FEDERAL REPUBLIC OF NIGERIA

NATIONAL GUIDELINES FOR THE REGULATION OF GENE EDITING

February, 2020

Foreword

List of abbreviations

CONTENT

PART 1 – INTRODUCTION

Cognizance of the rapid emergence of new genetic engineering techniques, the Federal Government of Nigeria took a proactive step in amending the National Biosafety Management Agency (NBMA) Act, 2015, (as amended) to include the regulation of such emerging gene technology approaches as gene drive, gene editing and synthetic biology, and to ensure biosecurity, as well as related matters. Thus, the National Biosafety Management Act, 2015, (as amended), in section 25(a), states *"No person, institution or body shall carryout gene drive, gene editing and synthetic biology except with the approval of the Agency"*.

The National Biosafety Management Agency (NBMA) Act, 2015 (as amended) empowers the National Biosafety Management Agency (NBMA) to identify and develop functional strategies to facilitate its implementation, hence the production of the National Guidelines on Gene Editing. This technical document provides pertinent information and guide to applicants, stakeholders and the general public on the NBMA's statutory oversight on gene editing activities. It explains processes and procedures of the NBMA in dealing with applications for gene editing, and highlights the requirements of an applicant.

PART 2- OBJECTIVE

The objectives of the document are to provide:

i. good understanding of the concept, techniques, global approaches and regulatory mechanism of gene editing;
ii. guidance and detailed information on general regulatory provisions for applications for gene editing including gene edited products packaging, identification and transport, import and export;
iii. processes & procedure for risk assessment and decision making.

PART 3 - SCOPE

Information contained in the National Guidelines on Gene Editing is limited to gene editing techniques as it relates to plants, animals and microorganisms - process and product - as it applies throughout the Federal Republic of Nigeria.

PART 4: BACKGROUND OF GENE EDITING

Throughout history, humans have taken actions to alter genomes of organisms with the aim of equipping them with useful properties to support human existence and wellbeing. A fundamental understanding of the mechanisms of inheritance and molecular genetics has increasingly allowed for deliberate manipulation of genes and allowed the development of gene technology since 1970s.

In recent years, gene editing techniques enable a targeted and precise modification of the genome with a high degree of specificity thus opening up new unforeseen applications. These modifications range from the replacement, insertion or deletion of one nucleotide at a specific locus to the site-specific integration of entire genes. Gene editing techniques include Transcription Activation-Like Effector Nucleases (TALENs), Zinc-Finger Nucleases (ZFNs), Oligonucleotide Directed Mutagenesis (ODMs) and Clustered Regularly Interspaced Palindromic Repeats (CRISPR).

Gene editing techniques, by way of principle, generate double strand breaks (DSBs) in DNA which is subsequently repaired by one of the endogenous cell repair mechanisms, Non-Homologous End Joining (NHEJ) or Homologous Directed Recombination (HDR). NHEJ is prone to errors and thus can be used to silence a gene (gene knock-out), but is unsuitable for correcting mutations as it may introduce additional mutations. In the HDR pathway, a homologous sequence serves as a template to repair the DSBs allowing an accurate repair. HDR can be used to introduce precise nucleotide sequence modifications or gene replacement/insertion at target loci in the presence of a foreign DNA as a repair template.

Gene editing techniques are categorized into; site-directed nuclease (SDN)-1, SDN-2, and SDN-3.

SDN-1 methods repair DSBs by NHEJ, thus allowing for site-directed mutagenesis. SDN-1 do not involve the use of foreign DNA. SDN-2 involves a template-guided repair of a targeted DSB using a sequence donor. The donor carries one or several small mutations flanked by two sequences matching both ends of the DSB, and is thus recognized as a repair template, allowing the introduction of the mutation(s) at the target site. SDN-3

involves a template-guided repair of a targeted DSB using a sequence donor, typically double-stranded DNA containing an entire gene or an even longer genetic element(s). Both ends of the donor are homologous to the ends of DSB, thus allowing for site-directed gene insertion.

PART 5: SCOPE OF GENE EDITING IN THE CARTAGENA PROTOCOL ON BIOSAFETY

The Article 8 (g) of the Convention on Biological Diversity (CBD) states the obligation of Parties to "establish or maintain means to regulate, manage or control the risks associated with the use and release of living modified organisms (LMOs)." Building on that, Article 1 of the Cartagena Protocol on Biosafety (CPB) aims "to contribute to ensuring an adequate level of protection in the field of the safe transfer, handling and use of living modified organisms resulting from modern biotechnology that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health, and specifically focusing on transboundary movements". According to the general provisions in Article 2 of the Protocol, each party shall take necessary and appropriate legal, administrative, and other measures to implement its obligations under this Protocol. Given that the Cartagena Protocol is the main international reference instrument for GMO/LMO regulation and was established in awareness of future technological developments, it has to be considered to what extent it applies to organisms derived by gene-editing techniques.

