भारत सरकार
विज्ञान और प्रौद्योगिकी मंत्रालय
जैव प्रौद्योगिकी विभाग
GOVERNMENT OF INDIA
MINISTRY OF SCIENCE & TECHNOLOGY
DEPARTMENT OF BIOTECHNOLOGY

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File No. PID-15011/1/2022-PPB-DBT **Dated: 17.05.2022**

OFFICE MEMORANDUM

Sub.: Guidelines for the Safety Assessment of Genome Edited Plants, 2022

1. In India, all activities related to Genetically Engineered organisms (GE organisms) or cells and hazardous microorganisms and products thereof are regulated as per the "Manufacture, Use/Import/Export and Storage of Hazardous Microorganisms/ Genetically Engineered Organisms or Cells, Rules, 1989" (Rules, 1989) notified by the Ministry of Environment, Forest and Climate Change (MoEF&CC), Government of India under the Environment (Protection) Act, 1986 (EPA 1986).

2. To harness the potential of Genome Editing technologies with proper appraisal of biosafety concerns, to ensure safety for the organisms and environment; the draft Guidelines were initiated proactively by the Department of Biotechnology under the power conferred to Review Committee on Genetic Manipulation (RCGM) through the sections 6, 8, & 25 of the Environment (Protection) Act, 1986 (EPA, 1986). The "Guidelines for the Safety Assessment of Genome Edited Plants, 2022" have undergone extensive deliberations by the Recombinant DNA Advisory Committee (RDAC), Genetic Engineering Appraisal Committee (GEAC), the Expert Committee constituted for this purpose and the Review Committee on Genetic Manipulation (RCGM).

3. MoEF&CC vide Office Memorandum (F. No. C-12013/3/2020-CS-III) dated 30.03.2022 Notified Exemption of the genome edited plants falling under the categories of SDN-1 and SDN-2 from the provisions of the rules 7 -11 (both inclusive) under the Rule 20 of the Rules, 1989. Review Committee on Genetic Manipulation (RCGM), the Competent Authority under Rules, 1989 of the Environment (Protection) Act, 1986 in its 231st meeting, held on 28.04.2022, approved and recommended to notify the "Guidelines for the Safety Assessment of Genome Edited Plants, 2022".

4. The Department of Biotechnology hereby notifies the "Guidelines for the Safety Assessment of Genome Edited Plants, 2022".

5. These guidelines shall be applicable for all public and private organizations involved in research, development and handling of the Genome Edited Plants from the date of notification.

6. The Guidelines provide a road map for the development and sustainable use of Genome Editing Technologies for plants in India, specifying the biosafety concerns, and describing the regulatory pathways to be adopted while undertaking Genome Editing of Plants.

7. The "Guidelines for the Safety Assessment of Genome Edited Plants, 2022" can be accessed from www.dbtindia.nic.in and https://ibkp.dbtindia.gov.in/.

(Nitin Kumar Jain)
Member Secretary, RCGM
Scientist F, DBT

DEPARTMENT OF BIOTECHNOLOGY
Ministry of Science and Technology
Government of India

Guidelines for the Safety Assessment of Genome Edited Plants

2022

सत्यमेव जयते

डॉ. राजेश सु. गोखले

Dr. RAJESH S. GOKHALE

आज़ादी का अमृत महोत्सव

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FOREWARD

Department of Biotechnology, Government of India is delighted to release "*Guidelines for the Safety Assessment of Genome Edited Plants, 2022*". This document was postulated in view of the advancements of modern plant biotechnology, complexity in biosafety assessment, and potential increase in research and development of Genome Edited Plants. This guideline is intended to provide detailed scientific guidance on regulatory requirements in context of Genome Edited Plants to all the stakeholders for research and product development.

These guidelines have been prepared through extensive deliberation in different committees as well as expert committees constituted for this purpose with members from academia, concerned Ministries/departments, public and private organizations and other concerned stakeholder to meet highest global standards. Considering huge growth and advancement in agriculture biotechnology research and applications, these guidelines are expected to bring transformational change in product development and commercialization and thereby would contribute towards increasing Farmer's income.

I congratulate Dr. Nitin K. Jain, Scientist-F, DBT & Member Secretary, RCGM for working with Chairs and members of various Committees and taking into consideration all issues required for biosafety assessment of Genome Edited Plants.

I am confident that these guidelines would be of immense help to all the stakeholders and ensure safe and efficient applications of genome editing technologies of global standard in the area of agriculture biotechnology.

(Rajesh S. Gokhale)

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सत्यमेव जयते

जय हिन्द

MINISTRY OF
SCIENCE & TECHNOLOGY

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PREFACE

In India, all types of gene technology research and development activities are regulated under the "Rules for the Manufacture, Use, Import, Export and Storage of Hazardous Microorganisms/Genetically Engineered Organisms or Cells 1989 (known as 'Rules, 1989') under the Environment (Protection) Act, 1986 (EPA 1986). Hence, unlike the ongoing global debates on the scope of existing legal and regulatory provisions in different countries, genome editing research and applications are regulated in India under provisions of the Rules, 1989.

Modern biotechnology has been advancing at a very rapid pace with the advent of several new molecular techniques and their potential applications in the field of agriculture, environment, food and human health. Genome editing technologies are currently amongst the most promising technologies in terms of applied biological research and innovation with a huge economic potential in a wide range of sectors. Genome Edited Plants expressing various traits are increasingly being developed globally.

However, as recognized globally, conduct of research and subsequent release of Genome Edited Plants requires proper appraisal of biosafety concerns to make it safe for the human, animals and environment.

