Republic of the Philippines
OFFICE OF THE SECRETARY
Elliptical Road, Diliman,
Quezon City 1100, Philippines

MEMORANDUM CIRCULAR
No. 08
Series of 2022

Subject: **RULES AND PROCEDURE TO EVALUATE AND DETERMINE WHEN PRODUCTS OF PLANT BREEDING INNOVATIONS (PBIs) ARE COVERED UNDER THE DOST-DA-DENR-DOH-DILG JOINT DEPARTMENT CIRCULAR NO. 1, SERIES OF 2021 (JDC1, s2021) BASED ON THE NCBP RESOLUTION NO. 1, SERIES OF 2020**

Pursuant to (a) the DOST-DA-DENR-DOH-DILG Joint Department Circular no. 1, series of 2021, ***Rules and Regulations for the Research and Development, Handling and Use, Transboundary Movement, Release into the Environment, and Management of Genetically Modified Plant and Plant Products Derived from the Use of Modern Biotechnology***, or JDC1, s2021 – which revised the previous DOST-DA-DENR-DOH-DILG Joint Department Circular no. 1, series of 2016, or JDC1, s2016 – and (b) the National Committee on Biosafety of the Philippines (NCBP) Resolution no. 001, series of 2020, ***The Regulation of Plant and Plant Products Derived from the Use of Plant Breeding Innovations (PBIs) or New Plant Breeding Techniques (NBTs),*** which tasked the Department of Agriculture to issue guidelines and take the lead in evaluating and monitoring products of PBIs, the following rules and procedure shall govern the evaluation of such products to determine when they would fall under the scope and coverage of the JDC1, s2021.

Section 1. **General Classification of Products of PBIs**.

As defined in the NCBP Resolution no. 1, series of 2020, PBIs are a new set of molecular, genomics and cellular tools that enable the targeted and efficient development of new varieties of crops with desired traits or characteristics in a way that is faster and more precise than conventional plant breeding techniques. These PBIs include site-directed nucleases (SDN), oligonucleotide-directed mutagenesis, cisgenesis and intragenesis, RNA-dependent DNA methylation (RdDM), grafting with GM material, reverse breeding, agroinfiltration, synthetic genomics, and other upcoming techniques, with the potential to produce both GM and non-GM plants as final products. Accordingly, products of PBIs may be classified as:

a. Genetically modified organisms (GMOs), if, as defined under Executive Order no. 514, series of 2006, they contain a novel combination of genetic material obtained through the use of modern biotechnology, which "novel combination" the NCBP defines as a resultant genetic combination in a living organism that is not possible through conventional breeding; or

b. Non-GMOs, or conventional products, if they do not contain a novel combination of genetic material in the final product.

Section 2. **PBI Products Falling under the Scope and Coverage of JDC1, s2021.** – The NCBP Resolution established that "only PBI-derived GM plants and plant products would be regulated under the JDC1 [s2016]. Consequently, PBI-derived non-GM plants and plant products," which are considered conventional products, "would not be regulated" under the JDC1, s2016.

Furthermore, the JDC1, s2021, under its Section 1 (Applicability), provides that, "Consistent with the National Committee on Biosafety of the Philippines Resolution No. 001, series of 2020, "The Regulation of Plant and Plant Products Derived from the Use of Plant Breeding Innovations (PBIs) or New Plant Breeding Techniques (NBTs)," products of PBIs or NBTs that do not contain novel combinations of genetic materials obtained through the use of modern biotechnology are not covered by this Circular."

Section 3. **Product Developer**. – A product developer refers to the natural or juridical person who developed the PBI product submitted for the evaluation and determination of its regulatory status under the JDC1, s2021. A product developer may include: (a) any of the departments or agencies of the Philippine Government; (b) a university with research institutions in the Philippines; (c) an international research organization duly recognized by the Philippine Government; (d) a corporation registered with the Securities and Exchange Commission of the Philippines; or (e) a cooperative registered with the Cooperative Development Authority of the Philippines.

