genome editing: means targeted methods to introduce new traits in organisms using various techniques which induce breaks in the DNA that can be repaired by endogenous mechanisms and lead to a range of changes at a targeted locus within the genome. This may be achieved by deleting, replacing, editing organism's own DNA or inserting a DNA sequence in the organism's genetic material;

Intentional introduction into the environment: means any deliberate use of genetically modified organisms beyond contained use;

Modern biotechnology: includes the application of—

a) in-vitro nucleic acid techniques including the use of recombinant deoxyribonucleic acid (DNA) and direct injection of nucleic acid into cells or organelles; or

b) fusion of cells beyond the taxonomic family, that overcome natural physiological, reproductive and recombination barriers and which are not techniques used in traditional breeding and selection;

Novel combination of genetic material: means an organism whose DNA has been altered with the addition or substitution of foreign DNA.

Regulatory agency: means a regulatory agency as set out in the First Schedule of the Biosafety Act, 2009 or such other agency as the Minister may, by Order in the Gazette, determine;

CHAPTER ONE

1.0 THE NATIONAL BIOSAFETY AUTHORITY

1.1 Background

The National Biosafety Authority (NBA) is a state corporation in Kenya established pursuant to the provisions of the Biosafety Act, 2009 to regulate all activities involving genetically modified organisms (GMOs) in food, feed, research, industry, trade and environmental release. Being the national focal point on biosafety matters, NBA fulfils its mandate by ensuring and assuring safe development, transfer, handling and use of GMOs with the aim of ensuring safety of human and animal health as well as provision of adequate protection of the environment.

NBA has made great strides in establishing a strong Biosafety regulatory framework in Kenya by developing and publishing the implementing Biosafety Regulations namely; The Biosafety (Contained Use) Regulations, 2011; the Biosafety (Environmental Release) Regulations, 2011; the Biosafety (Import, Export and Transit) Regulations, 2011; and the Biosafety (Labeling) Regulations, 2012. These regulations lay down a clear procedure on handling GMOs whether plants, animals or microorganisms. NBA is the National Focal Point for the Cartagena Protocol on Biosafety to the Convention on Biological Diversity (CBD) and is mandated to implement the provisions of the Cartagena Protocol on all Biosafety matters pertaining to GMOs.

1.2 Vision Statement

A World-class Biosafety Agency

1.3 Mission Statement

To ensure and assure safe development, transfer, handling and use of genetically modified organisms (GMOs) in Kenya.

1.4 Our Core Values

a) Integrity
b) Professionalism
c) Transparency
d) Accountability

1.5 Our Objectives

a) To facilitate responsible research and minimize risks that may be posed by genetically modified organisms;

b) To ensure adequate level of protection in the development, transfer, handling and use of genetically modified organisms that may have an adverse effect on the health of the people and the environment; and

c) To establish a transparent, science-based and predictable process for reviewing and making decisions on the development, transfer, handling and use of genetically modified organisms and related activities.

1.6 Our Core Functions

The Biosafety Act no.2 of 2009 lists the functions of NBA as follows:

a) Consider and determine applications for approval for the development, transfer, handling and use of genetically modified organisms, and related activities in accordance with the provisions of the Biosafety Act;
b) Co-ordinate, monitor and assess activities relating to the safe development, transfer, handling and use of genetically modified organisms in order to ensure that such activities do not have adverse effect on human health and the environment;
c) Co-ordinate research and surveys in matters relating to the safe development, transfer, handling and use of genetically modified organisms, and to collect, collate and disseminate information about the findings of such research, investigation or survey;
d) Identify national requirements for manpower development and capacity building in biosafety;
e) Advise the Government on legislative and other measures relating to the safe development, transfer, handling and use of genetically modified organisms;
f) Promote awareness and education among the general public in matters relating to biosafety;
g) Establish and maintain a Biosafety clearing house (BCH) to serve as a means through which information is made available to facilitate exchange of scientific, technical, environmental and legal information on, and experience with, genetically modified organisms; and
h) To exercise and perform all other functions and powers conferred on by the Act.

CHAPTER TWO

2.0 INTRODUCTION TO GENOME EDITING

2.1 Scope and Objective

2.1.1 Scope

These guidelines provide clarity on which genome edited organisms and/or derived products should be regulated under the Biosafety Act and which products would be exempted and managed as conventional varieties or breeds. The guidelines apply to genome edited plants, animals and microorganisms. Determination of genome edited organisms and/or products for possible regulation will be conducted on a case by case basis.

2.1.2 Objective

The objective is to provide technical guidance to applicants and reviewers on which genome editing organisms and/or products are regulated under the Biosafety Act, 2009.