The Department of Biotechnology is pleased to notify present "*Guidelines for the Safety Assessment of Genome Edited Plants, 2022*". These guidelines provide a pathway for regulatory requirements for biosafety assessment of Genome Edited Plants.

The guidelines define various categories of Genome Edited Plants and determines regulatory requirement for appropriate category and provide the regulatory framework and scientific guidance on data requirement in context of development of Genome Edited Plants.

I extend my sincere gratitude to all experts, members, stakeholders from industry, academia and civil societies for providing their vital inputs in preparation of this document. I also acknowledge the contribution of Biosafety Support Unit throughout the preparation of these guidelines.

(Dr. Nitin Kumar Jain)

Contents

1. INTRODUCTION

Genome editing (also called gene editing) is a group of technologies that enables change in the DNA/RNA of an organism. The key feature of these technologies is that these permit precise alteration of the targeted nucleotide(s) in DNA/RNA of an organism. The introduced changes could range from alteration of a single base to deletion/replacement/structural reorganization of a large genomic region. Such changes could be identical or comparable to natural mutations or obtainable through conventional mutagenesis. In some cases, genome editing could also introduce specific foreign DNA/RNA that is not available in the natural gene pool of the host plant species and thereby could introduce novel traits.

The applications of Genome Editing technology include crop improvement, enhancement of crop nutrition, crop protection, biofuels, pharmaceuticals, and other high-value secondary metabolites & nutraceuticals. This document, however, is specific to Gene/Genome Editing technologies for plants.

Since the technology involves genome manipulation, including introduction of foreign gene/genomic sequences in some cases, there is a need to consider in view of the ratification of the Cartagena Protocol by India, whether any of the products or the initial procedural phase of development of the product require to follow biosafety or environmental safety regulations[1,2].

Therefore, devising appropriate biosafety frameworks for research, development and commercial application of Genome Editing Technologies in agriculture & food sector is essential. This document provides a road map for the development and sustainable use of Genome Editing Technologies in India, specifying the biosafety and/or environmental safety concerns, and describing the regulatory pathways to be adopted while undertaking the genome editing of plants.

[1] Rules, 1989 of the Environment (Protection) Act, 1986
[2] Cartagena protocol

2. REGULATORY FRAMEWORK FOR GENOME EDITED PLANTS

In India, all activities related to Genetically Engineered organisms (GE organisms) or cells and hazardous microorganisms and products thereof are regulated as per the "*Manufacture, Use, Import, Export and Storage of Hazardous Microorganisms/ Genetically Engineered Organisms or Cells, Rules, 1989*" (Rules, 1989) notified by the Ministry of Environment, Forest and Climate Change (MoEF&CC), Government of India under the *Environment (Protection) Act, 1986* (EPA 1986). The mandate & functions of six competent authorities created under the Rules 1989 are shown in **Annexure I**.

All provisions under Rules, 1989 shall be applicable on genome edited plants except the rules 7 -11 (both inclusive) on which exemption from regulation has been granted under the Rule 20[3] by the Ministry of Environment, Forests and Climate Change vide Office Memorandum F. No. C -12013/3/2020-CS-III dated 30.03.2022, restricting the regulation of the process of genome editing of plants being carried out under containment, until free from exogenous introduced DNA, to be done by the Institutional Biosafety Committee following guidelines issued by Central government under information to Review Committee on Genetic Manipulation.

These guidelines shall be applicable to all the duly approved ongoing plant genome editing processes in containment conditions under the supervision of respective IBSCs and on those which will be taken up henceforth in India. The RCGM may formulate standard operating procedures (SOPs) and/or checklists to be followed for enabling biosafety regulation by IBSCs as required, time to time.

[3]**Rules 1989:** ***Rule 20.*** *EXEMPTION: The Ministry of Environment and Forests shall, wherever necessary, exempt an occupier handling a particular microorganism/genetically engineered organism from rule 7-11.*

A. Scope

The scope of this regulatory guidelines is limited to plants and products thereof developed using genome editing techniques employing site-directed nucleases (SDN) such as Zinc Finger Nucleases (ZFNs), Transcription Activator-Like Effector Nucleases (TALENs), Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR), and other nucleases with similar functions.

B. Definitions of genome edited plants derived from use of Site Directed Nucleases (SDNs)

The genome edited plants derived from the use of genome editing techniques employing site-directed nucleases (SDNs) such ZFNs, TALENs, CRISPR and other nucleases with similar functions are generally classified under three categories as

i) Site-Directed Nuclease (SDN)-1, a site-directed mutagenesis without using a DNA sequence template;

ii) SDN-2, a site-directed mutagenesis using a DNA sequence template; and

iii) SDN-3, site-directed insertion of gene/large DNA sequence using a DNA sequence template.

a) SDN-1

Involves the unguided repair of a targeted DNA break by natural endogenous DNA repair mechanism of the host organism such as non-homologous end joining. The spontaneous repair of this break can lead to a mutation causing gene silencing, gene knock-out or a change in the activity of a gene. The SDN-1 genome edited plants produced will be free from exogenous/foreign DNA. These mutations can be base substitution/indels/deletions including large deletions or structural changes. These resultant mutations are comparable to those occurring in nature, obtained through conventional mutagenic treatments or natural variation found in primary/secondary gene pool.

b) SDN-2

Involves a template-guided repair of a targeted DNA break using an externally supplied template sequence. The donor carries one or several small mutations flanked by two sequences matching both ends of the DNA break, and is thus recognized as a repair template, allowing the introduction of the mutation(s) at the target site. The resultant mutant carries modified sequence, leading to altered expression profile of the gene and/or altered activity of the encoded protein/RNA. Thus, the edited version could be regarded as allelic form comparable to those available in primary/secondary gene pool.

c) SDN-3

Involves a template-guided repair of a targeted DNA break using a sequence template, typically double-stranded DNA containing an entire gene or an even longer genetic element(s). Both ends of the template sequence are homologous to the DNA break ends (usually more than 800 bp each), which allows introduction of the target nucleotide sequence of the gene or genetic element(s) at the target site. SDN-3 Genome Edited plants shall have foreign gene(s) in a specific location of the genome conferring new/novel trait(s). These products will be clearly distinguishable from the naturally existing variations or mutations in the species.

