NATIONAL BIOTECHNOLOGY AUTHORITY

GUIDELINES ON GENOME EDITING REGULATORY PROCESSES

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Regulating Biotechnology for a Sustainable Future

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Abbreviations

CRISPR - Clustered Regularly Interspaced Short Palindromic Repeats

DNA - Deoxyribonucleic acid

DSB - Double-strand breaks

GE - Genome editing

GM - Genetically modified

GMO - Genetically modified organism

HDR - Homology-directed repair

NBA - National Biotechnology Authority

NHEJ - Non-homologous end joining

ODM - Oligonucleotide-Directed Mutagenesis

SDN - Site - Directed Nucleases

SI - Statutory Instrument

TALENs - Transcriptional Activator Like Effector Nucleases

ZFNs - Zinc Finger Nucleases

Interpretations

"prospective applicant" means any person submitting a prerequisite Form NBA (GED1) pursuant to the provisions of the National Biotechnology Authority Act [*Chapter 14:31*].

"genome editing" means altering the DNA sequence of an organism at specific positions by deleting, replacing or inserting nucleotides using various techniques which induce breaks in the DNA.

1 Genome Editing Guidelines

Genome editing has emerged as a transformative tool in biotechnology, enabling precise modifications to DNA. There is need to have guidelines to ensure that genome editing is applied responsibly to address scientific challenges and minimise risks in Zimbabwe. The guidelines will promote regulatory compliance and ensure that the application of genome editing techniques will support innovative, collaborative biotechnology research and development to benefit humanity.

1.1 Scope

These guidelines shall be read in line with the National Biotechnology Authority Act [*Chapter 14:31*] of 2006 and Regulations made thereunder.

Information contained in these guidelines is directed to all persons, institutions or bodies wishing to carry out genome editing work ranging from containment, confined field trial and general release.

1.2 Objectives

The objective is to provide technical guidance and information to applicants and stakeholders on general regulatory provisions for genome editing processes and products in Zimbabwe.

1.3 Genome Editing

Genome editing (GEd) involves the alteration of the genetic material of a living organism by inserting, replacing, or deleting a DNA sequence, typically with the aim of improving some characteristic or correcting a genetic disorder. The introduced change could range from alteration of a single base to deletion or replacement of a DNA sequence and such changes could be identical or comparable to natural mutations or obtainable through conventional mutagenesis.

Genome editing techniques include Base Editing, Prime Editing, Transcription Activator-like Effector Nucleases (TALENs), Zinc Finger Nucleases (ZFNs), Oligonucleotide-Directed Mutagenesis (ODM) and Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR).

Developments in genome editing have revolutionized our ability to make precise modifications to DNA, opening new frontiers in medicine, agriculture, industrial processes and the environment, (see Table 1 below). These advancements underscore the need for robust guidelines to ensure safe and equitable utilization of these technologies. There are several examples of genome editing activities being undertaken in Africa. In Kenya, *Sorghum bicolor* resistant to the parasitic weed, striga has been successfully produced through genome editing. Still in Kenya, preliminary research suggests that genome editing particular genes can shorten the cooking time of ordinary beans. In Mozambique, research is ongoing to develop liguleless sorghum, which is more suited for the production of biofuel and fodder because it lacks a particular structure in its leaves and has been demonstrated to have higher biomass and better light perception.

Table 1: An overview of some genome editing applications in various economic sectors

Sector	**Genome Editing Applications**
Agriculture	• Crop varieties with high yield performance, improved taste, early maturity, high nutritional content and quality, increased shelf life, improved biotic and abiotic stress tolerance. • Livestock with high productivity/yield, disease resistance and desirable morphological traits.
Health	• Gene function studies to elucidate genetic causes of neurodegenerative diseases and their treatment. • Precise manipulation of cellular function especially in cancer cell targeting and therapeutic repair of disease-causing mutations. • Antiviral therapeutics for treatment of viral infections by targeting host or viral genes. • Development of gene diagnostic tools for detection of low frequency mutations.
Environment	• Development of microbes and plants for bioremediation and bio-mining. • Development of plants with climate change resilience. • Development of plants for efficient production of biofuels.

Sector	Genome Editing Applications
	• Engineered gene drives for insect pests and disease vectors eradication (population suppression) and population modification.
Industry	• Product processing efficiency through manipulation of microbes for production of novel biocatalysts and additives.

Therefore, devising appropriate guidelines for research, development and general release of genome editing products is essential.

