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# Biotechnology and Biosafety Policy at OECD: Future Trends

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**The OECD Council Recommendation on Recombinant DNA Safety Considerations is a legal instrument which has been in force since 1986. It outlines the safety assessment practices that countries should have in place for agricultural and environmental biotechnology. This article suggests possible updates to make it suitable for the modern era.**

## OECD and Its Legal Instruments

The Organisation for Economic Co-operation and Development (OECD) is an intergovernmental organisation with 37 member countries. In 1986, the OECD Council adopted a Recommendation entitled *Recombinant DNA Safety Considerations: Safety Considerations for Industrial, Agricultural and Environmental Applications of Organisms Derived by Recombinant DNA Techniques* [1]. This OECD legal instrument was intended to promote international understanding of safety issues raised by recombinant DNA (rDNA) techniques so as to take steps towards an international consensus on the protection of health and the environment as well as a reduction of non-tariff barriers to trade. It also marked the start of OECD's engagement with modern biotechnology, which continues today with a track record of seminal events and publications that have facilitated the international harmonisation of risk assessment principles (Box 1). More information on the OECD Convention and OECD legal instruments is available on the OECD website (www.oecd.org/legal/oecd-convention.htm).

This article argues that the Recommendation remains important and should be more widely known. First, it remains in force today and, although it is a recommendation, OECD practice accords recommendations 'great moral force as representing the political will of Adherents. There is an expectation that Adherents will do their utmost to fully implement a Recommendation'. It is unclear whether OECD members or the wider biotechnology community are aware of the Recommendation and its content.

Second, candidate countries aspiring to OECD membership need to show that they are compliant with OECD legal instruments. Thirteen new members have joined the Organisation since the Recommendation was adopted. The OECD continues to expand its relationship with other non-members, many of which participate in its activities. In line with current OECD practice, the Recommendation is open to non-members. On December 2nd, 2020, Brazil became the first non-OECD country to adhere to the Recommendation.

Many elements of the Recommendation are relevant today despite subsequent developments in genomic technologies as well as risk/safety assessment initiatives. An accompanying text that underpins the Recommendation, entitled *Recombinant DNA Safety Considerations*, coined the 'Blue Book' [2], is an important reference to the thinking behind the Recommendation.

## Suggestions for an Update to the Recommendation

This article has several suggestions for an update to the Recommendation, bearing in mind that a revision can only be undertaken by OECD through its committee structure. However, these suggestions are made in the belief that this Recommendation is an important instrument that should be more widely known and should be updated to accommodate developments since 1986.

The Recommendation refers to 'recombinant DNA techniques' and rDNA organisms. Since 1986, however, a range of genomic techniques have been developed for modifying genomes that do not necessarily depend on rDNA. 'Genome editing', for instance, leads to some products that could also be produced using traditional techniques. In 2018, OECD held an international Conference on Genome Editing focusing on agricultural applications. It considered applications of genome editing in agriculture, including plant and animal breeding,

### Box 1. OECD and Modern Biotechnology Since 1986

The OECD has published many documents since 1986 that include principles and/or guidance related to the risk/safety assessment of genetically modified organisms (GMOs) as well as of foods and animal feed derived from them (Figure I). Today, these principles and guidance documents could be important additions to the Recommendation (a summary of relevant OECD principles and guidance is given in Table I).

The Recommendation was a good example of foresight when it was adopted in 1986, when most applications were restricted to containment facilities, although some of the first open-air field trials of GMOs were underway. It addresses issues relevant to human health, the environment, and agriculture that might be considered in a risk/safety assessment.