The CPB defines LMOs as "any living organism that possesses a novel combination of genetic material obtained through the use of modern biotechnology", where modern biotechnology means the application of:

i. In vitro nucleic acid techniques, including recombinant DNA and direct injection of nucleic acid into cells or organelles, or

ii. Fusion of cells beyond the taxonomic family, that overcome natural physiological reproductive or recombination barriers and that are not techniques used in traditional breeding and selection.

Although Gene Editing involves modern biotechnology techniques, it's not clear if the definition of LMOs captures all its forms. Here, it is questionable whether the development of point mutations and indels arising from NHEJ overcome "natural physiological reproductive or recombinant barriers" as is required by the definition. However, repair pathways involving homologous donor templates at the time of double stranded break (DSB) formation produce genetic modification that are novel because foreign DNA is integrated into the target organism`s genome. Such organisms are regarded as LMOs/GMOs and thus are subject to regulations guided by the CPB.

Furthermore, as a general exemption, the CPB does not apply to the transboundary movement of LMOs in the form of pharmaceuticals for humans which are addressed by other relevant international agreements or organizations.

PART 6: GENE EDITING TECHNIQUES

Gene editing comprises protein-mediated techniques (e.g., zinc-finger nucleases, TALENs), nucleic-acid-mediated genome modifications (e.g., ODM), or a combination thereof (e.g., CRISPR-techniques).

Zinc-Finger Nucleases (ZFNs)

ZFNs are synthetic restriction endonucleases, custom designed to cut DNA at specific sequences. They consist of zinc-finger domain that recognizes specific 3 base-pair DNA sequences at target sites in the genome and a nuclease domain (FokI) that cuts double-stranded DNA. The ZFN technology allows the introduction of site-specific mutations or the site-specific integration of genes in the plant genome.

Three variants of the ZFN technology are recognized in plant breeding with applications ranging from producing single mutations or short deletions/insertions in the case of ZFN-1 and -2 techniques up to targeted introduction of new genes in the case of the ZFN-3 technique. Literature shows that ZFNs have been used widely for targeted genome modifications in Arabidopsis, tobacco, and maize.

Transcription Activator-Like Effector Nucleases (TALENs)

TALENs were first identified in plant pathogenic bacteria (Xanthomonas) and function using the principle of ZFNs as engineered nucleases. They are however generated by fusing a transcription activator-like effector (TALE) DNA binding protein to the non-specific DNA endonuclease FokI. Studies have shown that TALENs have been used successfully to edit genomes of Arabidopsis, rice, Brachypodium, barley, maize, tobacco, soybean, wheat, tomato, potato and sugarcane (Lusser *et al.* 2012; Lusser *et al.*, 2011).

Clustered Regularly Interspaced Palindromic Repeats (CRISPR) CRISPR/Cas9

CRISPR/Cas9 was first used to edit plant genes in 2013 and is currently the prevalent gene editing tool. CRISPR was discovered as a prokaryotic immune system that protects cells by selectively targeting and destroying foreign DNA from viruses or plasmids. The engineered CRISPR/Cas9 is based on the type II CRISPR system that has the following three main components: the CRISPR associated protein 9 (Cas9), a trans-activating crRNA (tracrRNA) and a precursor crRNA (precrRNA). CRISPR/Cas9 is much simpler and easier to manipulate than the ZFNs and TALENs, and most importantly, it has a much higher efficiency in producing targeted mutations.

CRISPR/Cpf1

CRISPR from Prevotella and Francisella 1 (Cpf1) adds another option to the CRISPR toolbox. CRISPR/Cpf1 is an RNA-guided, class II CRISPR/Cas system that is similar to the CRISPR-Cas9, but shows features distinct from those of the CRISPR-Cas9 system.

Prime Editing

Prime editing techniques allow programmable base editors to fuse a catalytically impaired endonuclease (dCas9) to an engineered base editor (reverse transcriptase, cytidine deaminase) programmed with a prime editing guide RNA (pegRNA) that both specify the target site and encode the desired edit. These enzymes directly change individual nucleotides in the DNA and have the potential to correct disease-associated point mutations.

Oligonucleotide Directed Mutagenesis (ODM)

ODM is another tool for targeted mutagenesis in plant breeding. ODM is based on the use of oligonucleotides for the induction of targeted mutations in the plant genome, usually of one or a few adjacent nucleotides.

PART 7: GLOBAL REGULATORY APPROACHES TO GENE EDITING

Review of existing process-triggered Genetic Engineering (GE)/Genetic Modification (GM) regulatory systems: Australia, New Zealand, Europe, and India are using a process-driven regulatory trigger to regulate GE/GM organisms; these jurisdictions are reported to be currently reviewing the scope of their regulatory definitions, in order to clarify, if all forms of Gene Editing fall under their respective existing GE/GM regulatory framework.