2.1.3 Exemptions

These guidelines shall not apply to genome edited pharmaceuticals for human use and techniques listed in the first Schedule of the Biosafety (Contained Use) Regulations, 2011.

2.2 Background to genome editing

Modern biotechnology, involving the use of recombinant-DNA (r-DNA) technologies, also known as genetic engineering, emerged as a powerful tool with many potential applications in agriculture and healthcare in the 1980s. Organisms modified using r-DNA techniques, commonly referred to as genetically modified organisms (GMOs), have been and are being developed with traits intended to provide benefit to farmers, consumers, and industry. These traits include; abiotic stress tolerances, disease resistance, herbicide tolerance, pest resistance, improved nutrition, improved shelf life, more efficient vaccines, faster growth, production of useful by-products, among others.

Advancements in genome sequencing and comparative analysis, functional genomics, and the growing knowledge about function of various genes have motivated researchers to look at new ways to develop new traits by changing specific genes in the organism's own DNA, or to insert new DNA in a targeted manner. Over the last decade, researchers have developed many new precise techniques to develop new traits in a targeted manner through genome editing (Table 1). A growing number of countries have developed or are currently developing regulatory

policy/guidance for what genome editing products may be exempted from existing GMO regulatory frameworks, considering that genome editing can result in variety of outcomes: from outcomes comparable to those achieved by conventional breeding or found in nature, to outcomes comparable to transgenesis. Possible applications of genome editing in crops include biofortification, resistance to diseases and abiotic stress (e.g., drought), herbicide tolerance, male/female sterility, altering of flowering time etc. Applications in livestock include improved productivity e.g. muscle of meat, improved quality of products e.g. reduced allergenicity in milk, animal health and welfare e.g. resistance to diseases and hornless cows among others.

Table 1: Examples of Current Methods Used for Genome Editing

Genome editing technique		**Description**
Oligonucleotide Directed Mutagenesis (ODM)		Oligonucleotide Directed Mutagenesis (ODM) involves specific nucleotide changes and, without the use of enzymes (e.g. nucleases), result in targeted single nucleotide polymorphisms (SNPs).
Site Directed Nuclease (SDN)		Set of techniques based on the use of nucleases that introduce break in the DNA chain near a defined target sequence. Depending on the type of the endogenous DNA repair mechanism, different kind of site-directed modifications or genome editing possibilities may involve mutagenesis, gene replacement, gene insertion, and site-directed deletions or inversions.
a)	Meganuclease Technology	Meganucleases are naturally occurring restriction enzymes isolated from bacteria and yeasts that recognize and cleave DNA sequence targets, typically from 12 to 40 bp.
b)	Zinc Finger Nuclease Technology	Zinc finger nucleases (ZFN) are proteins composed of a zinc finger part and a nuclease part. The zinc finger protein binds to a specific DNA location on each side where the nucleases perform their function in pairs. Zinc finger sequence can be adjusted such that the nucleases can cut a target sequence in the plant.
c)	TALEN (Transcription Activator-Like Effector Nuclease) Technology	A type of site-directed nuclease that combines a customizable array of protein modules, found in bacterial proteins called transcription activator-like effectors, that each recognize a single DNA base and the catalytic domain of a DNA cutting enzyme called *Fok*I.

d)	CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)/Cas Technology	A precise form of site-directed nuclease technology based on CRISPR/Cas bacterial defense system against viruses. The nuclease is coupled to an RNA molecule which then binds to a specific DNA site. With this technology, scientists can elicit targeted DNA changes.

(The above table provides a short summary of some of the genome editing techniques currently being applied in breeding. Examples listed are for illustrative purposes and are not exhaustive).

With the emergence of genome editing techniques, there is need to consider the appropriate regulatory mechanisms for products of such technology. Regulators around the world have been developing regulations to assess and make decisions on genome editing techniques. The Authority, in collaboration with relevant regulatory agencies, has taken the initiative to develop these guidelines to establish the regulatory mechanisms taking into consideration other international guiding documents and genome editing regulations from other countries.

2.3 Genome editing in relation to Genetically Modified Organisms

The Cartagena Protocol on Biosafety (CPB) to the Convention on Biological Diversity (CBD) is the main international reference instrument for GMO regulation and Kenya is a signatory having signed in the year 2000 followed by ratification in 2003. Kenya's Biosafety laws are a domestication of the CPB. Under the protocol, GMOs (referred to as LMOs) are defined to mean any organism that possesses a novel combination of genetic material obtained through the use of modern biotechnology techniques. Genome editing techniques may alter the genome of organisms resulting in either a GMO or organisms that are not distinguishable from those developed from conventional breeding or natural selection. Those techniques that result to a GMO would be subject to the provisions of the Protocol and the Biosafety Act.