A non-resident product developer shall appoint an agent who is a resident of the Philippines and shall be in-charge with all submissions to and official communications with the Department of Agriculture particularly during the consultation process for the evaluation and determination of the regulatory status of a PBI product under the JDC1, s2021.

Section 4. **BPI Biotechnology Core Team-Plant Breeding Innovation**. – Within the Bureau of Plant Industry (BPI) is constituted a *Biotechnology Core Team-Plant Breeding Innovation (BCT-PBI)*. The BCT-PBI shall be composed of qualified technical staff from BPI and shall be chaired by the BPI Assistant Director for Regulatory Services. For every officially accepted request from a product developer for the conduct of a technical evaluation and determination, the BCT-PBI shall form a *Technical Consultation for*

Evaluation and Determination (TCED) Group. The TCED Group shall be composed of three (3) members, with at least two (2) members from the BCT-PBI selected based on availability and the other member appointed by the Chair of the BCT-PBI as an external expert, if deemed necessary, with expertise on genetics, molecular biology, molecular breeding, bioinformatics, and related disciplines. As further defined under Section 6 below, the TCED Group shall be responsible for the conduct of the technical evaluation and determination on the regulatory status of the PBI product under the JDC1, s2021. The BPI Director shall issue succeeding policy on the BCT-PBI on its composition, specific duties, and responsibilities in the implementation of this Circular.

Section 5. **Technical Consultation for Evaluation and Determination (TCED).** – A product developer who intends to introduce a PBI product into the country shall submit a request to the Director of BPI for *Technical Consultation for Evaluation and Determination* (TCED), which is a technical evaluation of the PBI product to determine whether or not the final product of the plant breeding process employed to produce the PBI product contain a novel combination of genetic material obtained through the use of modern biotechnology.

Section 6. **Procedural Requirements for the Conduct of a TCED**.

A. Submission of Request for TCED with Supporting Documents. The product developer shall submit the following documents to BPI.
   1. Both printed and electronic copy of the accomplished TCED Request Form, appended as *Attachment 1* to this Circular, that includes:
      a. Information on the name and contact details of the product developer and agent; and
      b. Sworn statement from the agent attesting to the authenticity and veracity of all documents being submitted.
   2. An accomplished *Prior Evaluation Form* (PEF), appended as *Attachment 2* to this Circular, that contains the following information on the PBI product:
      a. Type of organism and species involved;
      b. PBI technique used;
      c. Novel characteristic introduced and evidence of the desired genetic changes;
      d. Where the PBI technique employed uses a transient plasmid or an intermediate GMO, proof of their total absence in the final product; and
      e. As applicable, any additional information showing that the final product does not contain a novel combination of genetic material obtained through the use of modern biotechnology.
   3. Scientific studies, experimental evidence, and other documents to support claims in the PEF, when applicable; and
   4. Proof of payment of processing fee.

B. Acceptance of Submission. Upon receipt of the submission, the BPI shall examine it to determine its sufficiency in form and substance. If it complies with the format and contains all the required information, the submission shall officially be accepted. An accepted submission shall be posted immediately on the BPI website, and the public may submit to the BPI Director any technical information on the submission within ten (10) working days upon posting.

Within three (3) working days upon acceptance, the submission shall be forwarded to the BCT-PBI for the constitution of the TCED Group.