Existing product-triggered regulations: Canada is regulating GE/GM and Gene Editing products according to a product-trigger, under which the relevant novelty of the trait in question is considered on a case-by-case basis, irrespective of the technology used to develop it.

New regulations of Gene Editing: Argentina is reported to have introduced a new, customized regulatory resolution on New (Plant) Breeding Techniques (N(P)BTs) in 2015, making it one of the first countries to have passed a regulation on this novel set of techniques, covering the sub-category of Gene Editing in their course.

Israel also has recently issued a regulation, whose technical criteria resemble the ones applied in the Latin American countries mentioned before. Office of the Gene Technology Regulator (OGTR), Australia has launched a public consultation on GMO regulation amendments. As a consequence of the proposed changes, some cases of Gene Editing may be exempted from regulation. However, the scope of potentially exempted products in Australia would be quite narrow compared to the approaches of the other countries that have made regulatory decisions until now.

In the USA, current decisions on genome-edited plants have been based on the Plant Protection Act, as enforced by the USDA. The US Coordinated Framework for Biotechnology makes no special provisions for genome edited crops. As for any biotechnology-derived plant, if the genome-edited crop poses a plant pest risk, expresses a pesticide trait, or poses food safety risks different from other plants produced through traditional plant breeding then it is subject to regulatory considerations (by USDA, EPA and FDA, respectively); otherwise, the product can freely enter market channels.

In addition, both the FDA and the EPA could regulate genome-edited crops, but neither agency has indicated what their approach will be. Elsewhere, regulatory frameworks have been established that allow for progress in the development and commercial advancement of crops developed through Gene Editing, even as the specifics of the regulatory frameworks are being considered.

As explained in the previous sections, rules that determine whether or not an organism falls under a special GMO regulatory regime differ from one country to another. Quite often, their parameters for regulatory inclusion are based on product characteristics and/or the process used to obtain them. **However in Nigeria, if the gene editing process or the gene edited product does not lead to or have a new combination of genetic material (e.g. does not use a transgene/uses a transgene which is removed in the final product), a non-GM regulatory classification is applied: in this case, basic information on the overall breeding process, genetic changes, traits, bred-out of helper transgenes, etc. will be required.**

If on the other hand, the gene editing process requires the use of recombinant DNA sequences or the gene edited product has a new combination of genetic material (e.g. uses a transgene which remains in the final product), the regulatory classification stipulates that the final product falls under GM regulation.

PART 8 – GENERAL PROVISIONS FOR APPLICATION

I- Submission of Application

Any person, group of persons, institution or company that intends to have dealings with Gene Editing for any purpose must obtain and complete the application form (from the NBMA website - www.nbma.gov.ng or offices) and submit, with a dossier, to the Agency..

II- Acknowledgement of Application by the Agency

The Agency shall acknowledge in writing any application received to carry out any activity using gene editing stated in the NBMA Act, 2015 (as amended) or in the guideline.

III- Check for Completeness of Application Dossier/Internal Review of the Application

The Agency shall after acknowledging the application check for completeness of the dossier and also internally review the application to determine the regulatory status of the application.

IV- Request for Additional Information by the Agency, if need be

Where necessary, the Agency may request for additional information from an applicant to help guide the internal review. At this point, processing of the application will be stopped until response is received from the applicant.

V- Conveyance of Decision of the Internal Review

The Agency, after checking for completeness of the application and internally reviewing the application (if no additional information is required), will convey the regulatory status of the application, (in writing or electronically) to the applicant. Decision on the regulatory status of the application determines the next step of the application process.

VI- Payment of Prescribed Application Fees by the Applicant

An applicant will pay the required non-refundable application and processing fees that will be communicated to the applicant when forwarding the decision of the internal review if it falls within GMO classification. The evidence of payment must be submitted to the Agency for the application process to continue.

[**Note**: *The application will not require a fee if it does not fall within GMO classification.*

VII- Display of Application Dossier to the General Public

The Agency shall display the application in strategic locations for comments by the general public, if it falls within regulatory requirements. Notice of display of the application will be published in at least two national dailies and one local newspaper, Biosafety Clearing House, Agency website or such other news media as the Agency may from time to time determine. The notice shall contain summary of the application and brief information on the place and duration for the display, for public comments.

VIII- Constitution of National Biosafety Committee and National Biosafety Technical Sub-Committees

The Agency may constitute the National Biosafety Committee (NBC) and the National Biosafety Technical Sub-committees (NBTS) for further review of application that falls within GMO classification.

IX- Decision by NBMA

The Agency will issue Permit or reject application on the basis of recommendation by NBC and the decision of the DG/CEO. The decision may be forwarded to relevant regulatory agencies and also be made available in the Biosafety Clearing House (BCH) and NBMA website.

