

**National Organic Standards Board
Materials/GMO Subcommittee
Excluded Methods Terminology – Proposal
February 23, 2016**

Introduction and Background

In April 2013 the project was started to grapple with the definition of "excluded methods" in the USDA organic regulations. This is the definition that appears in the rule (7 CFR 205.2; Terms Defined):

Excluded methods. A variety of methods used to genetically modify organisms or influence their growth and development by means that are not possible under natural conditions or processes and are not considered compatible with organic production. Such methods include cell fusion, microencapsulation and macroencapsulation, and recombinant DNA technology (including gene deletion, gene doubling, introducing a foreign gene, and changing the positions of genes when achieved by recombinant DNA technology). Such methods do not include the use of traditional breeding, conjugation, fermentation, hybridization, in vitro fertilization, or tissue culture. (Federal Register / Vol. 65, No. 246 / Thursday, December 21, 2000 / Rules and Regulations p. 80639)

The definition was based on the best efforts of the NOSB in 1995 and has provided adequate guidance to prohibit the use of the most obvious genetically engineered crops such as herbicide-resistant corn and soybeans and Bt cotton, as well as prohibit processing inputs such as genetically engineered yeasts and enzymes. However, this definition is in need of re-examination and updating due to rapid advances in recombinant DNA biotechnology since 1995 that have made for gray areas for the organic standards regarding interpretation and enforcement.

In 2011 and 2012 a number of confusing issues came before the NOSB and to the NOP which made it necessary to revisit the definition. These include genetically engineered vaccines for livestock, the use of cell fusion within plant families to create male sterility in brassica hybrids, whether or not GMOs could be used in biodegradable bioplastic mulches, and the question of whether mutated algae might therefore be genetically engineered. The current definition is inadequate to clarify these issues. In the last few years the rise of gene editing with no insertion of foreign DNA, synthetic biology, and the genetically engineered insects that are starting to appear make this effort even more important.

The first NOSB Discussion Document on excluded methods in 2013,¹ discussed each of the terms in the above definition, defined and discussed other terms involved in traditional breeding, such as mutagenesis and conjugation, and brought up new terms that may be considered to be genetic engineering. No conclusions were suggested except that there is a need to do more work on the subject. The discussion questions posed asked commenters to suggest principles on which to base GE distinctions, to offer opinions on what terms were and were not excluded methods, and to bring forward new terms that may need consideration.

The second NOSB Discussion Document posted in September, 2014 and in April 2015² analyzed the comments received and proposed several options for an updated definition, and principles and criteria to use when evaluating the various genetic modification issues. Additional terms were collected and the beginnings of some definitions were started. A structure was proposed similar to the one in use by FiBL in Europe that involves an itemized chart with a yes/no column where the specific techniques could be itemized and evaluated. A recommendation was informally made by the subcommittee, but not voted upon, that these revisions to the definition and structure for evaluating techniques be regulated through NOP guidance rather than additional rulemaking. Lastly it was acknowledged that there will be some unresolved issues that will need continued public discussion because they pose enforcement challenges, are totally hidden from view, or not enough is known about them yet.

Goals of This Proposal/Document

The need for forward motion on this subject is more pressing every month. The fact that over 1000 pages of scientific references were submitted in public comment, with most of it being papers that came out since the NOSB GMO ad hoc Subcommittee was formed in 2012, indicates that the biotech community is rapidly outpacing any regulatory structure. The U.S. Department of Agriculture (USDA) has already ruled that certain plants produced with novel approaches to genetic manipulation will not be regulated as genetically modified organisms in the United States³. It is more imperative than ever that the organic community be very clear about where the line is drawn regarding genetic engineering.

Public Comment from the past two years has indicated strong support for this effort on the whole, although there is not consensus on some details. Every organic stakeholder is clear that genetic engineering is an imminent threat to organic integrity. Every effort must be made to protect that integrity to the extent that the NOSB is able to contribute to that.

The Materials Subcommittee is ready to move forward to create a structure for reviewing new technologies and disseminating the results of this review in a transparent manner. To this end, the proposal portion of this document includes supplements to the definition in the rule based on internationally accepted language, criteria to use in the reviews based on that definition, and a chart of those techniques that are clearly "excluded methods" based on the definition and criteria.