C. Conduct of the TCED.

1. The Chair of the BCT-PBI shall schedule the meeting of the TCED Group for the conduct of the TCED within seven (7) working days upon receipt of the officially accepted submission. The Chair shall also invite the product developer to be available for presentation and clarification on the submission during the scheduled technical consultation.
2. During the technical consultation, the TCED Group shall discuss and review the submission, particularly the PEF and other supporting documents, for the evaluation of the PBI product to determine whether or not a new combination of genetic material has been created in the final PBI product. Likewise, where appropriate, the TCED Group shall verify if there is enough scientific evidence of the absence of event(s) transiently used in the breeding process. In the conduct of the TCED, the TCED Group shall use Annex A of the NCBP Resolution no. 1, series of 2020 (Decision Tree), hereinafter appended as *Attachment 3* to this Circular.
3. The product developer shall ensure that its authorized representative is available to join the meeting in person or through tele- or video-conferencing in case the TCED Group requests for a presentation or has clarifications for the developer to answer.
4. Within five (5) working days from the first technical consultation, the TCED Group may set a second consultation if there are additional concerns that require further discussion. In such a case, the Chair of the BCT-PBI shall immediately communicate to the product developer the need to provide additional information and other studies in order to complete the evaluation. This information must be provided by the developer within five (5) working days from receipt of the request.
5. At the conclusion of TCED, the TCED Group shall make a technical determination on the regulatory status of the PBI product under the JDC1, s2021, which shall be indicated in the appropriate section of the PEF for evaluators, stating that the final PBI product:

a. Does contain a novel combination of genetic material obtained through the use of modern biotechnology, and thus shall be classified as a GMO and shall be under the scope and coverage of the JDC1, s2021; or
b. Does not contain a novel combination of genetic material obtained through the use of modern biotechnology, and thus shall be classified as a non-GMO or a conventional product and shall not be under the scope and coverage of the JDC1, s2021.

6. The BPI shall document the discussions of the TCED Group during the conduct of the TCED. The accomplished PEF indicating the technical determination of the TCED Group on the PBI product shall, within seven (7) working days after the conclusion of the TCED, be endorsed to the Director of BPI, who shall make an official determination on the regulatory status of the PBI product under the JDC1, s2021.

D. Action after Conduct of the TCED. Within five (5) working days from receipt of the accomplished PEF from the TCED Group, and considering any additional technical information from the public, if any, the Director of BPI shall make the official determination on the regulatory status of the PBI product; i.e.:
1. In case when the PBI product is officially determined as a GMO:
   a. Inform the product developer in writing that the GM PBI product is under the scope and coverage of the JDC1, s2021; and
   b. Advise the product developer to proceed with the application process under the JDC1, s2021 should the developer desire to secure a biosafety permit for any of the activities and use for regulated articles.
2. In case when the PBI product is officially determined as a non-GMO, issue to the product developer a *Certificate of Non-Coverage from the JDC1, s2021* for the non-GM PBI product, which shall also be made public by its posting on the BPI website.

   The Certificate of Non-Coverage from the JDC1, s2021 granted to a PBI product shall refer to the novel characteristic introduced in the current variety and the subsequent progenies. The certificate shall also apply to all germplasm or genetic backgrounds that will contain such characteristic produced by the product developer and/or its licensees in further breeding.

E. Monitoring. All PBI products officially determined as a GMO after the conduct of the TCED shall be monitored by the BPI to ensure compliance with the requirements of the JDC1, s2021 for regulated articles.

Section 7. **Compliance with Other Regulations.** – The Certificate of Non-Coverage from the JDC1, s2021 shall not excuse the product developer from complying with other relevant regulations of the Department of Agriculture and other government agencies, such as those involving quarantine, pest risk analysis, varietal registration, and crop-specific standards and programs, where warranted.

Section 8. **Target PBI Products.** – In the case of projects to develop or obtain PBI products that are still at the product concept or R&D phase, the product developer may file a request for TCED, following the same procedures as those specified in the foregoing sections, only for purposes of anticipating if the expected target product falls under the scope and coverage of the JDC1, s2021. In such a case, the TCED Group may perform a preliminary analysis and provide an indicative answer that will be communicated by BPI to the product developer. Upon the request of the product developer, portions of the submission may be treated as confidential information, subject to the provisions of Section 10 (*Confidential Information*) below. In the event that such PBI products are developed or obtained in the future, these shall be subject to the provisions of the foregoing sections, in order to confirm that such materialized PBI products contain the type of genetic change proposed in the preliminary consultation.