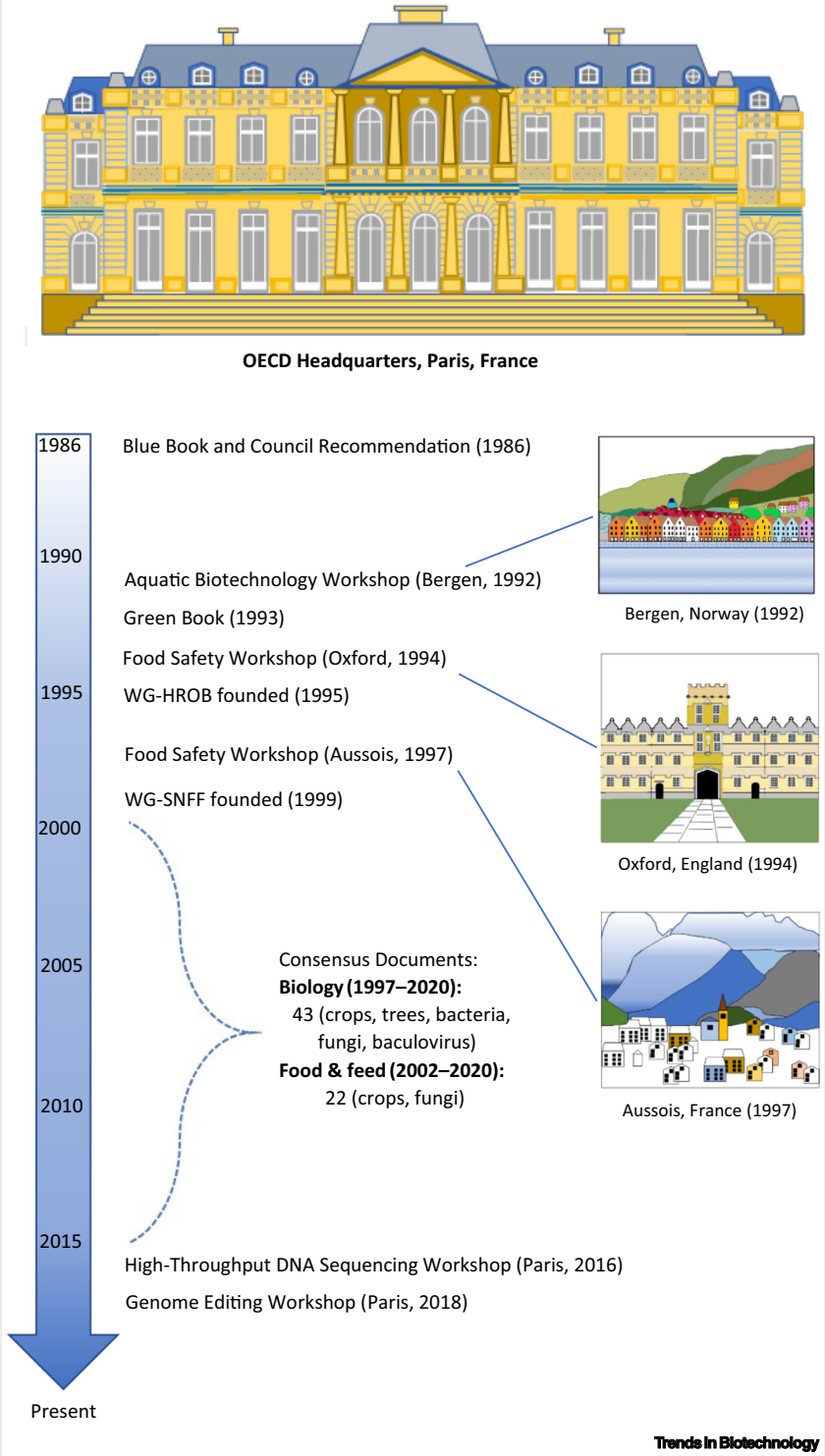


Figure I. Chronology of Seminal OECD Events and Publications on the Safety of Modern Biotechnology (1986–Present). Abbreviations: WG-HROB, OECD Working Group on Harmonisation of Regulatory Oversight in Biotechnology; WG-SNFF, OECD Working Group on the Safety of Novel Foods and Feeds.

