National Biosafety Authority

GUIDELINES FOR GENOME EDITING APPLICATIONS IN GHANA

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DECLARATION

I, Prof. Charles ANTWI-BOASIAKO, the Chairman of the Board of the National Biosafety Authority (NBA), acting under Section 40(3) of the Biosafety Act, 2011 (Act 831), hereby issue these Guidelines.

Dated this 30th day of October 2023.

Prof. Charles ANTWI-BOASIAKO, PhD

1.0 INTRODUCTION

Genome Editing is the precise targeted modification of the nucleotide sequence of the genome of an organism. Genome Editing (GE) techniques are rapidly being developed and deployed to serve agriculture and food production objectives leading to improved crops and other products. The process involves precise deletion, replacement, or the insertion of a single or a limited number of nucleotides. Genome edited organisms can have deoxyribonucleic acid (DNA) segments from the same or different species. There are a number of tools described as 'Genome Editing Technology'. Perhaps the most widely used tool is the Clustered Regularly Interspaced Short Palindromic Repeat (CRISPR)Cas (CRISPR-associated protein), but GE also refers to other methods such as Oligonucleotide Directed Mutagenesis (ODM), Transcription Activator-like Effector Nucleases (TALENs), Zinc-Finger Nucleases (ZFNs) and Meganucleases, as well as variations of these technologies. Whether using conventional breeding methods, recombinant DNA technologies, or GE Technologies, some genetic changes could be expected. The rates of genetic change can vary by species, and some methods introduce more changes than others. Random genetic changes can be stimulated deliberately to increase genetic variation, as is the case with random mutagenesis techniques. Random genetic changes can be silent (no observable effect), resulting in a desirable trait or combination that is selected in the breeding programme, or can result in unintended effects that would not be desirable, and which would be eliminated from the breeding programme.

Genome Editing Technologies do not present any unique or specifically identifiable environmental or human health concerns relative to other techniques of plant breeding. Genome Editing can be used to accomplish genetic outcomes similar to using conventional breeding practices. Notably, not all products of GE end up as GMOs. As such, only those GE processes or products that result in GMOs shall be subject to regulation under the Biosafety Act, 2011 (Act 831) and in accordance with Section 7 of these Guidelines. For end-users to benefit fully, products developed using GEd must be subjected to science-based safety regulations. Thus, GEd developers and other related stakeholders need to be aware of the Biosafety (Management of Biotechnology) Regulations, 2019 (L.I. 2383) and its requirements prior to the commencement of GE research activities and/or commercial release.

2.0 REGULATORY ALIGNMENT

The National Biosafety Authority (NBA) recognizes the value of international regulatory alignment. Ghana is a party to the Cartagena Protocol on Biosafety (CPB) to the Convention on Biological Diversity (CBD). The protocol defines a living modified organism (LMO) as any living organism that possesses a novel combination of genetic material obtained through the use of modern biotechnology. The objective of the CPB is to contribute to ensuring an adequate level of protection in the field of the safe transfer, handling, and use of LMOs resulting from modern biotechnology that may have adverse effects on the conservation and sustainable use of biological diversity, taking into account risks to human health. The definition of an LMO may vary between different jurisdictions; however, Ghana has adopted the term genetically modified organism (GMO) to be used interchangeably with the term LMO as found in the CPB. According to the general provision in Article 2 of the CPB, each

party shall take necessary and appropriate legal, administrative, and other measures to implement its obligations.

Pursuant to Section 20 and Section 40 (3) of the Biosafety Act, 2011 (Act 831), the NBA has developed these Guidelines to provide further clarity on the regulatory pathway to be adopted for different genome edited organisms within the framework of the Act. It is intended for use by GE developers and other relevant stakeholders wishing to understand whether their projects and/or products will be regulated under the prevailing provisions of the biosafety act or other applicable laws and steps to take when applying for biosafety approval on GE activities that would be regulated under the Biosafety Act in Ghana.

3.0 SCOPE

These Guidelines detail the procedures in determining which genome edited organisms or products may be regulated under the Biosafety Act, 2011 (Act 831).