C. Exemption for regulation of SDN-1 under the Rule 20 of Rules, 1989

Plants categorized as SDN-1 do not contain new combinations of genetic material as will be arising from the incorporation of exogenous DNA, and thus the final products are equivalent to naturally occurring loss of function or a change in the activity of a gene mutations or those induced via mutation breeding.

Similar products derived from naturally occurring mutations or those induced via mutation breeding are not regulated under Rules1989; therefore, the final of SDN-1 genome edited plants are exempted from the regulation and risk assessment under Rule 20 of the *Rules 1989* when

demonstrated to contain no exogenous DNA vide Office Memorandum F. No. C -12013/3/2020-CS-III dated 30.03.2022 issued by MoEF&CC. As per the Office Memorandum,

- *"Department of Biotechnology, Ministry of Science and Technology; Department of Agriculture Research and Education, Ministry of Agriculture and Farmers Welfare has recommended that the SDN1 and SDN2 Genome Edited Products free from exogenous introduced DNA be exempted from biosafety assessment in pursuance of Rule 20 of the Manufacture, Use, Import, Export and Storage of Hazardous Microorganisms/Genetically Engineered Organisms or Cells Rules 1989.Wherein, the process of genome edited plants to be carried out under containment, until free from exogenous introduced DNA, will be regulated by Institutional Biosafety Committee following guidelines issued by Central government under information to Review Committee on Genetic Manipulation.*
- *Therefore, the Central government hereby exempts the Genome Edited plants falling the categories of SDN1 and SDN2, which are free of exogenous introduced DNA, from the provisions of Rules 7 to 11 (both inclusive) of the above said rules.*
- *For such Genome edited plants to be released as new variety, further development and evaluation will be as per other applicable Laws/Acts/Rules*."

This is in accordance with the principle of equal treatment of products of equivalent risk profile. However, the early stages of research and development prior to the confirmation of the removal of gene editing reagents by genetic segregation or by any suitable method will remain subject to the existing requirements for rDNA research as described in *Regulations and Guidelines for Recombinant DNA Research and Biocontainment, 2017*[4].

Genome edited plants falling under SDN-1 category, which are demonstrated to contain no exogenous DNA, are either indistinguishable from naturally occurring variants or comparable to mutants derivable through conventional mutagenesis.

[4]https://ibkp.dbtindia.gov.in/DBT_Content_Test/CMS/Guidelines/20181115134719867_Regulations-Guidelines-for-Reocminant-DNA-Research-and-Biocontainment-2017.pdf

IBSCs would regulate the work during the containment phase as per Rules 1989 and approve for further handling of the material by the applicant after it is found to be free from any exogenous DNA and report the details to the RCGM at both stages, namely

i) at the time of accepting the experiments to be conducted under containment (Research and Development phase), and

ii) after granting approval to the product to be taken out of the containment conditions for further product development.

D. Exemption for regulation of SDN-2 under Rule 20 of the Rules 1989

Genome edited plants belonging to SDN-2 category carry specific nucleotide substitutions (*e.g.*, targeted edits or targeted allele replacements) introduced through DNA repair templates but do not carry any exogenous DNA and are comparable to naturally occurring variants or mutants obtainable through conventional mutagenesis. Similar products derived from naturally occurring mutations or those induced via mutation breeding are not regulated under Rules 1989, therefore, the final of SDN-2 genome edited plants are exempted from the regulation and risk assessment under Rule 20 of the Rules 1989 when demonstrated to contain no exogenous/foreign DNA vide Office Memorandum F. No. C -12013/3/2020-CS-III dated 30.03.2022 issued by MoEF&CC.

IBSCs would regulate the work during the containment phase as per Rules 1989 and approve for further handling of the material by the applicant after it is found to be free from any of the gene editing vector sequences or reagents and report the details to the RCGM at both stages, namely

i) at the time of accepting the experiments to be conducted under containment (Research and Development phase), and