A number of countries such as Argentina, Australia, Brazil, Canada, Chile, Colombia, Honduras, Japan and the US have made progress in developing regulatory frameworks that address regulation of genome edited products. Genome editing is an evolving technology and therefore regulatory frameworks developed need to be continually updated to facilitate innovation. It is in this context that these guidelines have been developed in order to provide a technical guidance to applicants and reviewers on the criteria for determining which genome editing techniques and/or derived end products are regulated under the Biosafety Act.

CHAPTER 3

3.0 REGULATORY CONSIDERATIONS FOR GENOME EDITING TECHNIQUES

3.1 Considerations for regulation of genome edited plants, animals and microorganisms

These guidelines provide a criterion to determine which genome editing processes and derived products are subject to Biosafety Act No. 2 of 2009. The decision thereof is made on a case by case basis (Table 2, Figure 1).

An applicant is required to submit an Early Consultation Form (Annex 1) and pay the applicable fees to the National Biosafety Authority (NBA) providing data on the experimental processes and end product to establish whether it should be regulated under the Biosafety Act, 2009 or not. The decision on early consultation by the NBA will be communicated to the applicant within **30 working days**. However, genome editing projects that do not have the required data will be regulated under the Biosafety (Contained Use) Regulations 2011.

This guideline may be reviewed based on new scientific information. NBA reserves the right to alter its decision if new scientific information previously unknown becomes available.

Table 2: Categories for regulation of genome editing techniques and derived products

Category	Considerations/scenarios
Regulated under the Biosafety Act	i). All genome editing projects without the required data*. ii). All cases of insertions (of foreign genes and/or regulatory elements) from a sexually non-compatible species. iii). All instances where foreign genetic material(s) are detectable. iv). All instances where markers used (selectable and reporter genes) for selection are present in the end-product. v). In cases where research and developmental phase starts with a GMO, NBA will regulate genome edited organisms up to the stage where GMO component is removed/segregated.
Not regulated under the Biosafety Act	i). All modifications by inserting genes from sexually compatible species and where regulatory elements (promoters and terminators) are also from the same species. ii). All deletions/knock outs provided that there is no insertion of foreign genetic material in the end-product. iii). Processed products whose inserted foreign genetic material cannot be detected.

	iv). Conventional breeding methods, mutagenesis, polyploidy and haploidy

Figure 1: Flowchart for the Early Consultation on genome editing processes in Kenya