Table I. Summary of Relevant OECD Principles and Guidance (Consensus Documents)

| Principle or guidance | Source |
|---|---|
| GMO development follows the principle of a stepwise approach, with risk/safety assessment being performed at each stage, from the laboratory to the growth chamber and greenhouse, to limited field testing, and finally to large-scale field testing. | OECD, 1986 (Blue Book) [2]<br>OECD, 1986 (Council Recommendation) [1] |
| Principle of case-by-case assessment. This principle implies that the risk/safety assessment of each case is performed individually using assessment criteria relevant to the particular case. | OECD, 1986 (Blue Book) [2].<br>OECD, 1986 (Council Recommendation) [1] |
| Principle of risk/safety assessment and risk management. This process includes hazard identification and, if a hazard is identified, risk assessment. The process is based on the characteristics of the organism, the trait introduced, and the environment into which the organism is introduced, as well as the intended application. | OECD, 1993 [6,7].<br><br>Published under the auspices of the former OECD Group of National Experts on Safety in Biotechnology |
| The principle of familiarity is used to address the environmental safety of GMOs. It is based on the understanding that most GMOs are developed from organisms such as crop plants whose biological characteristics are well understood. It allows risk assessors to use previous knowledge and experience with the introduction of GMOs into the environment, and this can indicate management measures. | OECD, 1993 [6,7].<br><br>Published under the auspices of the former OECD Group of National Experts on Safety in Biotechnology |
| The OECD regularly publishes environmental safety Consensus Documents. These are in line with the principle of familiarity in that they contain information that member countries have agreed is relevant to the risk/safety assessment of GM plants and other GMOs. The subject of each document is a crop plant or another organism where GM varieties have been commercialised or are expected in the future. | OECD, 2017 [8]. |
| The principle of 'substantial equivalence', otherwise known as the comparative approach, is used in the food and feed safety assessment of products derived from GMOs. It involves the comparison of a new food or feed derived from a GMO with a similar product having a history of safe use, such that the safety evaluation can subsequently focus on any differences identified. | OECD, 1993 [7].<br>Codex Alimentarius, 2009 [9]. |
| The OECD regularly publishes food/feed safety Consensus Documents which support the comparative approach. Each document has a crop plant as its subject, and includes data on key compositional parameters (nutrients, anti-nutrients, toxins, allergens) for the analysis of new variants of food- or feed-producing organisms including GM crops and several fungal species. | OECD, 2019 [10]. |

and their implications for risk and safety considerations as well as regulatory aspects [3]. From the panel discussions during this event, one of the findings that emerged was that there is a need for mutual understanding among nations about their respective regulatory approaches towards genome editing, possibly being even conducive to policy agreement. The need for such exchange among governments may be further compounded by the fact that genome editing is not solely the domain of major, globally operating biotechnology companies, and also engages small entrepreneurs and academics, as evident from the Argentinean experience [3]. The scope of the Recommendation could be revised to encompass these new techniques should OECD Member States indeed have a shared need for harmonisation and extension of the current focus on rDNA. This article suggests that the Recommendation should be renamed '*Safety Considerations for Products of Modern Biotechnology: Applications in the Environment, Agriculture, and Food/Feed Production*'.

Section I of the Recommendation focuses on sharing experiences with rDNA organisms so as to harmonise approaches to rDNA techniques, emphasising that regulatory oversight should not unduly hamper technological developments. Exchange of information has always been a recurrent theme of OECD activities. It would be good to review the texts about not hampering technological developments in the light of the regulatory practice of today. It would also be advisable to attach an Annex to the Recommendation that provides a continuously updated list of existing Consensus Documents and other OECD documents that support risk/safety assessment.

Section II could point out that the principle of good industrial large-scale practice, a topic which was last addressed at OECD in 1992 [4], remains valid for the handling of industrial microbial strains derived by modern biotechnology from safe parental strains.

Section III, on agricultural and environmental applications, recommends that risk/safety assessment should take into account the familiarity that has been gained with 'the environmental and human health effects of living organisms'. The recommendations describe approaches to risk assessment that have become commonplace since the publication of the Recommendation, such as prior risk assessment, stepwise development, and

the encouragement of 'research to improve the prediction, evaluation, and monitoring of the outcome of applications of rDNA organisms'. The footnote: '... this is not intended to imply that every case will require review by a national or other authority since various classes of proposals may be excluded' should be retained because probably not all member countries will wish to include all applications in their regulatory systems.