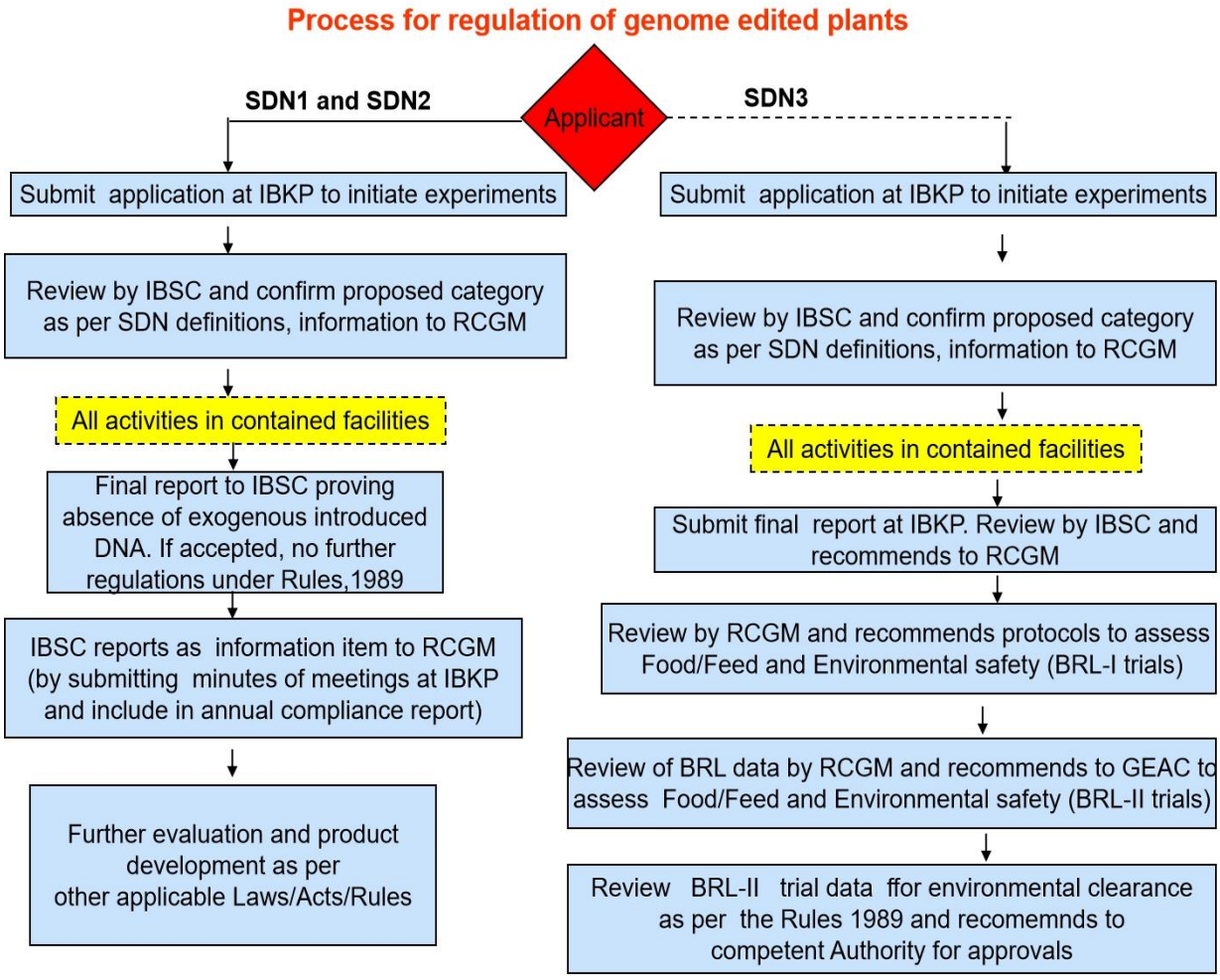
ii) after granting approval to the product to be taken out of the containment conditions for further product development.

E. Regulation of SDN-3 under the Rules 1989

Plants categorized as SDN-3 are subject to regulation under the Rules 1989 in the same manner as genetically engineered plants produced using other methods of genetic transformation.

3. PROCESS FOR REGULATION OF GENOME EDITED PLANTS

The regulatory process for genome-edited plants is summarized in Figure 1 and described in the text that follows



A. SDN-1 and SDN-2 Genome Edited Plants

a) Roles and Responsibilities of regulatory committees

Early phase research and development of SDN-1 and SDN-2 plants *i.e.*, prior to the removal of gene editing reagents by genetic segregation, is subject to regulation under *Rules, 1989*. The relevant Statutory Committees are as below:

Institutional Biosafety Committees (IBSCs)

The IBSC is constituted as a mandatory committee in all public or private research-based organizations handling hazardous microorganisms/ genetic engineered organisms and their production activities under the *Rules, 1989*[5].

The applicant including research institutions shall prepare, with the assistance of the IBSC, an up-to-date *on-site* emergency plan according to the manuals /guidelines of the RCGM and make available copies to the DLC/SBCC. IBSCs serve as the nodal point for interaction within an organization for implementation of the biosafety regulatory framework. Each IBSC has a nominee appointed by the Department of Biotechnology (DBT) and Biosafety Officer with medical qualifications. The role of an IBSC is extremely critical as it is a Competent Authority under the *Rules, 1989*, that functions within the premises of respective organization.

Functions and Compliance adherence of IBSCs are elaborated in the '*Handbook for Institutional Biosafety Committees (IBSCs), 2020*'.

Review Committee on Genetic Manipulation (RCGM)

RCGM functions in the DBT, and monitors the safety related aspects in respect of on-going research projects and activities involving genetically engineered organisms/hazardous microorganisms. It brings out Manuals of guidelines specifying procedure for regulatory process with respect to activities involving genetically engineered organisms in research, use and applications with a view to ensure environmental safety. RCGM shall lay down procedures restricting or prohibiting production, sale, importation and use of such genetically engineered organisms of cells as are mentioned in the Schedule of Rules, 1989.IBSCs are required to submit minutes of each meeting to RCGM to inform about projects reviewed and decisions taken. IBSCs also provide an annual report to RCGM for its review and consideration.

Operational requirements and guidance for containment of plants developed using rDNA techniques are described in *Regulations and Guidelines for Recombinant DNA Research and*

[5]Manufacture, Use, Import, Export and Storage Of Hazardous Micro Organisms/ Genetically Engineered Organisms or Cells, Rules, 1989 (Rules, 1989) notified under the Environment (Protection) Act, 1986 (EPA 1986)

Biocontainment, 2017, specifically section 3.4.2.1. Plant Biosafety Level 1 (PBSL-1) for SDN1 plants and section 3.4.2.2. Plant Biosafety Level 2 (PBSL-2) for SDN-2 and SDN-3 plants.