Section 9. **Appeal.** – An aggrieved party may file an appeal on the action taken by the BPI Director with the DA Secretary within fifteen (15) working days from (a) receipt by the product developer of the decision of the BPI Director, in the case when the PBI product is officially determined as a GMO; or (b) posting on the BPI website of the Certificate of Non-Coverage, in the case when the PBI product is officially determined as a non-GMO.

Section 10. **Confidential Information.**

a. If there are portions of the submission mentioned in this Circular that contain trade secrets or confidential business information, each page of the submission containing such information shall be marked "*Commercial-in-Confidence*" (CIC) by the product developer. In addition, portions of the submission which are deemed "CIC" shall be so designated. The product developer shall also submit one (1) copy of the submission with all the CIC deleted, marked with "CIC deleted" on each page where the CIC was deleted. If a submission does not contain any CIC, then the first page of all copies submitted to the BPI shall be marked "No CIC".

b. In no case, however, shall the following information be considered CIC:
   1. Name and address of the product developer and agent;
   2. Description of the PBI product, the type of organism and species involved;
   3. PBI technique used;
   4. New phenotypic features or novel characteristic introduced; and
   5. Any information that has been previously published or released in any format, media, or place.

c. The BPI shall inform the product developer if the information the latter identified as CIC does not qualify for such treatment and shall provide the product developer an opportunity for consultation and review of its decision prior to disclosure to any third party.

d. A product developer may refer to data or results from submissions previously provided by other developers: Provided, that (1) the information, data or results are not CIC, or (2) if the otherwise, the previous product developers have given their consent in writing to the use of their confidential information, data or results.

e. Documents that are made available to stakeholders and the public shall exclude portions that are marked as "CIC"; however, the documents shall clearly indicate with "CIC deleted" the part where the confidential information was removed.

Section 11. **Mutual Recognition Agreements**. – The Department of Agriculture, upon the recommendation and facilitation by BPI, may enhance cooperation with counterpart competent authorities of other countries to establish mutual recognition agreements or arrangements on the determination of classification of PBI products under international agreements to which the Philippines is a party.

Section 12. **Funding**. – BPI shall allocate resources for the implementation of this Circular. Funds necessary for the appointment of external experts to implement this Circular shall be provided by the DA Biotechnology Program.

Section 13. **Repealing Clause**. – All existing rules and regulations inconsistent with this Circular are hereby modified, revoked or repealed accordingly.

Section 14. **Separability**. – The provisions of this Circular are hereby declared to be separable. If any part or provision of this Circular shall be declared invalid, the remaining portions or provisions shall not be affected thereby and shall be construed as if it did not contain the particular invalid term or provision.

Section 15. **Effectivity**. – This Memorandum Circular shall take effect immediately upon completion of publication in a newspaper of general circulation and submission of a copy with the Office of the National Administrative Registrar, U.P. Law Center.

Done this 21st day of March 2022.

WILLIAM D. DAR, Ph.D.
Secretary

DEPARTMENT OF AGRICULTURE
in replying pls cite this code :
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Republic of the Philippines
Department of Agriculture
BUREAU OF PLANT INDUSTRY

Technical Consultation for Evaluation and Determination (TCED) Request Form

_____
(Date)

The Director
Bureau of Plant Industry

Sir/Madame:

We –

Information	Product Developer	Agent (if applicable)	Representative of Agent (if applicable)
Name			
Address			
Tel. No.			
Fax No.			
Email Address			

hereby request for the conduct of a Technical Consultation for Evaluation and Determination (TCED) for the plant/product of Plant Breeding Innovation (PBI) described below:

Name of the PBI Product	
Identification of the PBI Product (organism)	Scientific Name:
	Common Name:
Phenotypic feature before and after genetic change (Explain in detail.)	

The following supporting documents are attached:
1. Accomplished Prior Evaluation Form (PEF)
2. Scientific studies, experimental evidences, and other documents to support claims in the PEF
3. Proof of payment of fees.

The undersigned certifies that based on his/her personal knowledge and/or authentic documents: (i) all the information in this request form and accompanying submission are true and correct; (ii) the submission contains all information and views on which to base a decision and includes relevant data and information known to the product developer which are unfavorable to the submission.

