



Animal &
Plant Health
Agency

Guidance for companies importing and/or producing seed of species at risk of adventitious GM presence

APHA Genetic Modification Inspectorate

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Legal responsibilities of seed companies

In accordance with Part VI of the Environmental Protection Act 1990¹ (EPA), companies importing and/or producing seed are legally responsible for ensuring that they do not market or release unauthorised genetically modified organisms (GMOs). Such companies must ensure that appropriate controls are in place to minimise the risk of adventitious GM presence (AGMP). This guidance document provides advice on the actions companies should consider taking to demonstrate that they are managing AGMP risk appropriately, and meeting the requirements of the EPA. It also provides information on the seed audit programme run by the Genetic Modification Inspectorate (GMI) for England.

The GM Inspectorate seed audit programme

The GMI seed audit programme is designed to help companies based in England comply with the rules governing GMOs in seed. GM Inspectors achieve this by assessing which species are most at risk of AGMP, and by carrying out audits of companies that import and produce seed of these species. These audits are designed to evaluate the controls each company has in place to minimise the risk of AGMP and, where appropriate, suggest ways in which these controls can be improved. GMI seed audits are carried out on behalf of the Defra Varieties and Seeds Policy Team, and participation is voluntary. The audits include seed for marketing and seed for private and/or official trials.

It should be noted that participation in the GMI audit programme does not relieve companies of their legal obligations concerning GMOs in seed, nor should it be seen as an assurance that the GMI will not exercise its powers in appropriate cases under Part VI of the Environmental Protection Act 1990.

Crops most at risk of GM presence

The following crop species have been assessed by the GMI as being most at risk of GM presence²:

- **Brassica napus:** winter and spring oilseed rape, swede, swede fodder rape, salad rape, rape/kale hybrids, etc.
- **Brassica rapa:** turnip, turnip fodder rape, stubble turnips, Chinese cabbage, pak choi, oriental greens, rapid-cycling brassicas, etc.
- **Glycine max:** soya bean, edamame.

¹ Under Part VI of the Environmental Protection Act 1990 (see: <http://www.legislation.gov.uk/ukpga/1990/43/part/VI/>; accessed 08/05/2019), as read with the Genetically Modified Organisms (Deliberate Release) Regulations 2002 (S.I. 2002/2442; see: <http://www.legislation.gov.uk/uksi/2002/2443/contents/made>; accessed 08/05/2019), it is prohibited to release or market an unauthorised genetically modified organism.

² These species were identified using risk modelling, and have been included in the audit programme with the agreement of Defra's Varieties and Seeds Policy Team.

- **Zea mays:** fodder maize, grain maize and sweetcorn.

Ensuring suitable controls are in place

EU legislation concerning GMOs is not prescriptive in terms of the controls required to minimise the risk of AGMP in seed, hence there are various methods that companies can justifiably employ to safeguard the purity of their seed in terms of freedom from GMOs. The two main approaches are the use of **production controls** (see point 1, below) and the use of **analytical tests** (which can be used to check the efficacy of production controls; see point 2, overleaf). Further information on the definition of a GMO and the technical aspects of analytical testing, along with notes on GM crops authorised for cultivation in the EU, are given in Annex 1 at the end of this document.

1. Production controls

These include, but are not limited to:

- a) **Seed provenance** – documentation detailing the source of the germplasm, including the breeder and country of origin, and confirmation that the seed has been produced from non-GM lines;
- b) **Variety maintenance** – evidence that the variety has been maintained in isolation from transgenic lines (e.g. by the use of spatial, temporal, physical and/or procedural methods);
- c) **Seed production controls** – documentation detailing the controls in place to prevent contamination in the field, including at sowing, during the growing/flowering stage, and at harvest;
- d) **Controls relating to transport, storage and processing** – documentation confirming the use of suitable measures to prevent the introduction of AGMP due to admixture with other seed. Contracted processors should provide written assurances to demonstrate they have measures in place to minimise the risk of seed acquiring AGMP.

Note: If written statements ('letters of assurance') are requested from suppliers as a proxy for direct control or knowledge of production controls, such statements should refer to the specific relevant controls and how they have been applied to the seed in question.