The recitals, the introduction to the Recommendation, consider the future use of rDNA organisms. Many of the expectations in the recitals have come about. However, the landscape of 'rDNA' has changed, with many new possibilities. There is ongoing discussion about whether new products have the same novelty that led to the regulatory oversight that was deemed necessary for rDNA organisms. The recitals would also lend themselves to providing context and a future outlook. The approaches outlined by the Recommendation may be extended to other genomic techniques that do not entail the use of rDNA. A regular review and updating of the Recommendation would help to engender innovative safety assessment methodologies (e.g., analytical 'omic' approaches) that may be necessary to address the challenges that future synthetic biology products (e.g., xenobiotics, extensive engineering) may pose to the application of familiarity and the comparative safety assessment approach (Figure 1) [5].

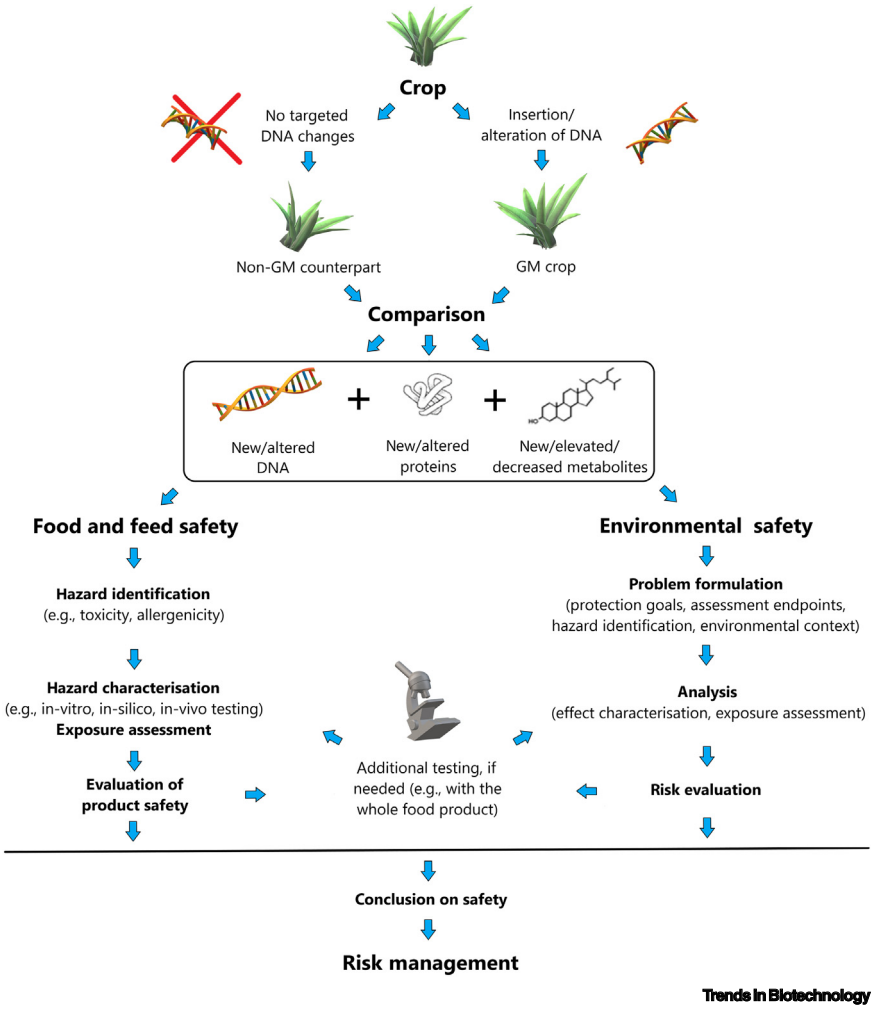


Figure 1. The Comparative Approach as Applied to Food/Feed and Environmental Safety Assessments of Genetically Modified (GM) Crops.