PART 9 – RISK ANALYSIS

Prior to approval of any activity concerning gene editing to be regulated, a comprehensive risk analysis shall be carried out to ascertain its safety to human health and the environment. This risk analysis process shall consist of three (3) interconnected elements: risk assessment, risk management and risk communication as provided in Part VIII of the NBMA Act, 2015, (as amended)(see Annex I of these guidelines).

PART 10 – SOCIO-ECONOMIC CONSIDERATION

I- Technology Assessment Based on Costs and Benefits Analysis

Though the potential costs and benefits, the socioeconomic risks, and the challenges for using gene-edited crops in agricultural value chains is not well established due to its novelty, if a gene edited product contains a novel DNA, it will be considered as a GMO, and socioeconomic consideration (SEC) on Article 26 of CPB and the provision of the NBMA Acts on the third schedule (79 to 84) shall apply. (See Annex II of these guidelines).

PART 11: PERMITS

General provisions for application process for permit shall apply as contained in Part 8 with exceptions in some cases.

I - Permit for Containment and Confined Field Trial

1) In accordance with the NBMA Act, 2015, (as amended), an applicant wishing to obtain a permit from the Agency to conduct any form of contained or confined use activity, including experiment on Gene Editing shall submit an application to the Agency providing all relevant information in the form prescribed by the Agency.

2) Any Institution(s) wishing to apply to the Agency for a permit under the regulation shall first submit the application to its IBC constituted by the NBMA for review and endorsement. An application shall not be accepted as completed by the Agency unless it contains a written endorsement from an IBC.

3) The IBC shall be a part of the institution where the applicant intends to carry out the contained use experiment. Where a critical mass of scientists to constitute the IBC is not available, the institution may jointly form one committee with other institution(s) or rely on the IBC of another institution.

II- Permit for Commercialization/General release

General provisions for application process for permit shall apply as contained in Part 8 with exception in some cases.

1) An applicant wishing to obtain permit for commercial release of gene edited product(s) classified as GMO shall submit an application to the Agency in the form prescribed by the Agency.

2) Prior to the submission of the application to the Agency, the applicant shall evaluate the socio-economic impact of the commercial release of the gene edited products in conformity with the provisions of the Act and guidelines issued by the Agency.

3) The Agency shall acknowledge the receipt of any application (in writing or electronically) for permit for the commercial release of the Gene Edited Product within twenty-one (21) working days from the date of receipt of the application.

4) The Agency shall ensure public awareness and participation in line with the provisions of the Act.

5) The Agency may constitute NBC and NBTS to review the application. The NBC shall give its expert opinions and recommendations to the Agency.

6) The Agency shall by a decision document, approve the application stating the terms and conditions of the permit or reject the application.
7) The decision will be forwarded to relevant regulatory agencies and also be made available in the Biosafety Clearing House (BCH) and NBMA website

Renewal of permit for commercialization

Where the applicant wishes to renew a permit for commercial release of Gene edited products classified as GMO, the applicant shall not later than nine (9) months before the expiration of the permit, submit an application to the Agency, which shall make a decision on the application before expiration of the permit.

The Agency upon the receipt of the application for renewal of permit shall-

- Acknowledge the receipt of the application in writing or electronically within twenty-one (21) working days from the date of receipt of application;
- Review the application for compliance with the Act, Regulation and Guidelines issued under the Act, and
- Request the applicant in writing or electronically for any further information which the Agency considers necessary.

III- Application for Permit for Import for Food, Feed and/or Processing (FFP)

Application for Permit for import for food, feed and/or processing (FFP) shall comply with provisions of the National Guidelines for Importation of GMOs for FFP (2020). However, the following procedures should be observed:

1) Applicant should submit a completed application form to the Agency providing all relevant information in the form prescribed by the Agency accompanied with a dossier containing risk assessment and risk management of the Gene edited product intended for importation.

2) The Agency shall acknowledge the receipt of an application in writing or electronically within twenty-one (21) working days of its receipt of the application.

3) The Agency shall after acknowledging the application, check for completeness of the dossier and also internally review the application to determine the regulatory status of the application.

4) Where necessary, the Agency may request for additional information from an applicant to help guide the internal review. At which point, processing of the application will be stopped until response (additional information) is received from the applicant.
5) The Agency will, after checking for completeness and internally reviewing the application (If no additional information is required), convey the regulatory status of the application, (in writing or electronically) to the applicant. Decision on the regulatory status of the application determines the next step of the application.

6) The applicant will proceed to pay the required non-refundable application fee that will be communicated to the applicant when forwarding the decision of the internal review. The evidence of payment must be submitted to the Agency for the application process to continue.

7) The Agency shall display the notice of the application in at least two national dailies, one local newspaper and the Agency's website. The notice shall contain summary of the application and brief information on the place and duration for the display, for public comments.

8) The Agency may constitute the National Biosafety Committee (NBC) and the National Biosafety Technical Sub-committees (NBTS) for further review of application.

9) The Director General shall issue Permit or reject application after the review of application. The decision will be forwarded to relevant regulatory agencies and also be made available in the Biosafety Clearing House (BCH) and NBMA website.