A separate discussion document contains the technologies, terms, and issues that we have not been able to agree on or do not yet have enough information on or that pose challenges that we have not yet taken up. These items are put out for discussion to collect further public comment. They will be reviewed at future NOSB meetings.

Definitions

In the previous Discussion Document we suggested a couple of possible definitions that would update the text in the rule to a more comprehensive one that would be flexible enough to accommodate future technologies and terms. We were inclined to favor the definitions in use by the Cartagena Protocol that are also in use by Codex Alimentarius.

During the course of public comment and subsequently, it has become clear that more than one definition is important to the organic community, but that all the terms we suggest defining here would fall under the Excluded Methods definition in the rule and would not change, but would strengthen that definition. These definitions are to be used in Guidance to supplement and update the definition in the regulations, while leaving the rule itself intact. It is important to adopt some definitions that are widely accepted internationally and thus give some common ground with other countries who are concerned about GMOs in organics.

In October 2015 the International Federation of Organic Agriculture Movements (IFOAM) put out a Discussion Paper on a proposed revision to their Position on Genetic Engineering.⁴⁵ Since they do not use the concept of "Excluded Methods" in other countries, they proposed new definitions for three terms: Genetic Engineering (GE), Genetically Modified Organism (GMO), and Synthetic Biology. After examining their definitions, the Materials/GMO Subcommittee (MS) agrees that these three terms are important to define in the guidance we are proposing. However, we do not wish to take the old approach (that IFOAM is still using) of trying to capture all the methods and terms into one definition, because it will be out of date as soon as the next round of new technologies arrives.

Therefore we are suggesting the following definitions of terms and acronyms, with sources, be adopted by the NOSB as being Excluded Methods:

Genetic engineering (GE) – A set of techniques from molecular biology (such as recombinant DNA and RNA) by which the genetic material of plants, animals, micro-organisms, cells and other biological units are altered and recombined (first sentence modified from IFOAM Position cited above)

Genetically Modified Organism (GMO) – A plant, animal, or microorganism that is transformed by genetic engineering as defined here. This term will also apply to products and derivatives from genetically engineered sources (first sentence from IFOAM Position cited above, second sentence modified from their definition)

Modern Biotechnology – (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 overcomes natural, physiological reproductive or recombination barriers, and that are not techniques used in conventional breeding and selection. (From the Cartagena Protocol⁶ and also used by Codex Alimentarius)

Non-GMO – The term that is used to describe or label a product that was produced without any of the excluded methods defined here. It is consistent with the NOP process-based standard that does not imply freedom from GMOs but does indicate that processes to prevent GMO contamination have been used (from the public comment by the Organic Trade Association, April 2015⁷)

Synthetic Biology⁸ – A further development and new dimension of modern biotechnology that combines science, technology and engineering to facilitate and accelerate the understanding,

design, redesign, manufacture and/or modification of genetic materials, living organisms and biological systems. (Operational Definition developed by the Ad Hoc Technical Expert Group on Synthetic Biology of the UN Convention on Biological Diversity⁹)

This series of definitions provide a better framework than solely the existing definition to further elaborate the various technologies that would be prohibited as well as those which would be allowed. We propose to combine these definitions, the principles and criteria discussed below, and the Terminology chart presented into this Proposal for Guidance on Excluded Methods.

Principles and Criteria

The NOSB has its own set of Principles of Organic Production and Handling in the Policy and Procedures Manual¹⁰. They start with:

1.1 Organic agriculture is an ecological production management system that promotes and enhances biodiversity, biological cycles, and soil biological activity. It emphasizes the use of management practices in preference to the use of off-farm inputs, taking into account that regional conditions require locally adapted systems. These goals are met, where possible, through the use of cultural, biological, and mechanical methods, as opposed to using synthetic materials to fulfill specific functions within the system.