B. SDN-3 Genome Edited Plants

Application of Rules, 1989, and Existing Guidance

The application of SDN-3 gene editing technology, including the final modified plants containing novel introduced DNA, are subject to regulation under the *Rules, 1989*, in the same manner as genetically engineered plants produced using other methods of genetic transformation. These products are subject to case-by-case risk assessment and oversight by IBSCs, RCGM, and GEAC.

Relevant guidance documents include:

i) *Regulations and Guidelines for Recombinant DNA Research and Biocontainment, 2017*
ii) *Guidelines for the Environmental Risk Assessment of Genetically Engineered Plants, 2016*
iii) *Guidelines for the Conduct of Confined Field Trials of Regulated, GE Plants, 2008*
iv) *Guidelines for the Monitoring of Confined Field Trials of Regulated, GE Plants, 2008*
v) *Guidelines for the Safety Assessment of Foods Derived from Genetically Engineered Plants, 2008*
vi) *Protocol for Food and Feed Safety Assessment of GE crops, 2008*
vii) *Revised Guidelines for Research in Transgenic Plants, 1998*

C. General Considerations for Risk Assessment of Genome Edited Plants

In general, for the safety assessment of genome edited plants, the basic risk assessment framework published in "*Risk Assessment Framework and Guidelines for the Environmental Risk Assessment of Genetically Engineered Plants 2016*" (http://geacindia.gov.in/resource-documents/biosafety-regulations/guidelines-and-protocols/ERA_GuideforStakeholders.pdf) & Guidelines for the Safety Assessment of Foods Derived from Genetically Engineered Plants (ICMR, 2008) shall be adopted. However, genome edited plants falling under SDN-1 and SDN-2 type that differ significantly from GE plants in several respects, and are exempted under Rule 20

of Rules 1989 as per the MoEFF&CCvide Office Memorandum F. No. C -12013/3/2020-CS-III dated 30.03.2022. Food/Feed and Environmental safety assessment may not be necessary, provided that the technology developer provides sufficient molecular and other documentary evidences to show that the genome edited plants carry proposed mutation(s) and fall under SDN-1 or SDN-2 type as per the definitions in the guidelines. Technology developer shall ensure that the SDN-1/SDN-2 type Genome edited plant under consideration for environmental release does not contain any foreign gene/DNA or sequences of vector used to create mutations and other components used in the editing process. Applicants' shall submit application for Genome editing of plants in prescribed forms at IBKP to seek approval of IBSC. For those Genome edited plants falling under SDN-3 type, additional data requirements that are over and above the information/data requirements prescribed for SDN-1 and SDN-2 type plants, will be required.

4. INFORMATION AND DATA REQUIREMENT FOR RISK ASSESSMENT

A. General information and data requirements for genome edited plants

a) Biology of host plant

Product developer shall refer the biology document for referring to common and scientific names of the host plant species and/or subspecies. Such documents are available for major crop plants at GEAC and IBKP web portals. For any new crop/plant, applicant may refer to similar documents available elsewhere in the public domain or in the published literature.

Information is to be provided on the origin, the center of diversity of the species, natural habitat of the host plant, and its range of distribution/cultivation in India, known predators/parasites/pests/pollinators of the host plant in India, cultivation and other agronomic practices followed by farmers, uses other than food & feed, if any, and any other relevant details.

b) Details on programmable nuclease/nickase and template nucleotide sequence(s)

Information and specific features of editing reagents/nuclease/nickase or other nucleases with similar functions including the kind of DNA break they create may be given along with details of vector DNA sequence and restriction Map (GenBank accession number wherever available with base pair positions), origin of replication(s), selection method followed and, biological source and DNA & amino acid sequence of nuclease/nickases or other nucleases with similar functions used in the experiments. Nucleotide sequence of the guide RNA(s) (sgRNA) for the target mutation site(s), if used.

c) Methods followed for genome editing

Site directed nucleases (SDNs) may be delivered to the cells in various ways, like transiently (without rDNA/exogenous DNA integration), or through stable co-integration into the

genome. Information on the methods followed for the delivery of vector and reagents used in editing (electroporation of protoplasts, biolistics, *Agrobacterium*-mediated transformation, and whisker-mediated transformation of cells, transient expression system, etc.) to be provided.

d) Selection of genome edited plants

Another important aspect of biosafety assessment is the presence/absence (removal) of selection marker in the finally selected genome edited plants. Molecular data providing evidence for the presence/absence of selection marker used (as the case may be) is to be provided.

e) Molecular characterization of genome edited plants

Detailed molecular characterization is to be carried out for all three types (SDN-1, SDN-2 and SDN-3) of genome edited plants. For all the three types of genome edited plants, molecular data confirming the precise target edit(s) in the stated genomic locations should be provided. In addition, evidence should be provided to demonstrate the absence of any exogenous DNA/transformation vector backbone that had been used. For SDN-1 and SDN-2 type edits, lack of integration of any foreign genes/DNA sequences should be proved. The molecular characterization data should reveal desired editing at the intended loci/site and lack of undesirable editing elsewhere in the genome by a suitable and appropriate method that can reveal off-target changes, if any. Also, molecular characterization shall reveal integration of vector DNA sequences and editing nucleases, if any. Details of the methods followed for segregating out the exogenous DNA/ transformation vector backbone/ editing reagents (selfing, back crossing, etc.) in the selected Genome edited plants are to be provided. Where available, provide information about natural mutants identical or comparable to the proposed/effected gene edit.

f) Characterization of off-target mutation(s)

Even though there is continuous improvement in the efficiency and precision of gene editing technologies, off-target effects *i.e*. changes elsewhere in the genome, are still likely. For seed propagated plants, the off-target mutations can be segregated out by appropriate breeding methodology which separate progeny plants in the forthcoming generations. Backcross breeding for sufficient number of generations to remove any possible off-target changes, if needed, should be carried out. In such case, the methodology followed and the extent of genome recovery of the wild-type genotype is to be elaborated.