PART 12: PROCEDURES FOR PACKAGING, LABELING AND TRANSPORT OF GENE EDITED PRODUCTS

Procedures for Packaging, Identification and Transportation for Gene Edited Products shall comply with provisions of Part IX the National Biosafety (Implementation) Regulations 2017.

PART 13: DOCUMENTATION AND RECORD KEEPING

In the case of documentation and record keeping, Part XI of the National Biosafety (Implementation) Regulations 2017 shall apply.

PART 14: MISCELLANEOUS

I- Transparency and Public Participation in Decision Making Process for Gene Edited Products

Part VII Sections 25(1-2) and 26(1) of the NBMA Act 2015 (As amended) shall apply to biosafety application for imported, exported or transported for contained use or for confined field trial and for commercial release of gene edited product.

II- Offences and Penalties

Provisions on offences, penalties and enforcement in Part IX of the NBMA Act 2015 (as amended) shall apply to gene editing activities.

III- Definition of Terms

a) The terms used in the NBMA Act 2015 (as amended) shall apply to this guideline
b) In this guideline-

"Act" means the National Biosafety Management Agency (NBMA) Act, 2015 (as amended).

"Applicant" means any person, institution, body or their authorized representative in Nigeria who applies for a permit under these guidelines.

"Biosafety Clearing House (BCH)" means a pool of information mechanism established under Article 20 of the Cartagena Protocol for exchange of scientific, technical, environmental and legal information on and experience in genetically modified organism (GMO), as part of the clearing house mechanism under Article 8 of the convention.

"Contained Use" means any operation using modern biotechnology undertaken within an enclosed facility, installation or other physical structure, such as a building, laboratory or greenhouse.

"Confined Field Trial" means a small scale experimental release into the environment of a GMO under physical and biological confinement conditions that limit the persistence of the GMO in the environment on completion of the experiment.

"DNA" means deoxyribonucleic acid: a molecule composed of two chains that coil around each other to form a double helix carrying genetic instructions for the development, functioning, growth and reproduction of all known organisms and many viruses. it is the hereditary material in all organisms. (What?)

"Gene Editing" means a type of genetic engineering in which DNA is inserted, deleted, modified or replaced in the genome of a living organism.

"Genetically Modified Organisms (GMOs) means any organism living or non-living that possesses a novel combination of genetic material obtained through the use of modern biotechnology.

"Institutional Biosafety Committee (IBC)" means a committee set up by any institution that carries out genetic engineering activities to ensure conformity with biosafety laws, regulations and guidelines

"Nuclease" means an enzyme capable of cleaving the phosphodiester bonds between nucleotides of nucleic acids.

"Nucleotide" means an organic molecule that is the building block of DNA and RNA. It is made up of three parts: a phosphate group, a 5-carbon sugar, and a nitrogenous base.

"Permit" means an official document giving an applicant authorization to either import for FFP, containment, confinement and/or commercial release.

"Product thereof" means something which is obtained from a gene edited product or organism