One of the points following this is in regard to Genetic Engineering:

1.11 Genetic engineering (recombinant and technology) is a synthetic process designed to control nature at the molecular level, with the potential for unforeseen consequences. As such, it is not compatible with the principles of organic agriculture (either production or handling). Genetically engineered/modified organisms (geo/gmo's) and products produced by or through the use of genetic engineering are prohibited.

The following principals of Organic Agriculture are used by IFOAM¹¹ and summarize well the guidance for developing a position on GMO technology.

- Principle of Health: Organic Agriculture should sustain and enhance the health of soil, plant, animal, human and planet as one and indivisible.
- Principle of Ecology: Organic Agriculture should be based on living ecological systems and cycles, work with them, emulate them and help sustain them.
- Principle of Fairness: Organic Agriculture should build on relationships that ensure fairness with regard to the common environment and life opportunities.
- Principle of Care: Organic Agriculture should be managed in a precautionary and responsible manner to protect the health and well-being of current and future generations and the environment.

Using the principles above, biotechnology processes will be reviewed to the following criteria to determine if they are excluded methods:

- The genome is respected as an indivisible entity and technical/physical invasion into the

plant genome is refrained from (e.g. through transmission of isolated DNA, RNA, or proteins). *In vitro* nucleic acid techniques are considered to be invasion into the plant genome.

- The ability of a variety to reproduce in species-specific manner has to be maintained and technologies that restrict the germination capacity of seed-propagated crops are refrained from (e.g. Terminator technology).¹²
- Novel proteins must be prevented from being introduced into the soil and water ecosystems and into the organic food supply.
- The exchange of genetic resources is encouraged and any patenting of living organisms, their metabolites, gene sequences or breeding processes are refrained from.¹³

Most of the techniques that are considered to be genetic engineering are clearly not compatible with the principal of ecology because they do not work within living ecological systems or sustain them. They are also at odds with the Principal of Fairness because they are not available equally to all stakeholders and are often patented or used to create patented traits. There are significant questions around the Principle of care for the health and well-being of future generations and the environment. These concerns do not change just because a technique cannot be tested for or does not use DNA foreign to the target organism.

The secondary effects from the use of GMOs are starting to emerge clearly in parallel with the new technologies. Issues such as reduction in diversity on farms where GMOs are grown, the demise of beneficial species both above and below the soil, the decline in soil fertility and resilience from increased use of herbicides, the evolution of weeds resistant to those herbicides, the altered nutritional profiles of the GMO crop products, and the displacement of small farmers from their land are all violations of the principals of organic agriculture.¹⁴

In the accompanying discussion document there will be additional discussion of how these concepts might be used in organic plant breeding.

Process and Product

Since the whole underpinning of the U.S. organic regulations is a process-based system, it makes sense that this concept carry over to defining excluded methods. This is indeed the basis of the current definition. However, this is not currently how U.S. government agencies regulate GMOs¹⁵, or handle other issues such as pesticide residues or water quality standards.

Newer technologies, known as Targeted genetic modification (TagMo) or targeted genome editing, are emerging and being adopted quickly.¹⁶ These are very clearly genetic engineering techniques but are not regulated by the current government structure because they do not involve DNA from a "pest" under the USDA APHIS regulatory structure. Many of these techniques involve precise changes in existing DNA without using foreign DNA from a different species. These new technologies make genetic modification much more accessible and less expensive. The resulting plants may not show up as genetically engineered in the commonly used testing methods because they contain no foreign DNA, just native DNA that has been changed at the allele level by humans.

Forward Movement towards Structure

FiBL Research Institute for Organic Agriculture from Switzerland submitted a comment in 2013 that included a chart that describes methods with a yes/no column for compatibility with organic standards for both plants and animals¹⁷. The NOSB posed adopting such a chart on the methods that receive consensus and can be incorporated into guidance. It is important to identify all of these terms so that it is clear that they fall under the definition of excluded methods, but these terms do not need to be added to the definition itself.

The first version of such a chart for the NOSB is presented here. Appendix A provides a brief description of each term with additional citations for those who want to find out more about the terms. There is so much terminology and so many techniques with similar or multiple names that we have added a column for additional names and types used for each general process. Along with lack of regulation of some of these processes, there is lack of standardization of the terms, so that new names and sometime proprietary ones are emerging all the time.