In case of perennials or clonally (vegetatively) propagated crops where sexual crossing option to segregate out off-target mutations cannot be employed, data demonstrating existence of such a variation in the species, if available, in nature or acceptability threshold of such off-target effects to the extent not to pose risk to environment and humans/animals needs to be given. In clonally propagated species, the *in vitro* options to select only those plants without such off-target variation may be employed, if established *in vitro* protocols are available in the species. In case of perennials or plants that reproduce mainly through vegetative propagation, additional molecular data may be required on a case-by-case basis.

g) Stability of edit(s) over the generations

Data showing stable inheritance of edited site(s) over the generations to be provided. In case of perennials or vegetatively propagated crops, presence of edited sequence in clonal generations is to be tested.

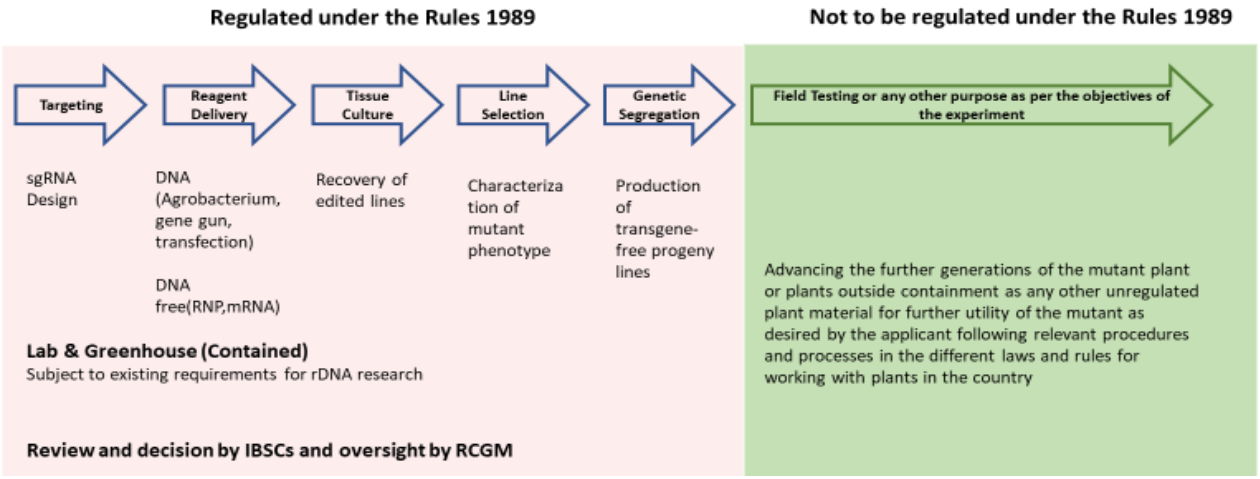


Fig.2. Genome Editing in plants: Work flow for SDN-1 and SDN-2 type modifications

B. Data requirements SDN-1 and SDN-2 for genome edited plants

The data requirements for the biosafety assessment of genome edited plants include, but are not limited to, existing trait value range in the species being targeted for change, editing reagents used, method of site directed nuclease and recombinant nucleic acid delivery, the nature of the modification, deletion, insertion of base pairs, number of mutants with desirable change, un-targeted alterations, edited loci and its direct or indirect effects, and molecular characteristics of the resulting trait/phenotype/product. In general, following aspects are relevant for biosafety assessment of the Genome edited plants that include SDN-1 and SDN-2 type:

I. Details of the plant species, its wild relatives, objectives of the experiment including the genomic region which is targeted for mutation with expected trait variant

II. Details of transformation/transient expression method followed for editing including reagents/programmable nucleases used.

III. Information on the characteristics and molecular mechanisms of editing reagents/programmable nucleases/nickases/base editors, etc., used, their mode of action, and type of breaks they create (single strand or double brakes).

IV. Information to support the claim that the selected Genome edited plant is SDN-1 or SDN-2 type only.

V. Molecular characterization confirming intended change at the target site.

VI. Comparative expression profile of target gene and/or product before and after editing.

VII. Detailed methods followed to ensure removal/lack of integration of vector DNA or any reagents used in editing process in the final selected mutant.

VIII. Methods followed to identify and/or remove off-target changes. Backcross breeding for sufficient number of generations to remove any possible off-target changes in case of genome edited plants. In case of perennials or plants that reproduce mainly through vegetative propagation, additional molecular data may be required on a case-by-case basis. In case of any off-target changes, information to show that they are not different

from any variant for that off-target trait found in the species or among segregating progenies in conventional breeding materials.

IX. Data (only for record purpose) on number of rejected plant types due to

(i). Off-target variation

(ii). Unacceptable level of targeted mutation

X. When the intended change is the introduction of novel food/feed trait by altering the composition in the edible parts beyond the existing normal range present in the food/feed crop and has no history of safe use, applications may be referred to Food Safety and Standards Authority of India (FSSAI) if meant for human consumption or Department Of Animal Husbandry, Dairying and Fisheries (DoAHDF) if meant for animal consumption for their approval.