_____

(Printed Name and Signature of Developer/Agent/Authorized Representative)

Republic of the Philippines)

SUBSCRIBED AND SWORN TO before me this ____ day of _____, 202__, affiant exhibiting to me his/her Community Tax Certificate No. _____ issued on _____ at _____.

Doc. No. _____;
Page No. _____;
NOTARY PUBLIC Book No. _____;
Series of 202__.

Prior Evaluation Form (PEF) for Products of Plant Breeding Innovation (PBI)

Part I. Background Information	
1. Name of Product Developer	
2. Office Address	
3. Telephone Number	
4. Email Address	
5. Website (if any)	
6. Name of Agent	
7. Position	
8. Mobile Number	
9. Email Address	

Part II. Description of the PBI Product	
1. Name of the PBI Product	
2. Identification of the PBI Product (organism)	Scientific Name:
	Common Name:
3. Phenotypic feature before and after genetic change (Explain in detail.)	

Part III. Description of the Plant Breeding Innovation (PBI) Procedure Used (To Be Used)		**Reference/s (If Applicable)**
1. Purpose of the PBI		
2. PBI procedure	☐ Oligonucleotide-directed mutagenesis (ODM) ☐ Site-directed nuclease 1 (SDN1) ☐ Site-directed nuclease 2 (SDN2) ☐ Site-directed nuclease 3 (SDN3) cis insert ☐ Site-directed nuclease 3 (SDN3) with trans insert ☐ Cisgenesis ☐ Intragenesis ☐ RNA-dependent DNA methylation (RdDM)	

	☐ Reverse breeding ☐ Agro-inoculation of non-germline tissues ☐ Agro-inoculation of germline tissues with cis insert ☐ Agro-inoculation of germline tissues with trans insert ☐ Agro-infiltration ☐ Grafting with GM material ☐ Synthetic genomics with cis-like sequence integration or faithful genome reconstruction ☐ Synthetic genomics with trans-like sequence integration ☐ Others: _____	
3. Genetic change in the organism		
a. Name of the molecular tools used		
b. Description and nucleotide sequence of the molecular tools used i. Guide RNA ii. Nuclease iii. Nucleotide sequence to be introduced (if applicable) iv. Vectors (if applicable) v. Selection markers (if applicable) vi. Reporter gene (if applicable)		
c. Delivery system	☐ Agrobacterium-mediated ☐ Particle bombardment/biolistic method ☐ Floral-dip ☐ PEG-mediated protoplast method ☐ Others (specify) _____	
d. Nature of DNA changes	Original sequences (underline target bases): _____ Sequences after gene editing (underline new bases): _____	

	☐ Deletions → *Proceed to Question 4.* ☐ Additions and/or substitutions; involve a few base changes (specify how many bases) _____ → *Proceed to Question 4.* ☐ Insertions and/or gene replacements; involve more than a few base changes (specify how many bases) _____ → *Proceed to Question 3e.*	
e. Source of insertion or genes	☐ Same species (specify) _____ → *Proceed to Question 4.* ☐ Cross-compatible species (specify) _____ → *Proceed to Question 4.* ☐ Cross-incompatible species (specify) _____ → End of inquiry.	
4. Experimental evidence showing the final PBI product has no new combination of genetic material in the form of foreign DNA insert or sequences from gene editing tool construct using appropriate molecular techniques. For PBI products developed with the introduction of whole genes into the cells of the target/host organism, molecular evidence must be presented to show that such gene/s was/were not incorporated in any part of the genome where it is/they are not intended to be.		
5. Any existing regulatory precedence on the PBI Product in the issuing country and purpose of the decision (if applicable).		