We would especially like to acknowledge the work done by the Center for Food Safety in their public comment for the April 2015 meeting. They have helped organize all the various terminology and provided substantial scientific papers that discuss all the terms.¹⁸ The technologies are grouped by the tasks that the methods accomplish and the types of changes made to the engineered organism. In the context of this proposal we are not able to discuss most of the terms at length so please see the Appendix and the CFS cited comment for the full reference list.

The ones marked "TBD" in the chart below are discussed further in the accompanying Discussion Document.

Terminology Chart			
Method and synonyms	Types	Excluded Methods	Notes
Targeted genetic modification (TagMo) syn. Synthetic gene technologies syn. Genome engineering syn. Gene editing syn. Gene targeting	Sequence-specific nucleases (SSNs) Meganucleases Zinc finger nuclease (ZFN) Mutagenesis via oligonucleotides CRISPR-Cas system* TALENs** Oligonucleotide directed mutagenesis (ODM) Rapid Trait Development System (RTDS) (Cibus)	YES	Most of these new techniques are not regulated by USDA and are hard to test for.
Gene Silencing	RNA-dependent DNA methylation (RdDM) Silencing via RNAi pathway RNAi pesticides	YES	
Accelerated plant breeding	Reverse Breeding	YES	These may pose

techniques	Genome Elimination FasTrack Fast flowering Dupont Seed Production Technology (SPT)		an enforcement problem for organics because they are not detectable in tests.
Synthetic Biology	Creating new DNA sequences Synthetic chromosomes Engineered biological functions and systems.	YES	
Embryo transfer in animals	Embryo rescue in animals	YES	FIBL distinguishes embryo rescue in plants from animals.
Cloned animals and offspring	Somatic nuclear transfer	YES	
Plastid Transformation		YES	
Marker Assisted Selection		NO	
Protoplast Fusion		TBD	
Cisgenesis		TBD	
Intragenesis		TBD	
Transposons		TBD	
Transduction		TBD	
Cell Fusion within Plant Family		TBD	
Embryo rescue in plants		TBD	
TILLING	Eco-TILLING	TBD	
Agro-infiltration		TBD	
Doubled Haploid Technology		TBD	
Induced Mutagenesis		TBD	

* CRISPR-Cas = Clustered regularly interspaced short palindromic repeats and associated protein genes.

** TALENs = Transcription activator-like effector nucleases.

Proposal

This proposal has three sections, to be used in NOP Guidance on Excluded Methods:

1. Approve the definitions of Genetic Engineering (GE), Genetically Modified Organism (GMO), Modern Biotechnology, Non-GMO, and Synthetic Biology as written above.
2. Approve the Principles and Criteria above that will be used in the evaluation of new technologies and terminologies.
3. Adopt the Terminology chart proposed above and the listings in it as presented, recognizing that this will be added to as further deliberations occur in the future.

Subcommittee Vote

The NOSB Materials/GMO subcommittee approves the three sections of this proposal as stated above.

Motion by: Zea Sonnabend

Second: Tracy Favre

Yes: 5 No: 0 Abstain: 1 Absent: 0 Recuse: 0

Appendix A –

Brief Description and Additional Citations for Terms used in Excluded Methods Terminology Chart.

Only terms that are marked YES or NO as Excluded Methods are defined here. All those marked TBD are still being worked on in discussion. Those marked "syn." are defined in cited reference from Center for Food Safety Public Comment in April 2015¹⁹. Some other definitions are from the NOSB previous Discussion Document²⁰ and from the FiBL 2015 plant breeding dossier.²¹

Targeted genetic modification (TaqMo) (Kuzma and Kokotovich 2011, Kokotovich and Kuzma 2014) - a collective term for the zinc finger nuclease techniques that create DNA double-stranded breaks at specific genomic locations that can then be used to alter the target gene. The genetic modification would not necessarily involve transfer of nucleic acids from another species, nor would it be easy to detect in a final product.