2. Analytical tests

Such tests, on individual seed batches or lots, could include polymerase chain reaction (PCR) DNA-based tests, protein-based tests (e.g. lateral flow devices), and spray tests (e.g. for herbicide tolerance).

As a **minimum**, each analytical test should:

- a) Be carried out on a **representative sample** of the seed lot³;
- b) Be carried out on a minimum working sample for analysis that contains **no less than 3000 seeds**⁴ (which may need to be tested in batches to align with analytical sensitivity);
- c) Include appropriate **positive and negative controls**;
- d) Address the risk of **possible false positives**⁵;
- e) Be conducted to **an analytical sensitivity level of at least 0.1%** (i.e. limit of detection $\leq 0.1\%$)⁶;
- f) Provide a clear indication of any **standards or accreditation** to which the analysis conforms, e.g. ISO17025, UKAS, AFNOR, GLP, etc.;
- g) **Report the actual result for the test** with the associated measurement uncertainty for the result (e.g. $\pm 95\%$ confidence limits).

In addition, for PCR-based tests the analysis should ideally consist of testing with a **combination of commonly used promoter and terminator sequences** (e.g. cauliflower mosaic virus promoter - CaMV p35S and nopaline synthase terminator - tNOS), as well as **antibiotic markers** appropriate to the crop in question (e.g. NptII, the selectable marker for kanamycin resistance). Testing for sequences that encode **specific traits** such as PAT/BAR (LibertyLink) and GOX (Roundup Ready) may also be appropriate to strengthen the assurance provided by the testing regime.

Assurance should be provided on the separate handling of the seed subsequent to any testing. Test certificates should clearly identify the lots or batches to which they refer.

³ For example, sample obtained by systematic sampling to prepare a working sample in accordance with the International Seed Testing Association (ISTA) rules for seed purity.

⁴ In line with the proposed protocol submitted to the EC Standing Committee on Seeds in 2001.

⁵ For example, by including controls that reduce the likelihood of positive test results due to environmental contamination with DNA from, for example, cauliflower mosaic virus and/or soil-borne bacteria.

⁶ In line with the opinion of the EC Scientific Committee on Plants, adopted 07/03/2001, stating that the limit of analytical sensitivity of available detection methods is about 0.1% for routine analysis (see: https://ec.europa.eu/food/sites/food/files/safety/docs/sci-com_scp_out93_gmo_en.pdf; accessed 08/05/2019).

Additional notes on mutagenesis and gene editing

On 25 July 2018, in case C-528/16⁷, the European Court of Justice ruled that the use of certain gene editing techniques, such as oligonucleotide-directed mutagenesis (including CRISPR-Cas9 techniques), constitute genetic modification. This means that a number of new breeding techniques that were previously unregulated are now considered to produce GMOs⁸. Plant varieties produced using these techniques need to go through the EU authorisation process before being marketed and/or cultivated in the EU.

Prior to the ruling some breeders were known to be preparing to market varieties produced using these now-regulated techniques. The GM Inspectorate does not believe that any such products have been marketed in the EU, however, companies should remain vigilant to the potential use of regulated gene-editing techniques. If you have any concerns regarding the provenance of varieties you are intending to market please contact the Inspectorate (details below).

Contacting the APHA GM Inspectorate:

The GM Inspectorate can provide practical help on what steps companies should take if they have evidence of, or suspect, AGMP in seed. Detection of AGMP **at any level** should always be notified to the GM Inspectorate. If you have any questions regarding your company's obligations, the suitability of production assurances and/or testing, please contact us:

Email: gm-inspec@apha.gov.uk

Web: <https://www.gov.uk/guidance/gm-inspectorate-seed-audit-programme#contact>

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⁷ C-528/16 Confédération paysanne and Others v Premier ministre and Ministre de l'agriculture, de l'agroalimentaire et de la forêt. See:

<http://curia.europa.eu/juris/celex.jsf?celex=62016CJ0528&lang1=en&type=TXT&ancre=> (accessed 08/05/2019)

⁸ So-called 'classical' mutagenesis, for example using ionising radiation or chemical mutagens, retains exemption from GM regulations due to a long history of safe use.

Annex 1: additional technical information

Definitions:

- **Genetically modified organisms** and **genetic modification** are as defined in European Directive 2001/18/EC⁹.
- **Adventitious GM presence** (AGMP) is the accidental or technically unavoidable presence of GMOs in a non-GM commodity, in this case seed.