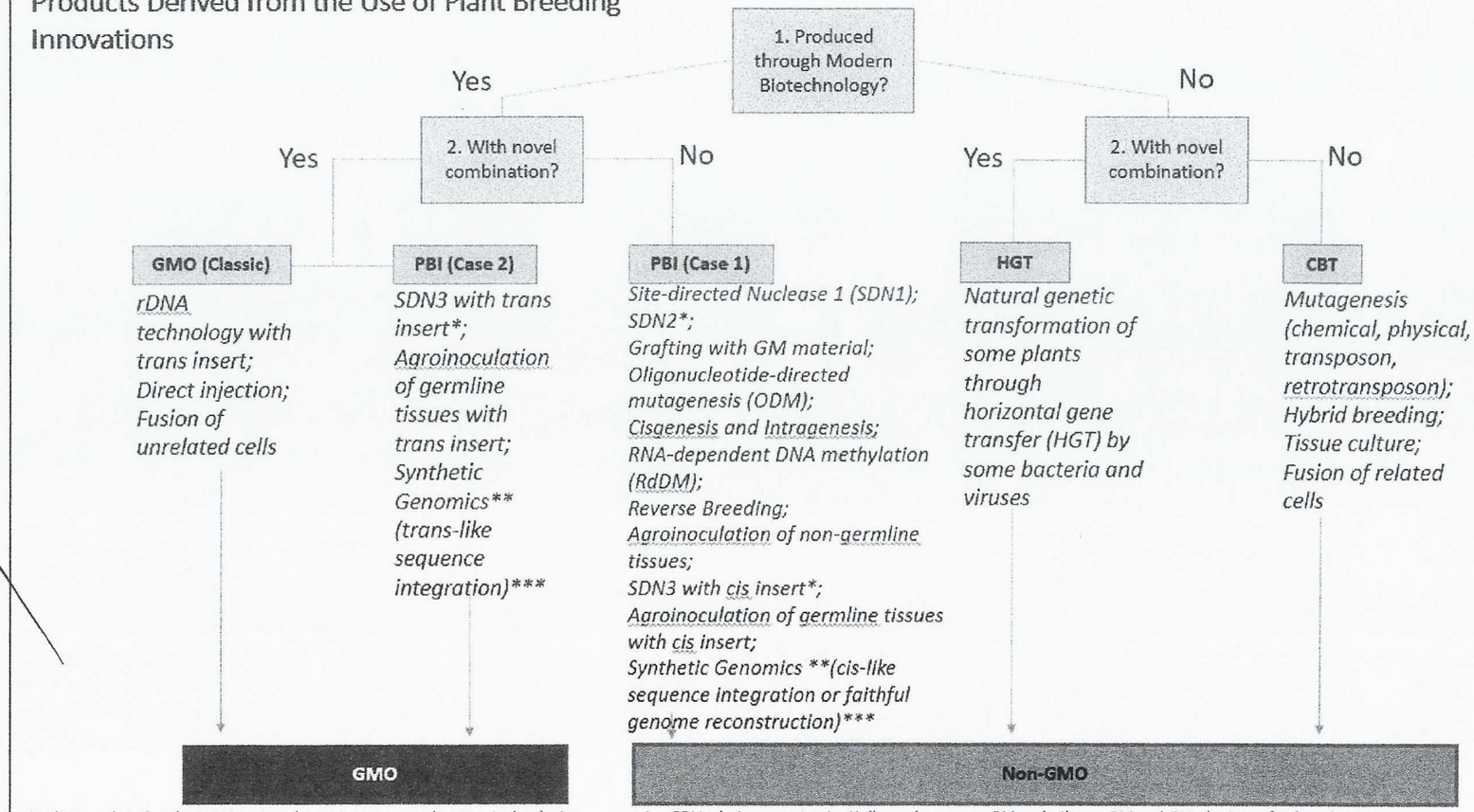
Part IV. Scientific Studies, Experimental Evidences, and Others Submitted with This Form
1. _____
2. _____
3. _____
4. _____
5. _____

Name	*Designation*	*Signature*	*Date*

For the Biotech Core Team-Plant Breeding Innovation (BCT-PBI) TCED Group: Please check the appropriate box.	
	Determined that the PBI Product is not a GMO and does not fall under the scope and coverage of the JDC1, s2021 based on the scientific evidence(s) presented by the Product Developer.
	Determined that the PBI Product is a GMO and falls under the scope and coverage of the JDC1, s2021 based on the scientific evidence(s) presented by the Product Developer.