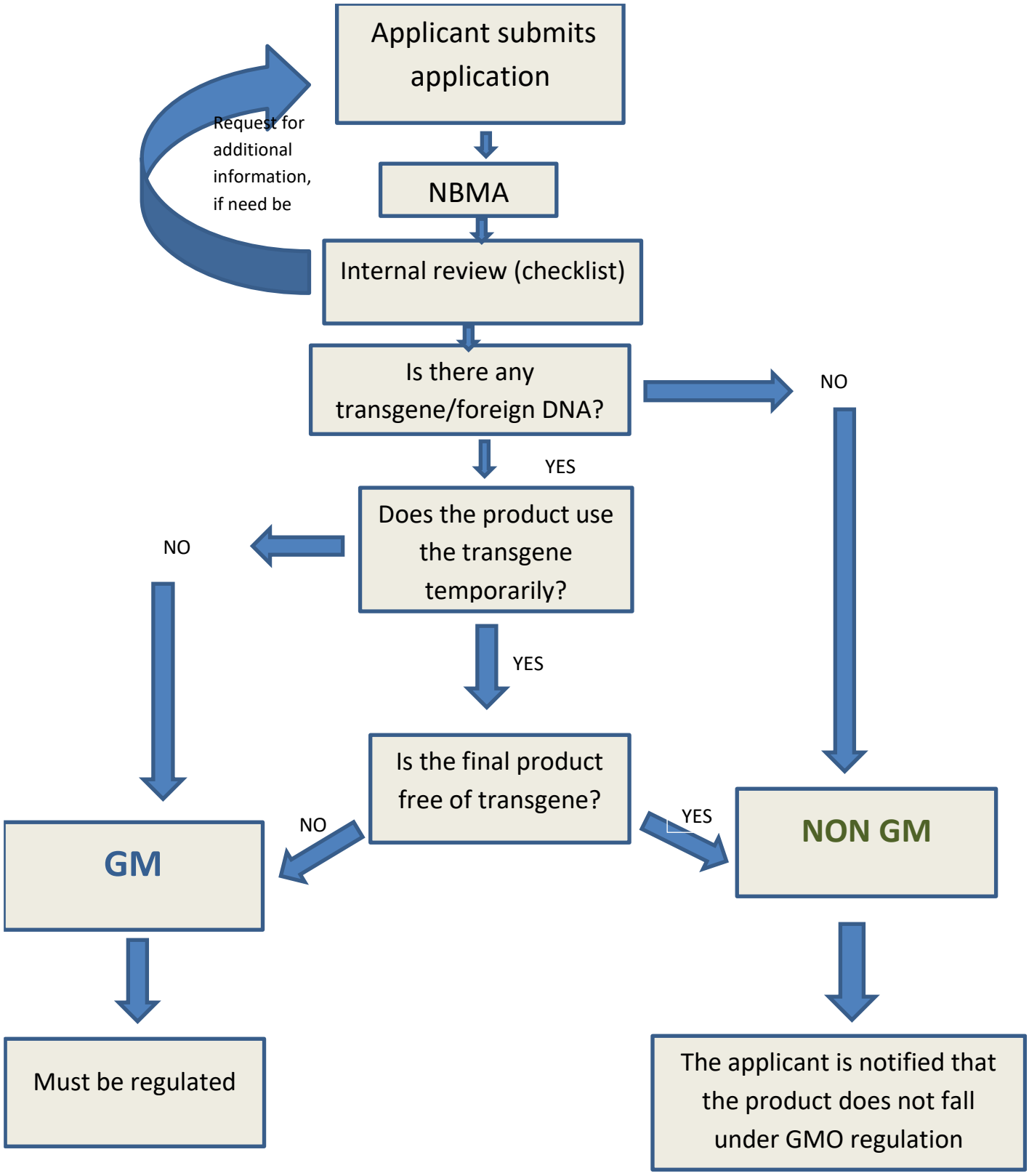
"Risk Assessment" means the process of identification, characterization, identification of risk elements and evaluation through scientific methods such as tests, analyses and trials of risks and risk sources that GMOs may pose to animal, human and plant health, biological diversity and the environment.

"Risk Communication" means is an interactive process of exchange of information and opinion on risk that GMOs may pose among experts and the public.

"Risk Management" means the process of assessing, choosing and implementing suitable options to effectively manage risks identified in the risk assessment process.

"Transgene" means a gene which is artificially introduced into the genome of another organism using any of a number of genetic engineering techniques.

PART 15: PROCESS MAP FOR GENE EDITING APPLICATION FOR DETERMINATION OF REGULATORY STATUS


Applicant submits application
Request for additional information, if need be
NBMA
Internal review (checklist)
Is there any transgene/foreign DNA?
NO
YES
Does the product use the transgene temporarily?
NO
YES
Is the final product free of transgene?
NO
YES
GM
NON GM
Must be regulated
The applicant is notified that the product does not fall under GMO regulation

Explanatory Note of the Process Map for Gene Editing Application for Determination of Regulatory Status

- The applicant after filling the application form submits the form with the dossier to NBMA.
- The NBMA conducts an internal review/check-listing to determine the next step of the application process and may request for additional information, if need be.
- If the product is found to contain transgene/foreign DNA, it will be further assessed to determine if the transgene or foreign DNA is used temporarily.
- If the transgene is used temporarily, then it will be confirmed that the final product is free of transgene to be considered as Non-GMO and the applicant will be notified that the product does not fall under GMO regulation.
- However, if the transgene is used permanently, it will be considered as GMO and will be subjected to the Agency's process of GMO regulation.
- In the event where the product is found not to contain any transgene or foreign DNA, it will be considered as Non-GMO and the applicant notified that the product does not fall under GMO regulation.

ANNEX I

I- Risk Assessment

(a) The objective of the risk assessment is to identify and evaluate potential adverse effects of the genetically edited material, direct or indirect, immediate or delayed, on human and animal health and the environment.
(b) Risk assessment of any genetically edited material shall be carried out for gene editing techniques involving Site Directed Nuclease 3 on case by case basis.
(c) Risk assessment shall however also be carried out on a case by case and step by step basis for techniques involving Site Directed Nuclease 2 as well as other editing techniques such as Oligonucleotide Directed Mutagenesis if unintended effects are observed.
(d) The scientific data to be used for risk assessment shall be of adequate quantity, based on sound research methodologies, carried out using appropriate techniques and analyzed using appropriate analytical techniques.
(e) The data and information shall be peer reviewed or able to stand a scientific peer review.
(f) Data and information shall be obtained from the developer of the product, peer-reviewed scientific literature, regulatory agencies, international bodies, independent scientists, and other appropriate sources.
(g) Scientific data from other sources generated using other different methodologies and in different environs may also be considered.