## Concluding Remarks

The Recommendation should take into account the accomplishments since 1986, and how the intentions of the Recommendation have largely come true, stating the importance of the principles of familiarity and the comparative approach as well as the case-by-case nature of the pre-market safety assessment of products of modern biotechnology. The revised Recommendation (an overview of detailed suggestions for amendments is given in Table 1) could look forward to the likely and preferred future developments within the purview of modern biotechnology, reflecting present-day discussions similarly to the original Recommendation.

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### Declaration of Interests

The authors declare no conflicts of interest. The views presented here are solely those of the authors and do not necessarily represent those of the OECD, the EFSA, or any other institution with which the authors are or have been associated.

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Table 1. OECD Council Recommendations Parts I and III[a], and Suggested Amendments

| Section | 1986 Recommendation | Suggested amendments |
|---|---|---|
| I-a | Share, as freely as possible, information on principles or guidelines for national regulations, on developments in risk analysis and on practical experience in risk management with a view to facilitating harmonization of approaches to recombinant DNA techniques. | Expand scope by including non-recombinant DNA techniques.<br>Also include non-agricultural applications.<br>Mention OECD BioTrack[b] as a platform to exchange information.<br>Expand the use of unique identifiers to microorganisms and animals. |
| I-b | Examine their existing oversight and review mechanisms to ensure that adequate review and control of the implementation of recombinant DNA techniques and applications can be achieved while avoiding any undue burdens that may hamper technological developments in this field. | (same as for I-a above) |
| I-c | Recognise, when aiming at international harmonization, that any approach to implementing guidelines should not impede future developments in recombinant DNA techniques. | Refer to internationally harmonised guidelines for food safety assessment (Codex Alimentarius Commission). |
| I-d | Examine at both national and international levels further developments such as testing methods, equipment design, and knowledge of microbial taxonomy to facilitate data exchange and minimise trade barriers between countries. Due account should be taken of ongoing work on standards within international organisations. | Expand the scope (beyond microorganisms) to plants and animals. |
| I-e | Make special efforts to improve public understanding of the various aspects of recombinant DNA techniques. | Include recent developments such as new breeding techniques. |
| I-f | Watch the development of recombinant DNA techniques for applications in industry, agriculture and the environment, while recognising that for certain industrial applications, and for environmental and agricultural applications of recombinant DNA organisms, some countries may wish to have a notification scheme. | Replace 'recombinant DNA' by 'recently emerging genome-editing methods'. |
| I-g | Ensure that assessment and review procedures protect intellectual property and confidentiality interests in applications of recombinant DNA, recognising the need for innovation while still ensuring that all necessary information is made available to assess safety. | Add that maximum transparency should be pursued, for example by making data accessible to public scrutiny. |
| | RECOMMENDS, with specific reference to agricultural and environmental applications, that Member countries: | |
| III-a | Use the existing considerable data on the environmental and human health effects of living organisms to guide risk assessments. | Refer to familiarity with particular modifications and/or traits.<br>Acknowledge lack of familiarity with, for example, gene drives and synthetic organisms. |
| III-b | Ensure that recombinant DNA organisms are evaluated for potential risk, prior to applications in agriculture and the environment by means of an independent review of potential risks on a case-by-case basis. | Require that safety assessments follow the principle of the comparative approach/substantial equivalence.<br>Allow the assessment to be expedited based on familiarity. |
| III-c | Conduct the development of recombinant DNA organisms for agricultural or environmental applications in a stepwise fashion, moving, where appropriate, from the laboratory to the growth chamber and greenhouse, to limited field testing and finally, to large-scale field testing. | Maintain this recommendation for a stepwise approach. |
| III-d | Encourage further research to improve the prediction, evaluation, and monitoring of the outcome of applications of recombinant DNA organisms. | Refer to the various Consensus Documents that will inform the risk assessment (to be appended). |

[a]Sections I and III contain recommendations to member countries on risk management in general (I) and specifically for environmental and agricultural purposes (III) [1].
[b]www.oecd.org/science/biotrack/

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