C. Data requirements for SDN-3 type genome edited plants

In addition to the data requirements in 4.B suggested for SDN-1 and SDN-2 type Genome edited plants, additional data requirements as per the GE organisms prescribed for food/feed safety assessment as per the Guidelines for the Safety Assessment of Foods Derived from Genetically Engineered Plants (ICMR, 2008) and Environmental safety assessment as per the Guidelines for the conduct of Confined Field Trial of GE plant (Environmental risk Assessment (ERA) guidelines of MoEF&CC, (2016) will be required, on a case by case basis. Data on trait efficacy, and agronomic performance at multi-locations through Biosafety Research Level (BRL) confined field trials as per the SOPs prescribed for GE crop plants are to be followed.

ANNEXURE-I: The Six Competent Authorities, their mandate & functions as defined under Rules 1989

Competent Authorities	Mandate & Functions
Recombinant DNA Advisory Committee (**RDAC**)	The RDAC functions in Department of Biotechnology (DBT) and shall review developments in biotechnology at national and international levels and shall recommend suitable and appropriate safety regulations for India in recombinant research, use and applications from time to time
Institutional Biosafety Committee (**IBSC**)	The IBSC is constituted by an occupier or any person including research institutions, handling hazardous microorganisms/ genetic engineered organisms {at Research & Development (R&D) level}. The occupier or any person including research institutions shall prepare, with the assistance of the IBSC, an up-to-date on site emergency plan according to the manuals /guidelines of the RCGM and make available copies to the DLC/SBCC and RCGM/GEAC
Review Committee on Genetic Manipulation (**RCGM**)	RCGM functions in the DBT to monitor the safety related aspects in respect of on-going research projects and activities involving genetically engineered organisms/hazardous microorganisms. It shall bring out Manuals of guidelines specifying procedure for regulatory process with respect to activities involving genetically engineered organisms in research, use and applications with a view to ensure environmental safety. RCGM shall lay down procedures restricting or prohibiting production, sale, importation and use of such genetically engineered organisms of cells as are mentioned in the Schedule of Rules, 1989
Genetic Engineering Appraisal Committee (**GEAC**)	The GEAC functions in the MOEF &CC and is responsible for approval of (i) activities involving large scale use of hazardous microorganisms and recombinants in research and industrial production from environmental angle (ii) proposals relating to release of genetically engineered organisms and products into the environment including experimental field trials. The GEAC or any person/s authorised by it shall have powers to take punitive

	action under the Environment (Protection) Act
State Biotechnology Coordination Committee (**SBCC**)	SBCC review periodically the safety and control measures in the various installations/institutions handling genetically engineered organisms/hazardous microorganisms. SBCC have powers to inspect, investigate and take punitive action in case of violations of statutory provisions through the Nodal Department and the State Pollution Control Board/Directorate of Health &/ Medical Services
District Level Committee (**DLC**)	DLC monitor the safety regulations in installations/institutions engaged in the use of genetically modified organisms/ hazardous microorganisms and its applications in the environment. DLC/or any other person/s authorized in this behalf shall visit the installation engaged in activity involving genetically engineered organisms, hazardous microorganisms, formulate information chart, find out hazards and risks associated with each of these installations and coordinate activities with a view to meet any emergency. DLC shall also prepare an off-site emergency plan for field trials. DLC shall regularly submit its report to the SBCC/GEAC

While the RDAC plays an advisory role, IBSC, RCGM and GEAC are involved in regulatory and approval functions. SBCC and DLC are responsible for monitoring the activities related to GMOs at state and district levels respectively.

ANNEXURE-II: Other applicable Laws, Acts and Procedures Governing Genome Editing

The Genome Editing Technologies also have implications to International treaties/ agreements like Cartagena Protocol on Biosafety to the Convention on Biological Diversity, Biological Weapons Convention, Wassenaar Arrangement on Export Controls for Conventional Arms and Dual-Use Goods and Technologies, Australia Group (AG). India being a party to these treaties/ agreements shall remain committed to the fulfilment of its obligations and shall take necessary steps to regulate genome editing whenever required.

The other applicable laws, acts & procedures related to biosafety and biosecurity are The Biological Diversity Act, 2002[6]; Drugs and Cosmetic Act 1940[7]; Seed Act, 1966[8]; Protection of Plant Varieties and Farmers Rights (PPVFR), 2001[9]; Food Safety and Standards Act, 2006[10]; Plant Quarantine Order 2003[11]; The Unlawful Activities (Prevention) Act, 1967[12]; Disaster Management Act, 2005[13]; Weapons of Mass Destruction and Their Delivery System (Prohibition of Unlawful Activities) Act, 2005[14]. Further, India is a signatory to The Convention on Biological Diversity (CBD)[15] and its subordinate protocols (Cartagena and Nagoya protocols)[16].