The comparative approach, considering closely related microorganisms or their products with a history of safe use, is a key general principle in risk assessment of gene editing.

A risk assessment shall involve the following steps;

(a) an identification of any genotypic and phenotypic characteristics associated with the genetically edited material that may have adverse effects on the environment and on human health.

(b) an evaluation of the likelihood of these adverse effects being realized, taking into account the level and the kind of exposure of the likely potential receiving environment of the genetically edited material.

(c) an evaluation of the consequences should those effects be realized.

(d) an estimation of the overall risk posed by the genetically edited material based on the evaluation of the likelihood and consequences of the identified adverse effects being realized.

(e) a recommendation as to whether or not the risks are acceptable or manageable, including identification of strategies to manage these risks.

(f) consideration of any relevant legislation both locally and internationally.

(g) Following steps (a) to (f), identify the level of risk associated with the genetically edited material

(h) Identification of the appropriate containment measures taking into consideration the level of the risk associated with the genetically edited organism.

(i) classification of the contained use according to the NBMA's containment guidelines.

(j) where there is uncertainty regarding the level of risk, the Agency may request for further information on the specific issues of concern or may recommend implementing appropriate risk management strategies and monitoring the genetically edited organism in the receiving environment.

(k) review of the classification based on the assessment.

According to Codex Alimentarius Commission, a safety assessment of food derived from genetically modified organisms which can equally apply to gene edited organisms contain a foreign transgene is characterized by the assessment of the whole or part of the food compared to an equal portion of the conventional counterpart. This process entails:

i) **Identification of new or altered hazards**: In the identification of new hazards in gene edited organisms, hazard identification should involve the identification of biological, chemical, and physical agents capable of causing adverse health effects and which may be present in a particular food or group of foods. It is the first step of risk assessment and seeks to identify any similarities and/or differences between the rDNA organism or its product thereof and their equivalent conventional counterparts. It should take into account the compositional analysis and agronomic and phenotypic characteristics.

ii) **Hazard characterization**: In the characterization of hazards it should involve the qualitative and/or quantitative evaluation of the nature of the adverse health effects associated with biological, chemical and physical agents which may be present in food. It should be aimed to evaluate the differences present (toxicological and nutritional effects) in the rDNA organism or its product thereof and assess its implications on human health.

iii) **Exposure assessment**: Assessment of exposure, should involve the qualitative and/or quantitative evaluation of the exposure to products and derivatives of recombinant-DNA organisms compared to their conventional counterparts. It

should take into account the magnitude, frequency and duration of the exposure. A post-market surveillance may be necessary to confirm the findings of the exposure assessment.

iv) **Risk characterization**: Risk characterization should involve the qualitative and/or quantitative estimation, including attendant uncertainties, of the probability of occurrence and severity of known or potential adverse health effects in a given population based on hazard identification, characterization and exposure assessment.

v) Based on the assessments (i-iv) above, it may be possible to determine if the risk characterization is sufficient or not. If the exposure to the genetically edited organism is expected to be significantly high, then more data on toxicity may be required.

Risk assessment for facilities handling genetically modified organisms-

If a genetically edited organism has been assessed and falls under the category of being a GMO, then facilities should strictly adhere to the Containment Facility Guidelines of the NBMA (2017). These regulations guide all activities involving GMOs under containment and are applied during research on GMOs while still in the laboratory, greenhouse, and animal house.

II- Risk management

(a) The purpose of risk management in gene edited organisms is to protect the health and safety of people and the environment by controlling or mitigating risk.

(b) It should encompass preparation of a risk management plan which includes training on general risk management measures, evaluation and mitigation of risks, and proposed permit conditions.

(c) It should also include monitoring and reviewing which details measures to assess effectiveness of all steps in risk analysis including post release review of commercial release of the genetically edited organism.

Risk management should involve the following steps:

(a) Based on risk assessment outcomes, a risk evaluation should be carried out during this phase (risk management) to determine, which risks need mitigation. (Risk evaluation may also aid in consideration of whether the proposed dealings should proceed, need further assessment or, require collection of additional information during the release.)

(b) Risk should be evaluated against the objective of protecting the health and safety of people and the environment.

(c) When the risk evaluated requires mitigation, options to reduce, eliminate or avoid the risk should be identified and assessed. Options to reduce exposure to the GMO or its products and limit opportunities for the spread and persistence of the GMO, its progeny or the introduced genes to the environment should be considered.
(d) Selected management measures should be implemented. Selection of risk management measures should be made according to their efficacy and efficiency, commensurate with the level of risk. If risk treatment measures are selected for an identified risk, then risk should be reduced sufficiently such that any residual risk does not compromise protection of the health and safety of the people and the environment.