3. Application and Review Process

A prospective applicant for genome editing activities shall submit a requisite pre-submission form, **NBA (GEd) 1** to the Authority (NBA) providing applicant's details, organism information, molecular techniques, genome edited product and declaration by applicant.

Upon receipt of the requisite pre-submission form, the Authority shall determine whether the activity or end product should be regulated under the GMO Regulations i.e., **Statutory Instrument 105 of 2026** or otherwise (see Figure 1 below). The outcome of the determination shall be communicated to the applicant within fourteen (14) working days. The Authority shall determine all applications on a case-by-case basis.

NBA reserves the right to review this outcome if new scientific information becomes available.

4.Considerations for regulation of genome edited processes and products

The scope of these regulatory guidelines is limited to processes and products which utilise genome editing techniques such as base editing, prime editing and site-directed nucleases (SDN) and other nucleases with similar functions. The application of the aforementioned nucleases are categorised into three groups as indicated in Table 2 below.

Table 2: *Categories of Gene editing events.*

Category	Description	GMO Classification
Site-Directed Nuclease (SDN)-1	• Involves repair of Double-Strand Break (DSB) in the target DNA by non-homologous end joining (NHEJ) through endogenous	**Non GMO** • Single nucleotide /point alteration • Do not contain new combinations of genetic material.

Category	Description	GMO Classification
	repair mechanism without homology-directed repair (HDR). • Such repairs create small indels at the joining point resulting in gene silencing, knock-out or a change in gene activity.	• Final products are equivalent to naturally occurring loss of function or a change in the activity of gene mutations or those induced via mutation breeding. • Indistinguishable from naturally occurring variants or comparable to mutants derivable through conventional mutagenesis.
Site-Directed Nuclease (SDN)-2	• Involves template-guided or HDR repair of the targeted DSB using a short single-stranded donor DNA. • The donor DNA carries one or more small mutations flanked by sequences matching one or both ends of the targeted DSB (known as repair template), allowing desired changes in the target gene.	**Non GMO** • Several nucleotide alterations i.e. between 2 and 20. • Carry specific nucleotide substitutions (*e.g.*, targeted edits or targeted allele replacements) introduced through DNA repair templates but do not carry any exogenous DNA. • Comparable to naturally occurring variants or mutants obtainable through conventional mutagenesis.
Site-Directed Nuclease (SDN)-3	• Involves template-guided HDR of the targeted DSB using a double-stranded donor DNA, containing a complete gene or even longer genetic element. The ends of the donor are homologous to the two DSB ends (typically over 800 bp each). • This allows gene replacement or insertion of a new gene from the same, related or a distant species at the target site.	**GMO**