Crop-specific information:

- **Brassica napus, Brassica rapa** and **Glycine max**: currently there are no authorisations for the commercial cultivation of GM seed of these species in the EU. Therefore, if a PCR test on an individual batch or seed lot indicates an AGMP at any detection level, none of the seed can be marketed or planted and further advice should be sought from the GM Inspectorate.
- **Zea mays**: currently there is just one consent authorising commercial cultivation of GM maize in the EU, for MON810 (C/F/95/12, Monsanto). There are currently more than 100 varieties of maize containing MON810 listed in the EC Common Catalogue of Varieties¹⁰.

There is no marketing restriction on approved GMOs which have been cleared as presenting no risk to human health or to the environment (but note that labelling requirements, as described in Regulation (EC) 1831/2003¹¹, apply).

In the absence of specific labelling thresholds in European legislation for the adventitious presence of approved GMOs in conventional seed, UK industry has chosen to adopt a precautionary approach and operates to the level of detection (0.1% or less, as described above). Any company contemplating marketing seed in the UK with a detectable level of an approved GMO must declare that level on the seed label.

⁹ <https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32001L0018&from=EN> (accessed 08/05/2019).

¹⁰ http://ec.europa.eu/food/plant/plant_propagation_material/plant_variety_catalogues_databases/search/public/index.cfm (accessed 08/05/2019).

¹¹ <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2003:268:0024:0028:EN:PDF> (accessed 08/05/2019).

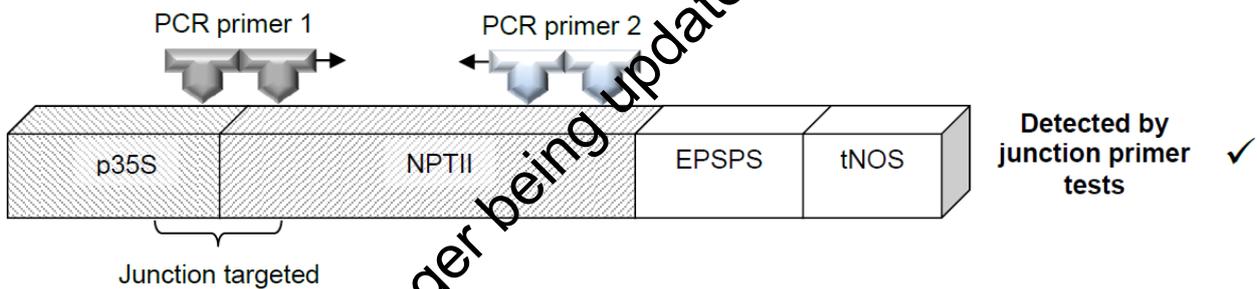
Information relating to PCR junction primer tests

A number of GM elements are derived from naturally occurring bacteria and viruses. PCR tests targeting these elements can give false positive results, as the presence of such bacteria and viruses in seed can erroneously appear to be a GM presence.

PCR junction primer tests work by targeting the adjoining regions between neighbouring GM elements that would not normally be associated in nature. This makes such tests less likely to produce false positive results compared to standard PCR tests which target individual elements. Companies commissioning junction-spanning tests should, however, be aware that their increased specificity is at the expense of the range of elements targeted, resulting in a potential reduction in the number of GM lines the test can detect. This is illustrated in Figure 1, below, which represents a test targeting the p35S/NPTII junction (the bracketed area in Construct A); note that in Construct B, the p35S and NPTII elements are present but not detected as they are not adjacent.

Figure 1 - examples of gene positions in two hypothetical GM constructs and detection using a specific junction-spanning GM test

Construct A



Construct B



Despite the p35S and NPTII elements being present in both constructs, the junction-spanning test only returns a positive result for Construct A. Consequently, such junction-spanning tests could fail to detect a range of GM lines containing p35S and/or NPTII.

Companies that employ junction-spanning PCR tests should ensure that the names of the specific genetic elements, constructs or events that are targeted are included on the certificate.



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Any enquiries regarding this publication should be sent to us at

Email: gm-inspec@apha.gov.uk

Web: <https://www.gov.uk/guidance/gm-inspectorate-seed-audit-programme#contact>

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