Additional Risk management information

(a) Applicants should have contingency plans in case of an emergency.
(b) The nature of such plans may vary depending on the Permit and nature of dealings. All approvals include a requirement that NBMA be informed if there is an unintentional release of the genetically edited organism.
(c) There should be monitoring and reviewing of all steps in risk analysis to ensure the right procedures are undertaken. Each step should be done correctly to ensure that the outcomes remain valid in the light of future findings or changes in circumstances.
(d) A number of both internal and external feedback mechanisms should be used to maintain the effectiveness and efficacy of risk assessment and risk management, and which consider the concerns of all interested and affected stakeholders. Monitoring and reviewing should contribute to identifying situations where treatment measures are not adequately managing the risks, either as a result of non-compliance or because of changed circumstances or unintended or unexpected effects. It should also facilitate ongoing review of the conclusion of risk assessment and of the risk treatment options.

III- Risk Communication

(a) Good risk communication should promote a clear understanding of all aspects of risk and provide information about risk to help people make decisions, to minimize conflicts, to improve understanding of perceptions and positions and to achieve equitable outcomes.
(b) To be effective, risk communication should consist of an exchange of knowledge rather than a one-way transfer of information. It is most effective when it is two-way and with an opportunity for discussion and feedback.
(c) Appropriate communication channels should include the Agency's website - www.nbma.gov.ng , email: nbma@nbma.gov.ng and the BCH (www.bch.cbd.int).

IV- Emergence of new information which identifies actual risks after the grant of permit

(a) In the case where additional information identifying risk regarding a genetically edited organism arises after the grant of a permit, the Agency may suspend or revoke the permit.
(b) The Agency should follow laid down contingency plan and subsequently subject it to risk assessment, management and mitigation measures.

V- Considerations of unintended effects in Gene Editing applications

Unintended effects are changes other than the intended changes in the genetically edited organism resulting from its genetic modification. Some unintended effects may be predicted or explained in terms of current knowledge of biology and of the integration of metabolic pathways.

(a) Intended and predicted unintended effects should be analyzed based on the most appropriate methodology.
(b) Overall data on different levels, such as molecular characterization, comparative compositional analysis, phenotypic characteristics, etc. should be used to detect unintended effects.
(c) A contingency plan which may involve re-assessment and management should be followed for any genetically edited organism displaying an unintended effect.

ANNEX II

The socio-economic considerations should focus on those with impacts on the conservation and sustainable use of biological diversity, especially with regard to the value of biological diversity to indigenous and local communities.

The National Biosafety Management Act, 2015 (As amended) has been developed to ensure that production and use of genetically modified organisms take place in an ethical and socially justifiable way, in accordance with the principle of sustainable development and without detrimental effects on human health and environment.

1. Approval will not be given to the placing on the market of a gene edited product except it is considered and duly determined by the Agency to:
    a. Benefit Nigeria without causing significant risk to human health, biological diversity and in general the environment;
    b. Contribute to sustainable development;
    c. Not have adverse socio-economic impacts; and
    d. Accord with the ethical values and concerns of communities and does not undermine indigenous knowledge and technologies.
2. An applicant should subject to the directive of the Agency, prior to placing on the market of gene edited products;
    a. Conduct a comprehensive socio-economic assessment of each product on each application, on a case by case basis.
    b. Submit socio economic literature review and analysed data of the baseline survey done in the vicinity.
    c. Conduct socio economic impact assessment within the vicinity amongst:
        i. Farmers, households and community;
        ii. Industry and markets;
        iii. Consumers; and
        iv. Traders.
3. The Agency shall conduct broad review of all the necessary documents as submitted by the applicant and may establish relevant committee to review such documents for advice.

4. In assessing the socio economic impact the applicant should take into considerations the following:

    a) Anticipated changes in the existing social and economic patterns resulting from the introduction of the genetically edited organism or products.
    b) Possible treats to biological diversity, traditional crops or other products and in particular, farmer's varieties and sustainable agriculture.
    c) Impacts likely to be posed by the possibility of substituting traditional crops, products and indigenous technologies through modern/emerging biotechnology outside of their agroclimatic zones.
    d) Anticipated social and economic costs due to loss of genetic diversity, employment, market opportunities and in general, means of livelihood of the communities likely to be affected by the introduction of thr gene edited organisms or products.
    e) Possible countries and communities to be affected in terms of disruptions to their social and economic welfare
    f) Possible effects which are contrary to the social, cultural, ethical and religious values of communities arising from the use of release of the gene edited organism or the product.

ANNEX III

Contents for a permit for commercial release of Gene edited products

A permit for commercial release of Gene edited product shall state the -

- Objective of the release
- Identity of the Gene edited product released or imported
- Period of validity of the permit
- Conditions for the releases
- Monitoring requirement in accordance with schedule 4 of the act including the time or periods in the monitoring plan, and
- Reporting obligations of the applicant to the agency.

Duration of a permit for commercialization

A permit for commercialization shall be for a period not exceeding 10years.