- syn. Synthetic gene technologies (Then 2015)
- syn. Genome engineering (Voytas and Gao 2014)
- syn. Gene editing (Puchta and Fauser 2013)
- syn. Gene targeting (GT) (Puchta and Fauser 2013, Endo et al. 2015)
- syn. Sequence-specific nucleases (SSNs) (Voytas and Gao 2014):
- syn. Meganucleases (Gao et al. 2011, as cited in FSANZ 2013)
- syn. Site directed mutagenesis via oligonucleotides, zinc finger nuclease (ZFN) (Dow, APHIS 2012) - an introduction of recombinant DNA through transient molecules that are identified by zinc-finger nucleases, with or without a repair template. The techniques resemble transgenesis but the end products are similar to, and indistinguishable from, conventionally bred plants.
- syn. Clustered regularly interspaced short palindromic repeats and associated protein genes (CRISPR-Cas system) (NYTs 3/20/2015) – a protein called Cas9 enables breaks in DNA at specific spots so that additional pieces of DNA and RNA can be inserted.
- syn. Transcription activator-like effector nucleases (TALENs) (Sprink et al. 2014).
- syn. Oligonucleotide directed mutagenesis (ODM) (Lusser et al. 2011)
- syn. Cibus Rapid Trait Development System (RTDS) (Beetham et al. 2012 patent) - Similar to the oligonucleotide targeted DNA modification it does not leave behind transgenic material, only uses it to create a change in a precise area of a gene.

Gene silencing via RNAi and DNA methylation - Interfering with the regulation of gene expression through inserting methyl groups onto RNA and DNA that then suppress the expression of the gene. Can occur in nature, but is used as a recombinant technique in cancer research and plant breeding.

- syn. RNA-dependent DNA methylation (RdDM) (Lusser et al. 2011)
- syn. Gene silencing via RNAi pathway (Casacuberta et al. 2015, Baier et al. 2014, Lubasik and Zielenkiewicz 2014, Hirschi 2012, Heinemann et al. 2013, Lundgren and Duan 2013, Wagner et al. 2015) – A technique in which a small strand of RNA is inserted into a DNA sequence to regulate the expression of the gene. There is no change to the DNA sequence, but there is technical interference with the genome.

- RNAi-based pesticides (Palli 2014, Zhu 2013) – RNA interference (RNAi) is a technique in which gene silencing RNA strands are inserted into a target genome in order to regulate the expression of target genes. It was used to engineer rootworm resistant corn as well as to genetically engineer insects themselves.

Accelerated Plant Breeding Techniques

- Reverse Breeding (Dirks et al. 2009) – A process that uses several other techniques such as RNAi to suppress meiotic recombination, tissue culture, and then double haploidization to create parental lines that are homozygous to use in breeding F1 hybrids.
- Genome elimination (Comai 2014)
- FasTrack (Waltz 2012) – a breeding scheme that has so far been used in plums where an early-flowering gene from poplar is inserted into a plum tree. When the plum flowers in less than a year, it is crossed with non-transgenic varieties carrying desirable traits. Markers are used to identify the right traits and, at the end of the breeding program, only those are selected that do not have the transgene.
- Fast flowering (Flachowsky et al. 2011)
- DuPont’s Seed Production Technology (SPT) (Waltz 2012)

Synthetic Biology (see definition in main document)

- Synthetic chromosomes (Shenoy and Sarma 2010, pp. 12-13; Gaeta et al. 2012)

Embryo Transfer in animals – a technique used in animal breeding. It involves inducing superovulation of donor with gonadotropins, artificial insemination, recovery of embryos, isolation and storage of embryos, transfer of embryos back into animals, and then pregnancy.

Plastid transformation (Maliga 2004, as cited in NOSB discussion 2014) – Plastids are semi-autonomous organelles within higher plants with a small, highly polyploid genome. Technology has been developed for genetic modification of this genome independent of nuclear DNA. Currently used commercially in tobacco, and widely researched.

Marker Assisted Selection – Molecular markers are used as diagnostic aids to determine differences in the DNA sequence. They can help in selecting desired traits. The markers do not change the DNA of living plants and are not considered to be genetic engineering.

¹ NOSB 2013. Excluded Methods Terminology Discussion Document. April 2013.