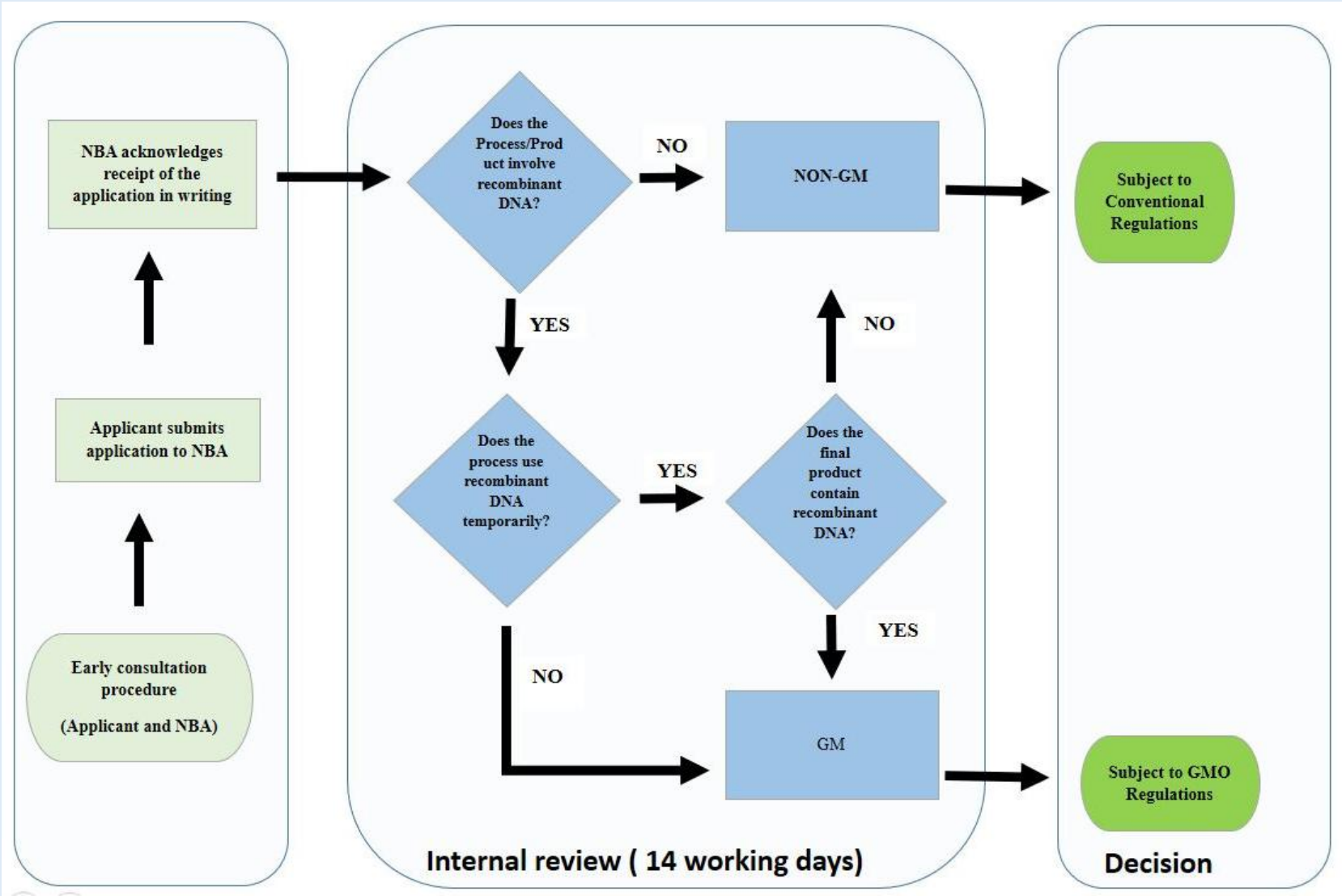

Figure 1: *Determination of regulatory status of Genome Editing activity or end product process flow*.

ANNEX

NBA (GEd) 1

ANNEX 1: REQUISITE PRE-SUBMISSION FORM ON GENOME EDITING ACTIVITIES IN ZIMBABWE

This form will guide in determining whether genome editing activities (organisms or end products) are regulated under the NBA Act of 2006 or otherwise.

SECTION I

Applicant Details

i. Name of Applicant: _____

Physical address

_____

_____

_____

ii. Postal address

_____

_____

_____

iii. Telephone Number_____

iv. Email Address_____

Responsible person details

v. Name of Responsible Person:

_____

Physical address

_____

_____

Telephone Number _____

Email Address_____

Affiliated Institution:

_____

Physical address

_____

_____

Postal address

_____

_____

Telephone Number_____

Email Address_____

Website_____

1.2 Project co-funders or sponsors or partners

a. Name of co-funders or sponsors or partners

_____

_____

b. Physical Address

_____

_____

_____

c. Postal address

_____

_____

_____

d. Telephone Number_____

e. Email address_____

SECTION II

ORGANISM INFORMATION

2 (a) Organism Taxonomic description

(b) (Breed/ Strain/ Variety/ Line – where applicable)

(c) Rationale for genome editing

(i) Purpose of genome editing (provide brief description):

(ii) Intended use:

Contained Use	☐
Import	☐
Confined Field Trial	☐
General Release	☐
Placing on market	☐
Export	☐

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?	**YES**	**NO**
3.6.2. Is the vector disarmed?	**YES**	**NO**
3.6.3. If yes, how was the vector disarmed?		
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**
4.2. If not, describe the techniques used to remove the inserted genetic sequences and evidence for the same*		
4.2.1. Describe detection protocols used to confirm absence of inserted genetic sequences in the genome edited end products and provide data to support this assertion*		

4.3. Has the genome edited product been exempted from respective relevant GMO legislation anywhere in:- (i) Africa, and (ii) the rest of the world ?	4.3.1. If yes, where and for what purpose? (Provide supporting evidence)

***Where the required data is not available, the application shall be subjected to the National Biotechnology Authority Act [*Chap. 14:31*] of 2006 and its enabling Regulations.**

SECTION V

DECLARATION BY APPLICANT

I hereby certify that the above information is true and accurate to the best of my knowledge

Name of Applicant _____

Position within the applying organisation: _____

Date: _____

Signature: _____

Official Stamp of applying Organisation should be placed here