Information herein is directed at all relevant stakeholders, but not limited to persons wishing to use GE Techniques relating to animals, plants, and microorganisms. This ranges from contained use, confined field trial, introduction into the environment and /or placing on the market, and imports intended for direct use as food, feed, or for processing, exports, and transit in Ghana.

4.0 OBJECTIVE

To provide procedural guidance to potential applicants on the categories of Genome Edited organisms and/or their products that shall be regulated under the Biosafety Act, 2011 (Act 831).

5.0 APPLICATION PROCESS

5.1 Pre-submission consultation

As part of the NBA administrative processes, applicants shall complete and submit a pre-submission consultation form to the secretariat which will help to determine the regulatory status of the application.

5.2 Procedure for submitting an application

In case the product would be regulated under the Act, the applicant shall complete and submit the appropriate application form. The completed application requesting approval to carry out GE shall be addressed to the Chief Executive Officer, National Biosafety Authority (NBA).

The NBA may request further information/clarification from the applicant in accordance with Section 17(2) of the Biosafety Act, 2011 (Act 831).

6.0 EXEMPTIONS

Generally, these Guidelines do not apply to the use of GE or genome edited organisms for purposes of developing pharmaceuticals for human use, and which are the subject of any other enactment, as stated in Section 1 (2) of the Biosafety Act, 2011 (Act 831). Details of other exempted genome edited-related matters are captured in section 7 of these Guidelines.