<http://www.ams.usda.gov/AMSV1.0/getfile?dDocName=STELPRDC5102656>

² National Organic Standards Board Materials/GMO Subcommittee. (2014). *Discussion Document on Excluded Methods Terminology*. August 22.

³ Waltz, E. (2012). Tiptoeing around transgenics. *Nature Biotechnology*, 30, 215-217. doi:10.1038/nbt.2143

⁴ IFOAM – Organics International, 2015, 2015 Discussion Paper on a Proposed Revision to Position on Genetic Engineering and Genetically Modified Organisms in Organic Agriculture.

https://gallery.mailchimp.com/75bdf144a46c1e451eecd10/files/Discussion_paper_on_GMO_position_2015.pdf

⁵ IFOAM – Organics International, 2002, Position on Genetic Engineering and Genetically Modified Organisms, P01, https://gallery.mailchimp.com/75bdf144a46c1e451eecd10/files/IFOAM_GMO_Position_Paper.pdf

⁶ Convention on Biological Diversity. 2013. The Cartagena Protocol on Biosafety. Available at:

<http://bch.cbd.int/protocol>.

⁷ Organic Trade Association Comments to the NOSB, <http://www.regulations.gov/#!documentDetail;D=AMS-NOP-15-0002-0814>

⁸ Two other definitions were looked at when this one was chosen: **Synthetic Biology** – Designing and constructing biological devices, biological systems, biological machines and biological organisms using a range of methods derived from molecular biology and biotechnology, including in virtually all cases the techniques of genetic engineering or genetic modification (from IFOAM Position cited above). **Synthetic biology** is a maturing scientific discipline that combines science and engineering in order to design and build novel biological functions and systems. This includes the design and construction of new biological parts, devices, and systems, as well as the re-design of existing, natural biological systems for useful purposes.” (from SynBerc, the University of California/Department of Energy synthetic biology research consortium)

⁹ Link to the European Commission's draft definition with discussion:

http://ec.europa.eu/health/scientific_committees/consultations/public_consultations/scenih_r_consultation_21_en.htm

¹⁰ NOSB Policy and Procedures Manual: <https://www.ams.usda.gov/sites/default/files/media/NOSB-PolicyManual.pdf>
<https://www.ams.usda.gov/sites/default/files/media/NOSB-PolicyManual.pdf>

¹¹ http://www.ifoam.bio/sites/default/files/poa_english_web.pdf

¹² FiBL Research Institute of Organic Agriculture 2013. Public Comment to NOSB. Docket AMS-NOP-12-0070

¹³ FiBL Research Institute of Organic Agriculture 2015. Dossier No. 2 Plant Breeding Techniques: an assessment for organic farming.

¹⁴ IFOAM – Organics International, 2015, 2015 Discussion Paper on a Proposed Revision to Position on Genetic Engineering and Genetically Modified Organisms in Organic Agriculture.

https://gallery.mailchimp.com/75bdff144a46c1e451eecd10/files/Discussion_paper_on_GMO_position_2015.pdf

¹⁵ Kuzma J, Kokotovich A (2011) Renegotiating GM crop regulation. EMBO reports 12: 883–888.

¹⁶ Kokotovich A, Kuzma J (2014) Conflicting Futures: Environmental Regulation of Plant Targeted Genetic Modification. Bulletin of Science, Technology & Society 34: 108–120.

¹⁷ FiBL Research Institute of Organic Agriculture 2013. Public Comment to NOSB. Docket AMS-NOP-12-0070

¹⁸ CFS Comments to the NOSB, 2015, Docket #AMS_NOP_15-0002-0874

¹⁹ CFS Comments to the NOSB, 2015. Reference List. <http://www.regulations.gov/#!documentDetail;D=AMS-NOP-15-0002-0875>

²⁰ National Organic Standards Board Materials/GMO Subcommittee. (2014). *Discussion Document on Excluded Methods Terminology*. August 22.

²¹ FiBL Research Institute of Organic Agriculture 2015. Dossier No. 2 Plant Breeding Techniques: an assessment for organic farming.