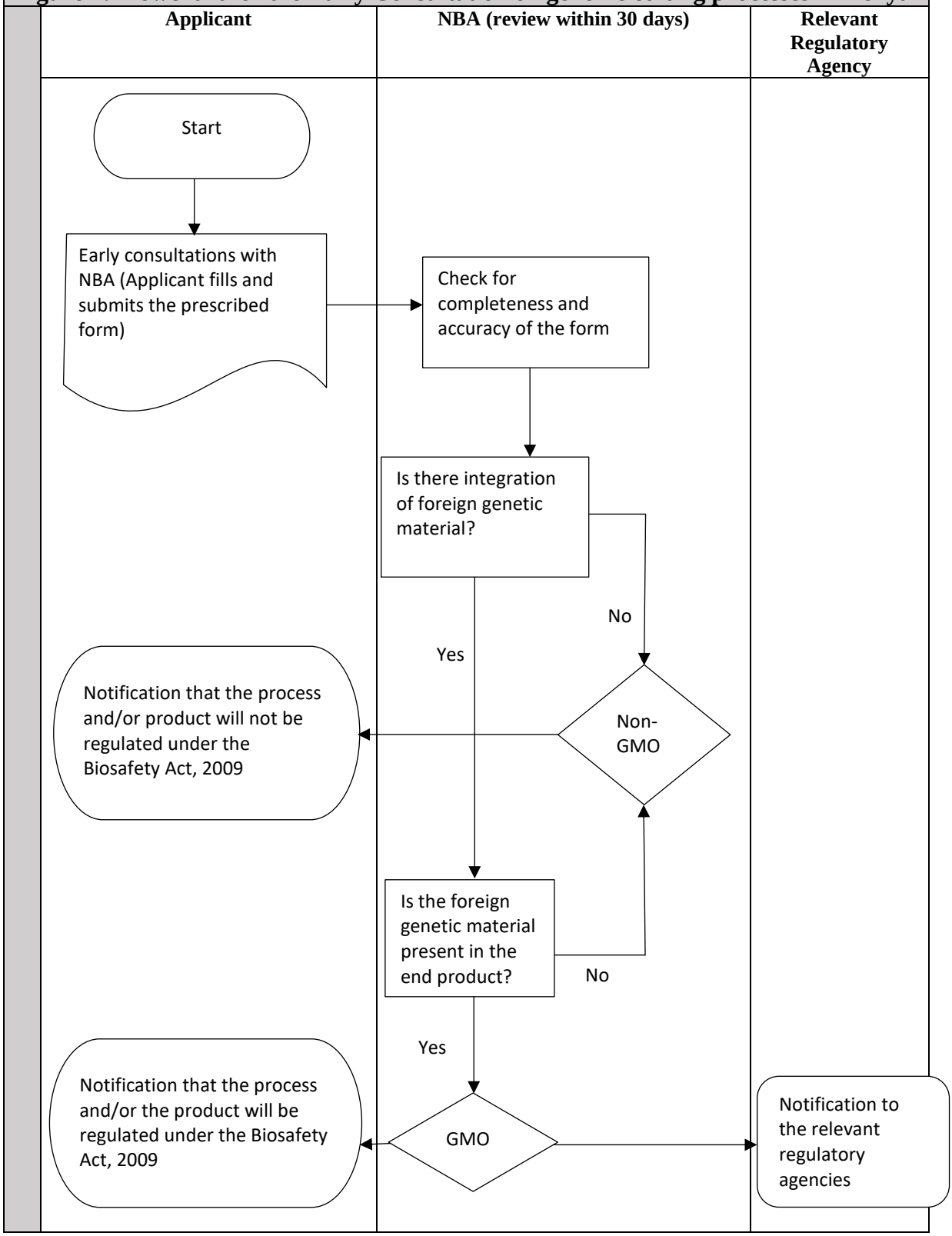

Figure 1: Flowchart for the early consultation on genome editing. The above chart shows the decision process for determining whether the developmental process or products for genome editing are regulated under the Biosafety Act, 2009.

CHAPTER FOUR

3.0 REFERENCES

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ANNEX

ANNEX 1: APPLICATION FOR EARLY CONSULTATION ON GENOME EDITING TECHNOLOGY IN KENYA

This form will guide in determining whether genome editing organisms or their derived products are regulated under the Biosafety Act, 2009 or not.

SECTION I: APPLICANT INFORMATION
1.1 Name of Applicant, Address, Email, Telephone
1.2. Affiliated Institution, Address Email, Telephone, Website
SECTION II: ORGANISM INFORMATION
2.1. Taxonomic description of the organism: Genus, Species (Breed/ Strain/ Variety/ Line – where applicable)
2.2. Rationale for genome editing
Purpose of genome editing: Intended use: Research, Import, Environmental release, Placing in the market, etc (Tick as appropriate)
SECTION III: MOLECULAR TECHNIQUES
3.1. Give a summary of the molecular techniques used: 3.2. State the gene or DNA sequence(s) modified: 3.3. Describe the type of genome editing done (deletion, insertion, substitution, replacement) with supporting data*; 3.4. Molecular description of the target organism's nucleotide target sequences, before and after genome editing with supporting data*; 3.5. Molecular description of the gene edited organisms, their functions and the affected pathways (where applicable) before and after genome editing*;
3.6. Provide the names of vectors to be used and show their genetic map (if not applicable, go to 3.7.)

3.6.1 Is the vector naturally pathogenic?	3.6.2 Is the vector disarmed?	3.6.3 If yes, how was the vector disarmed?
☐ Yes ☐ No	☐ Yes ☐ No	
3.7. Describe delivery methods used for genome editing		
SECTION IV: GENOME EDITED PRODUCT		
4.1. Is the inserted foreign DNA sequence(s) present in the final product?		
☐ Yes ☐ No If No; Describe the techniques used to remove the inserted genetic sequences and evidence for the same*; Describe detection protocols used to confirm absence of inserted genetic sequences in the genome edited end products and provide data to support this assertion*;		
4.2. Has the genome edited product been exempted from respective relevant GMO legislation anywhere in the World? If YES, where and for what purpose?		

Where the required data is not available, the application shall be subjected to the Biosafety Act, 2009 and its enabling regulations.

SECTION V: DECLARATION OF CORRECTNESS OF INFORMATION

I certify that the above information is true to the best of my knowledge.

Principal Investigator/Applicant

Name _____

Signature _____ Date _____

Collaborator(s) (*if applicable*)

Name(s) _____

Signature _____ Date _____