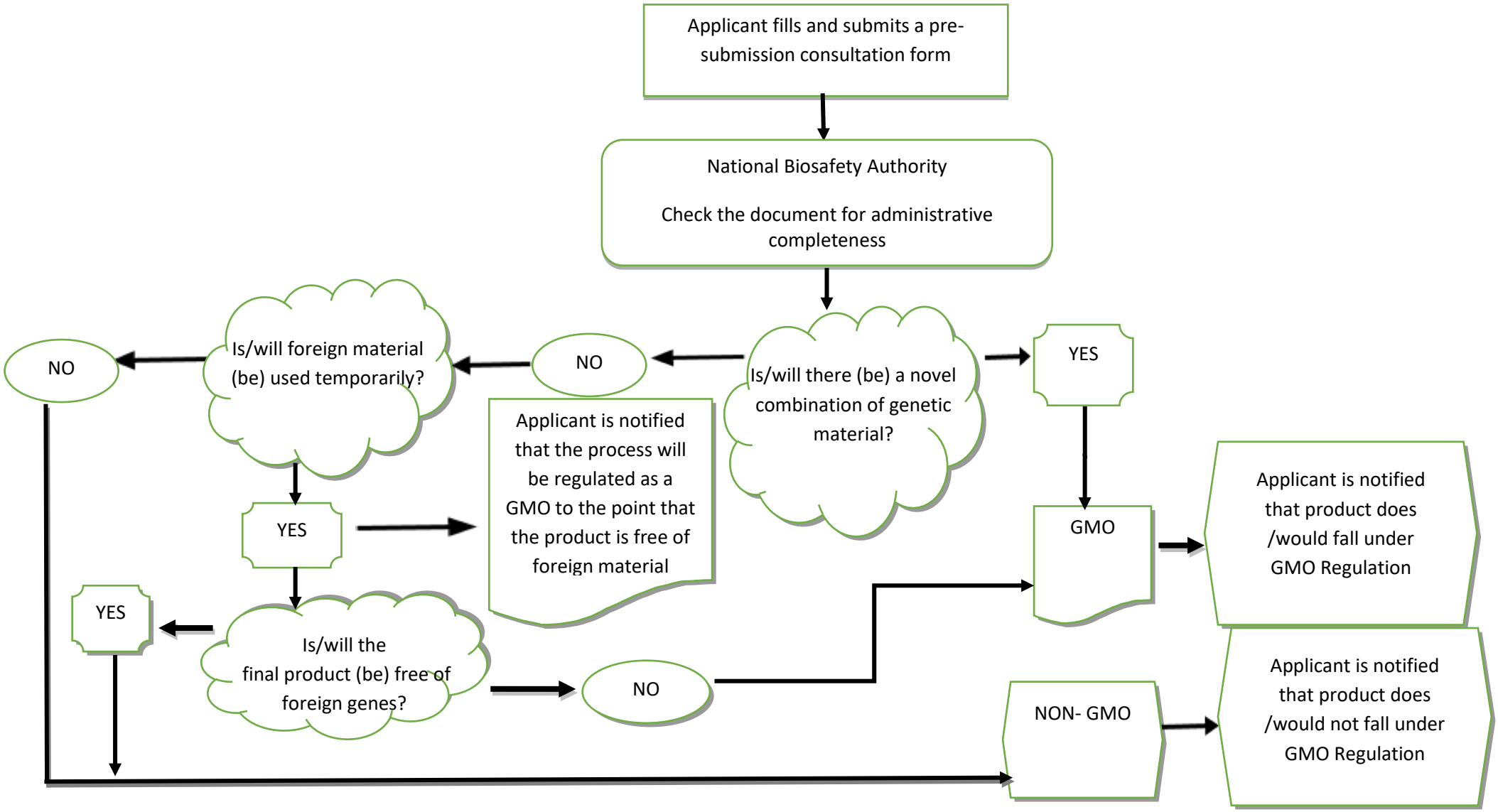
7.0 REGULATORY CONSIDERATIONS FOR GENOME EDITING TECHNIQUES

Products of GE would be regulated on a case-by-case basis. Depending on the kind of genetic modification, products of GE containing foreign genes shall be regulated under the Act. However, in instances where the product of GE does not contain foreign genes then it will not be regulated under the Biosafety Act. As such, products of GE shall be regulated on a case-by-case basis until the foreign gene is completely removed in the process. These Guidelines provide the criteria to determine which organisms and/or products shall be regulated or not (Table 1) under the Biosafety Act, 2011 (Act 831).

Table 1: Categories of Genome Editing Techniques and their derived products for regulation in Ghana.

Category	Considerations
Regulated under the Biosafety Act, 2011 (Act 831)	• All cases of insertions (for foreign gene (s) and/or regulatory elements) from a non-sexually compatible species where the foreign gene remains in the final product. • All instances where foreign gene (s) are detectable. • All instances where markers used (selectable and reporter genes) for selection are present in the product in subsequent generations.
Exempt From Regulation	• The end products from SDN-1 methods that do not contain inserted nucleic acids or its replicated product. • All deletions/knock outs provided that regulatory elements used are from the same species that is, no insertion of new elements. • Processed products where foreign gene (s) cannot be detected. • Natural processes such as conventional breeding, mutations, polyploidy.

8.0 PROCESS MAP FOR PRE-SUBMISSION CONSULTATION FOR GENOME EDITING APPLICATIONS



9.0 SANCTIONS UNDER THE BIOSAFETY ACT, 2011 (Act 831), SECTION 41

(1) A person commits an offence and is liable on conviction to a fine of not less than two thousand five hundred penalty units and not more than five thousand penalty units or to a term of imprisonment of not less than five years and not more than ten years or to both the fine and the term of imprisonment if that person.

(a) makes contained or confined use, releases into the environment, places on the market, imports or exports, a genetically modified organism without the approval of the Authority, or

(b) contravenes a condition attached to an approval under the Act, or

(c) fails to furnish information as required by or under the Act, or

(d) uses or releases confidential information for a purpose not authorised by or under the Act, or

(e) uses a genetically modified organism for mischievous or unethical purposes, or

(f) obstructs or fails to assist the Authority or officers of the Authority in the performance of a function under the Act, or

(g) contravenes any other provision of the Act.

(2) Where a body corporate is convicted of an offence specified in subsection (1) above a Director and any other officer of that body corporate shall be deemed to have committed the offence for which the body corporate is convicted.

(3) A person shall not be convicted of an offence pursuant to subsection (2) where it is proved to the satisfaction of the Court that, having regard to the nature of the offence,

(a) that person did not consent to, or did not connive at, the commission of the offence, or

(b) that person did exercise the degree of reasonable diligence as ought in the circumstances to have been exercised to prevent the commission of the offence.