Printed Name	***Signature***	***Date***

Decision Tree on the Regulation of Plants and Plant Products Derived from the Use of Plant Breeding Innovations



Techniques listed under PBI Case 1 and Case 2 may expand as new technologies emerge. Any PBI technique must potentially produce a non-GM or both non-GM and GM plant as a final product..

*Includes the new CRISPR-CAS with Prime Editing (Science, 2019) ** Different from Synthetic Biology which specializes on artificial organisms ***Pertains to a largely synthetic assembled genome

Glossary to the Decision Tree

Agroinfiltration – also known as agroinoculation, an Agrobacterium-mediated transfer of a gene construct into plant cells for the transient expression of the introduced gene. Mainly used in research, agroinfiltration is currently being explored for plant and human disease management and the commercial production of recombinant protein in plants (Chen et al., 2013; Hariharan et al., 2021)

Cis – from a sexually compatible species

Cisgenesis – the transfer through genetic engineering of one of more genes originating either from the host species itself or from a close relative (cross-compatible species). A typical cisgene comprises the target gene itself along with its native promoter and terminator region (Moglia and Portis, 2016)

CRISPR/Cas9 or Clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated protein 9 – a type of site-directed nuclease (SDN) tool comprising the DNA-cutting enzyme, Cas9, and the sgRNA that guides the complex to the target sequence to be edited.

Conventional breeding Techniques (CBT) – refer to the procedures of selection, hybridization, assisted pollination and induced mutagenesis

Genetic engineering (GE) – refers to the process of producing a genetically modified organism or GMO

Genetically modified organism (GMO) – also known as living modified organism (LMO); any living organism that possesses a novel combination of genetic material obtained through the use of modern biotechnology or recombinant DNA technology (Cartagena Protocol on Biosafety)

Germline – the population of germ cells (e.g., egg, sperm) of an organism that passes on its genetic material to the progeny (offspring) (https://en.wikipedia.org/wiki/Germline)

Grafting with GM material – an NBT that produces non-transgenic products from a chimeric plant in which one part (either rootstock or scion) is a GMO and the part with the harvestable product is a non-GMO

Horizontal gene transfer (HGT) – also known as lateral gene transfer; the non-sexual movement of genetic information between genomes. Incoming DNA or RNA can replace existing genes, or can introduce new genes into a genome (Keeling & Palmer, 2008)

Intragenesis – similar to cisgenesis except that the gene being transferred is a combination of genetic parts (promoter, CDS, terminator, etc.) obtained from other genes of the same species

Modern biotechnology – the application of: a) in vitro nucleic acid techniques, including recombinant deoxyribonucleic (rDNA) and direct injection of nucleic acid into cells or organelles or b) fusion of cells beyond the taxonomic family that overcome natural physiological, reproductive or recombination barriers and that are techniques used in traditional breeding and selection (Cartagena Protocol on Biosafety)

Mutagenesis – the process of generating a genetic mutation or variation

Novel combination – a resultant combination of genetic material that is not possible through conventional breeding

Oligonucleotide-Directed Mutagenesis (ODM) – a technique that makes use of synthetic oligonucleotides that share homology with a target sequence(s) with the exception of the nucleotide(s) to be modified. Oligonucleotides "target" the homologous sequence in the genome, and create a mismatch at the base pair that is to be modified. This mismatch is recognized by the DNA repair machinery of the cell and the mismatch is repaired using the synthetic sequence as template to change the target nucleotides (Modrzejewski et al., 2018)

Palindromic – the state in which the nucleotides are ordered such that they have the same sequence as the complementary DNA-strand when read in the opposite direction

