



**Submission of information on detection and identification of living modified organisms
pursuant to paragraph 3 of decision CP-10/11
Response to CBD notification ntf-2023-100 (Reference: SCBD/CPU/DC/WM/AMC/MW/91277)**

Submission by GERMANY

Part I. Endorsement of submission

Name of Country/Organization: GERMANY

Name of Cartagena Protocol Focal point/ endorsing: Nina OPITZ (Federal Ministry of Food and Agriculture)

Signature of the Cartagena Protocol Focal Point/ Head of Organization:

Date: 09 November 2023

Part II. Submission of information

In Germany, substantial expertise in the field of detection and identification of LMO has been established in more than 30 years of activities in LMO control. In general, LMO in food, feed and seeds are detected by means of DNA analysis.

1. New techniques or tools for the detection and identification of living modified organisms

PCR based methods – most commonly real-time PCR – have been applied as the method of choice for the detection and identification of LMO. Recently, digital PCR (ddPCR), is coming into play in LMO analytics. In addition, in Germany, next generation sequencing (NGS) approaches using different highly reproducible NGS techniques¹ in combination with continually improving NGS-data analysis pipelines are currently evaluated. They are still at the stage of research and development but have the potential to complement and guide PCR-based methods. Approaches such as targeted sequencing may be applied for the simultaneous detection of numerous known LMO. Further molecular characterization and identification of unauthorized LMO might be achieved e.g. by NGS using primer-walking strategies or

¹ Reproducibility of next-generation-sequencing-based analysis of a CRISPR/Cas9 genome edited oil seed rape, Steffen Pallarz, Stefan Fiedler, Daniela Wahler, Jörn Lämke, Lutz Grohmann, 09/10/2023, <https://doi.org/10.1016/j.fochms.2023.100182>

whole genome sequencing approaches. Additionally, in the area of detection and, if possible, identification of genome edited organisms, NGS is becoming invaluable due to the single-nucleotide resolution and generalized character of the technology.

2. Experience with

- a. New detection techniques
- b. Detecting newly developed and/or unauthorized living modified organisms

Newly developed LMO include classical LMO with rare genetic elements and organisms produced using genome editing. Many if not most of these cannot be detected using standard screening approaches. The same problem is faced regarding numerous unauthorized LMO. However, the increasing number of newly developed and unauthorized LMO has become a widespread problem. In Germany, several approaches are used to tackle this problem:

- i. New element- and/or construct-specific screening methods are developed and validated on a regular basis considering the prevalence of genetic elements and constructs in LMO. Respectively, the German table of screening methods is continuously being extended (https://euginius.eu/euginius/pages/methodSearch_searchview.jsf, select method set ABC)
- ii. Pre-spotted plates with oligonucleotides for all events which are currently authorized or in the process of being authorized in the European Union (EU) have been developed by the European Union Reference Laboratory for Genetically Modified Food and Feed (EURL-GMFF).
- iii. In order to detect commercialized LMO that are not authorized in the EU, numerous official validated methods have been developed.
- iv. Initial experience has been gained in Germany regarding the detection and identification of genome edited organisms that are classified as LMO in the European Union. For each individual event a specific detection method is being developed². In addition, two methods for the detection of scaffold RNA of CRISPR/Cas9 nucleotide sequences have been developed but are not applied in routine official control, yet.
- v. As mentioned above, NGS approaches complement the toolbox for the detection and identification of newly developed and unauthorized LMO. Due to the high resolution of the technology they allow for the simultaneous detection of numerous known LMO, the further molecular characterization and identification of unauthorized LMO, and detection and, if possible, identification of genome edited organisms. Furthermore, the continually collected NGS data allows for the development of AI models to detect even unknown LMO.

- c. Experience with developing reference materials:

In case of LMO which are authorized in the EU, the availability of certified reference material is guaranteed and it is provided by few accredited producers. Regarding unauthorized LMO, the access to suitable reference material and/or sufficient information on the genetic modification is a challenge. Therefore, reference material for unauthorized LMO is produced and characterized in Germany by the German National Reference Laboratory for genetically modified organisms (NRL-GVO) which is part of

² Detection of commercialized plant products derived from new genomic techniques (NGT) – Practical examples and current perspectives, Patrick Gürtler, Steffen Pallarz, Anke Belter, Kolja Neil Eckermann, Lutz Grohmann, 05/13/2023, <https://doi.org/10.1016/j.foodcont.2023.109869>

the Federal Office of Consumer Protection and Food Safety (BVL). This is done on an ad hoc basis and with regard to the relevance for the official control, whether routine screening methods can reveal the abundance of the LMO and whether biomass or genomic DNA can be obtained from the producer. The procurement of such material is often the biggest hurdle.

On the analytical level, the decisive factor is what type of material or information is available. If biomass of the LMO is available, parameters such as extractability of the DNA, homogeneity, zygosity and the number of insertions must be determined. The resulting reference material is most suitable in analytical controls as it is most similar to the sample material. If pure genomic DNA is obtained, a long shelf life is ensured. However, such material is often unsuitable for use in NGS analyses as DNA extraction and purification for NGS has to follow very specific protocols. If neither biomass nor genomic DNA can be obtained, in Germany, artificial plasmids are synthesized. They then contain the sequence of the known genetic modification. The use of artificial plasmids as reference material is treated with caution, as they behave differently in the analysis than the sample material.

3. Collaborations or agreements between national and/or regional laboratories

In Germany, competent national and private laboratories are involved in various collaborations and networks.

At a national level, German laboratories work together in working groups such as the § 28b GenTG and § 64 LFGB working groups. They have been founded on a legal mandate and consist of members of the competent national laboratories as well as representatives of the industry and academia. They develop and/ or validate analytical methods for official control activities which are legally valid and are published in an Official Collection of Methods. At the European/ EU-wide level, German laboratories are member of the European Network of GMO Laboratories (ENGL). ENGL plays an eminent role in the development, harmonisation and standardisation of means and methods for sampling, detection, identification and quantification of LMO in a wide variety of products in Europe. Regarding the standardization of LMO detection methods German laboratories work on a national (DIN), European (CEN), and international (ISO) level.

As a means to support LMO detection laboratories in their work, the BVL (Germany) and the Wageningen Food Safety Research (WFSR, The Netherlands) collaborate on the Euginius database (www.euginius.eu) which provides information on authorization status, reference materials and detection methods for LMO.

4. Summary and recommendation

The above mentioned techniques are still in a stage of development regarding their use for the detection and identification of LMO. They include highly academic approaches that may not be easy to implement as they require access to high-end technical equipment. Therefore, and because the access to suitable reference materials is a major challenge, newly developed and unauthorized LMO are not yet covered by routine LMO detection in Germany.

Considering the above information, Germany is of the opinion that there is no need to update the Biosafety Technical Series 05: Training Manual on the Detection and Identification of Living Modified Organisms in the Context of the Cartagena Protocol on Biosafety, yet. It provides a good overview of current methods for LMO analysis. A re-evaluation at a later date should be considered.

Submission of supporting documentation:

- Pallarz *et al.*, 2023, Food Chemistry, <https://doi.org/10.1016/j.fochms.2023.100182>
- Guertler *et al.*, 2023, Food Control, <https://doi.org/10.1016/j.foodcont.2023.109869>