[6] The Biological Diversity Act, 2002 (The http://nbaindia.org/uploaded/Biodiversityindia/Legal/31.%20Biological%20Diversity%20%20Act,%202002.pdf)
[7] Drugs and Cosmetic Act 1940 (http://legislative.gov.in/sites/default/files/A1940-23.pdf)
[8] Seed Act, 1966 (https://seednet.gov.in/cms/home/readyreckoner/Seed_4/16_The_Seed_Act_1966.pdf
[9] PPVFR (https://indiacode.nic.in/bitstream/123456789/1909/1/200153.pdf)
[10] Food Safety and Standards Act, 2006 (https://indiacode.nic.in/bitstream/123456789/7800/1/200634_food_safety_and_standards_act%2C_2006.pdf)
[11] Plant Quarantine Order 2003 (http://ppqs.gov.in/plant-quarantine-order-2003-consolidated-version)
[12] The Unlawful Activities (Prevention) Act, 1967 (https://indiacode.nic.in/bitstream/123456789/6853/1/unlawful_activities_prevention_act1967.pdf)
[13]"Disease, disability or death from natural (epidemics or pandemics), emerging or re-emerging diseases and man-made (intentional use) in Biological Warfare (BW) operations or incidents of Bioterrorism (BT)."
[14] Weapons of Mass Destruction and Their Delivery System (Prohibition of Unlawful Activities) Act, 2005 (http://www.mea.gov.in/Uploads/PublicationDocs/148_The-Weapons-Mass-destruction-And-Delivery-Systems-Act-2005.pdf)
[15]The Convention on Biological Diversity (CBD) entered into force on 29 December 1993 (https://www.cbd.int/convention/).
[16]The Cartagena Protocol on Biosafety. The Cartagena Protocol on Biosafety to the Convention on Biological Diversity is an international agreement which aims to ensure the safe handling, transport and use of living modified organisms (LMOs) resulting from modern biotechnology that may have adverse effects on biological diversity, taking also into account risks to human health.(http://bch.cbd.int/protocol/).

Biological Diversity Act, 2002 prohibits the acquisition of any biological resource[17] occurring in India or knowledge associated thereto for research or for commercial utilization or for bio-survey and bio-utilization without the approval of National Biodiversity Authority. FSSAI under Food Safety and Standards Acts, 2006 is responsible to assess the safety of food and its ingredients where food contains or consists of genome edited products.

[17] "Biological resources" means plants, animals and micro-organisms or parts thereof, their genetic material and by-products (excluding value added products) with actual or potential use or value, but does not include human genetic material.

ANNEXURE-III: MoEF&CC Office Memorandum F. No. C -12013/3/2020-CS-III dated 30.03.2022 regarding Exemption of the Genome Edited plants under Rule 20 of Rules, 1989

F. No. C -12013/3/2020-CS-III
Government of India
Ministry of Environment, Forest and Climate Change
CS-III (Biosafety) Division
Indira Paryavaran Bhawan
Jor Bagh Road, Ali Ganj
New Delhi-110 003
Date:30th March, 2022

OFFICE MEMORANDUM

Sub: Exemption of the Genome Edited plants falling under the categories of SDN1 and SDN2 from the provisions of the Rules, 1989.

The Ministry of Environment, Forest and Climate Change has notified the rules for the Manufacture, Use, Import, Export and Storage of Hazardous Microorganisms/Genetically Engineered Organisms of Cells, Rules 1989 hereinafter referred as Rule vide No. GSR 1037 (E) dated 5th December 1989, -

2. Rule 20 of the Manufacture, Use, Import, Export and Storage of Hazardous Microorganisms/Genetically Engineered Organisms or Cells Rules 1989 empowers the Ministry of Environment, Forest and Climate Change to exempt an occupier handling a particular microorganism/genetically engineered organism form the application of the provisions of Rule 7 and 11 (both inclusive).

3. Department of Biotechnology, Ministry of Science and Technology; Department of Agriculture Research and Education, Ministry of Agriculture and Farmers Welfare has recommended that the SDN1 and SDN2 Genome Edited Products free from exogenous introduced DNA be exempted from biosafety assessment in pursuance of Rule 20 of the Manufacture, Use, Import, Export and Storage of Hazardous Microorganisms/Genetically Engineered Organisms or Cells Rules 1989. Wherein, the process of genome edited plants to be carried out under containment, until free from exogenous introduced DNA, will be regulated by Institutional Biosafety Committee following guidelines issued by Central government under information to Review Committee on Genetic Manipulation.

4. Therefore, the Central government hereby exempts the Genome Edited plants falling the categories of SDN1 and SDN2, which are free of exogenous introduced DNA, from the provisions of Rules 7 to 11 (both inclusive) of the above said rules.

5. For such Genome edited plants to be released as new variety, further development and evaluation will be as per other applicable Laws/Acts/Rules.

6. This issues with the approval of Competent Authority.

30/3/2022

(Naresh Pal Gangwar)
Additional Secretary
mail id: asnpg.mefcc@gov.in

To

1. Secretary, Deptt. of Biotechnology
2. Secretary, Deptt. of Agriculture & Farmers Welfare
3. Secretary, Deptt. of Agriculture Research & Education
4. Chief Secretary (All States/UTs)

Copy to:

1. PPS to Cabinet Secretary
2. PPS to Secretary, MoEFCC

ACKNOWLEDGEMENTS

- ✓ **Apex Committee** constituted by DBT under the Chairmanship of Prof. K. Veluthambi, Professor (Retd), MKU, Madurai; to Work Out General Principles and Guidelines on Genome Editing Technologies, Applications & Regulations, and to identify specific Sub-committees for data requirements
- ✓ **Sub Committee** constituted under the Chairmanship of Dr. Ramesh V. Sonti, Director, NIPGR, New Delhi; to Work Out General Principles and Data Requirements for Biosafety Assessment on Genome Editing Technologies, Applications & Regulation on Plants
- ✓ **Drafting Committee** constituted under the Chairmanship of Dr. K. V. Prabhu, Chairperson, PPV&FR Authority, New Delhi
- ✓ **Expert Committee** under the Chairmanship of Prof. Y.K. Gupta, to discuss guideline and SOPs on Genome Edited plants
- ✓ **Review Committee of Genetic Manipulation** (RCGM)
- ✓ **Genetic Engineering Appraisal Committee** (GEAC)
- ✓ **Biosafety Support Unit**, Regional Centre for Biotechnology, Faridabad

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DEPARTMENT OF BIOTECHNOLOGY
Ministry of Science and Technology
Government of India

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