Plant Breeding Innovations (PBI) – also known as New Plant Breeding Techniques (NBT) are a new set of molecular, genomics and cellular tools that enables the targeted and efficient development of new varieties of crops with desired traits in a way that is faster and more precise than conventional plant breeding techniques, which PBIs include Site Directed Nucleases (SDN), Oligonucleotide Directed Mutagenesis, Cisgenesis and Intragenesis, RNA-dependent DNA Methylation (RdDM), grafting with GM material, Reverse Breeding, Reverse Breeding, Agroinfiltration, Synthetic Genomics, and other upcoming techniques with the potential to produce GM and/or non-GM plants as final products (NCBP Res 1 ser 2020)

Recombinant DNA (rDNA) – a technology that uses enzymes to cut and paste together DNA sequences of interest. The recombined DNA sequences can be placed into vehicles called vectors that ferry the DNA into a suitable host cell where it can be copied or expressed (National Human Genome Research Institute, NIH, USA)

Reverse Breeding (RB) – an NBT designed to directly produce parental lines for any heterozygous plant. RB generates perfectly complementing homozygous parental lines through engineered meiosis. The method is based on reducing genetic recombination in the selected heterozygote by eliminating meiotic crossing over (Dirks et al., 2009).

RNA-dependent DNA Methylation (RdDM) – an NBT that uses RNA molecules to knock down or silence target genes by attaching a $-CH_3$ (methyl group) within their promoter sequence, particularly involving the carbon 5 of cytosine without introducing mutational changes in the relevant DNA sequences. These epigenetic effects may be achieved through stable insertion of a construct or by transient expression.

Site-Directed Nuclease (SDN) – a genome editing tool that involves the use of different DNA-cutting enzymes (nucleases) that are directed to cut the DNA at a predetermined location by a range of different DNA binding systems. After the cut is made, the cell's own DNA repair mechanism recognizes the break and repairs the damage, using one of two pathways that are naturally present in cells: non-homologous end-joining (NHEJ) and homology-directed repair (HDR) (https://prri.net/scientific-topics/new-breeding-techniques/genome-editing/site-directed-nuclease-sdn-genome-editing). SDN

applications are divided into three techniques: SDN-1, SDN-2 and SDN-3. SDN-1 produces a double-stranded break in the genome of a plant without the addition of foreign DNA. The spontaneous repair of this break can lead to a mutation or deletion, causing gene silencing, gene knock-out or a change in the activity of a gene. SDN-2 produces a double-stranded break, and while the break is repaired by the cell, a small nucleotide template is supplied that is complementary to the area of the break, which in turn, is used by the cell to repair the break. The template contains one or several small sequence changes in the genomic code, which the repair mechanism copies into the plant's genetic material resulting in a mutation of the target gene. SDN-3 also induces a double-stranded break in the DNA, but is accompanied by a template containing a gene or other DNA sequences. The cell's natural repair process then utilizes this template to repair the break, resulting in the introduction of the gene or new sequences (https://www.nbtplatform.org/background-documents/factsheets/factsheet-site-directed-nucleases.pdf).

Synthetic genomics – encompasses technologies for the generation of chemically-synthesized whole genomes or larger parts of genomes, allowing to simultaneously engineer a myriad of changes to the genetic material of organisms (Konig et al., 2013)

Trans – from a sexually incompatible species

Transcription activator-like effector nucleases (TALEN) – a site-directed nuclease (SDN) technology that possesses the nuclease FokI as DNA-cleaving domain and an array of TAL effector proteins as the DNA-binding domain engineered to recognize specific DNA sequences (Joung & Sander, 2013)

Zinc finger nucleases (ZFNs) – an SDN technology comprising a class of engineered DNA-binding proteins that facilitate targeted editing of the genome by creating double-strand breaks in DNA at user-specified locations (https://www.sigmaaldrich.com/PH/en/technical-documents/technical-article/genomics/advanced-gene-editing/learning-centerwhat-is-zfn). The double strand breaks are repaired by the cell's own DNA repair system where nucleotide changes may be introduced.

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