(4) For the purposes of subsections (2) and (3), a body corporate includes a firm or partnership, and those subsections shall be construed accordingly in the case of a firm or partnership.

10.0 REVIEW AND UPDATE OF THE GUIDELINES

These Guidelines shall be subjected to review every five (5) years and/or based on new, relevant available scientific information.

11.0 ANNEX

Table 2: Examples of Current Methods and Related Mechanisms Used for Genome Editing

Genome Editing Techniques	Description
Oligonucleotide Directed Mutagenesis (ODM)	Oligonucleotide Directed Mutagenesis (ODM) involves specific nucleotide changes and, without the use of enzymes (e.g., nucleases), resulting in targeted single nucleotide polymorphisms (SNPs).
Site Directed Nuclease (SDN)	Set of techniques based on the use of nucleases that introduce breaks in the DNA chain near a defined target sequence. Depending on the type of the endogenous DNA repair mechanism, different kinds of site-directed modifications or GE possibilities may occur, resulting in mutation. It may involve mutagenesis processes such as gene replacement, gene insertion, and site-directed deletions or inversions. There are three types of Site-Directed Nucleases (SDN) Genome Editing and these are; i. SDN-1: no donor DNA template is supplied to force Non-homologous DNA end-joining (NHEJ). It is a naturally occurring DNA repair mechanism. In most cases, NHEJ introduces small insertions or deletions that lead to a loss in gene function i.e. targeted gene knockouts. ii. SDN-2: a homologous donor DNA template, which is a copy of the target gene sequence with only a small modification, is used. During repair, this homologous modified sequence will be introduced into the Genome, causing a targeted mutation that could restore or modify gene function. iii. SDN-3: these applications are similar to SDN 2 applications, except that in this case the homologous donor DNA involves complete gene sequence (s) which could be cis-, intra-, and/or transgene sequences. SDN 2 and SDN 3 therefore enable targeted gene knock-ins.
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 (ZFNs) 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. The zinc finger sequence can be adjusted such that the nucleases can cut a target sequence in the plant.

c. TALENs (Transcription Activator-Like Effector Nucleases) Technology	TALENs are restriction enzymes that can be engineered to cut specific sequences of DNA. They are made by fusing a TAL effector DNA-binding domain to a DNA cleavage domain (a nuclease that cuts DNA strands). TALENs can be engineered to bind practically any desired DNA sequence, so when combined with a nuclease, DNA can cut at specific locations. The restriction enzymes can be introduced into cells, for use in gene editing or for GE in situ, a technique known as GE nucleases.
d. CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)/Cas (CRISPR-associated) Technology	A precise form of site-directed nuclease technology based on CRISPR/Cas bacterial defence 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.
Prime Editing	Prime Editing is a 'search-and-replace' GE technology that introduces all base-to-base conversions, as well as small insertions and deletions, without the need for double-stranded breaks (DSBs) or donor DNA templates.
Base Editing	Base editing is a technique that uses CRISPR-guided RNA to bind its target sequences, but instead of cutting the DNA strand, it chemically changes one DNA base letter into another.

12.0 DEFINITION OF TERMS

For the purposes of these Guidelines:

"Act" the Biosafety Act, 2011 (Act 831).

"Applicant" is a person who submits an application pursuant to a provision of the Biosafety Act.

"Application" the complete dossier submitted by an applicant.

"Biosafety" is a term used to describe efforts to reduce and eliminate the potential risks resulting from biotechnology and its products.

"Biotechnology" is a technological application that uses biological systems, living organisms, or derivatives of those systems and organisms to make or modify products or processes for a specific use.

"Conventional Breeding" involves identifying parent plants with desirable characteristics to create favorable combinations in the next generation.

"Developer" is any individual or organization that works on developing and advancing technologies and techniques for genome editing

"Foreign Gene" in the context of these Guidelines refers to a gene from a sexually non-compatible species.

"**Sexually Compatible**" a viable zygote can be formed through the union of two gametes through techniques used in conventional breeding.