Annual report on scientific method validation activities performed in support of GMO Food and Feed Authorisation (Great Britain)

FSA Contract Reference Number: FS430418
GMO Food and Feed Authorisation (Great Britain)

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Glossary

CRM - Certified Reference Material

DNA - Deoxyribonucleic acid

EFSA - European Food Safety Authority

ENGL - European Network of GMO Laboratories

EURL - EU Reference Laboratory for GMOs in food and feed

FSA - Food Standards Agency

GE – Gene Editing

GMM - genetically modified microorganisms

GMO - Genetically Modified Organism

JRC – Joint Research Centre (Italy, Ispra)

NRL - National Reference Laboratory (appointed under (retained) Regulation (EC) 2017/625)

OL – Official Laboratory based in the UK

PA - Public Analyst

PCR - Polymerase Chain Reaction

SC – Steering Committee

WG – Working Group

Role of the GMO Authorisations (Great Britain) position

The Food Standards Agency (FSA) is the Competent Authority for the purpose of Regulation (EU) 2017/625 on Official Feed and Food Controls in the UK. To fulfil the FSA's obligation under Article 8 of Commission Implementing Regulation (EU) No 503/2013, the FSA appointed LGC to deliver the functions currently performed by the EU Reference Laboratory (EURL) for supporting the authorisation of Genetically Modified Organisms (GMO) for food and feed uses, in Great Britain (England, Wales and Scotland). Applications for authorisations may include analysis of genetic material derived from plant, animal and microorganism sources.

The GMO Authorisations role is responsible for delivering the provision of method validation laboratory services for the authorisation of new GMO applications for Great Britain (GB), renewal GMO applications for GB and the review and re-validation of existing and ongoing applications as and when necessary on behalf of the FSA.

GMO Authorisations (Great Britain) Services

The basic duty is to deliver the document review and method validation stage of the GMO Food and Feed authorisation process which forms part of the risk assessment for the FSA. The validation process includes the following six steps:

1. Reception of valid application including relevant documentation and data on method and samples
2. Scientific assessment of documentation and data (primarily DNA extraction method and method of detection)
3. Experimental testing of samples and methods
4. Method validation through collaborative ring trials
5. Reporting to the Authority (FSA)
6. Secure storage of relevant GMO food and feed samples and control materials for the duration of the contract.

LGC was awarded the GMO Authorisations (Great Britain) position by the Food Standards Agency in August 2021 following open competitive tender. Pursuant to this role, LGC conducts the following activities, as specified in the contract with the FSA:

Core Function
Objective 01 – Infrastructure development
This objective underpins the provision of a support structure to build a resilient base for all GMO method validation authorisations:

- New GMO event applications in Great Britain;
- Pipeline applications - applications which were part-way through the EU authorisation process, prior to the end of the transition period of the UK away from the EU on 1st January 2021;
- Renewals – GMOs which are authorised for use in the EU/UK, but are due for renewal following expiration of the initial 10 year validity period of their authorisation (retained Regulation (EC) No 1829/2003, and retained Regulation (EC) No 641/2004, as amended by retained Regulation (EU) No 503/2013).

Objective 02 – Core support activities
This objective ensures maintenance of competency of core activities (e.g. reporting structure, storage facilities, internet presence, and contract management) in support of the method validation of GMOs as part of the GB authorisation process.

Objective 03 – Core authorisation activities

This objective follows a six-point scientific technical plan to ensure a due process is in place for provision of method validation services as part of the GB based GMO authorisation process:

03/1 – Reception of the application
03/2 – Scientific assessment of dossiers and data
03/3 – Experimental testing of samples and methods
03/4 – Method validation through collaborative ring trials
03/5 – Reporting to the Authority (FSA)
03/6 – Control materials housing

Core Function

Production of the GMO Authorisations (Great Britain) annual report

This report details the activities carried out during the 1st year of the GMO Authorisations (Great Britain) operation (April 2021-March 2022) in relation to the duties of the role.

Objective 01 – Infrastructure development

Tasks:

01/0 - Agree an operational protocol with the FSA at the project kick-off meeting
01/1 - Establishment of new quality procedures to ISO 9001 of the processes for quality control of method validation of new GMOs applications as part of the UK GMO authorisation process
01/2 - Description of the method validation process published
01/3 - Guidance on the submission process and expected timeframes published
01/4 - Publication of a note to the applicants on the type and nature of control samples provided in the context of applications for authorisation
01/5 - Publication of an explanatory note to applicants regarding practical instructions concerning the method validation task of the authorisation laboratory pursuant to relevant UK legislation (e.g. retained Regulation (EU) No 503/2013 on applications for authorisation)
01/6 - Publication of an explanatory note for the payment of financial contributions under Commission implementing regulation (EU) No 120/2014 of 7th February 2014, amending Regulation (EC) No 1981/2006, on detailed rules for the implementation of Article 32 of Regulation (EC) No 1829/2003
01/7 - Publication of document templates for submission of method validation data
01/8 - Initial maintenance activities

Example activities in relation to these Tasks:

- Development of an operational protocol:
    - A kick-off meeting was held with the FSA in order to discuss and agree an operational protocol for delivery and maintenance of the GMO Authorisations function going forward;
    - Initial versions of T&C's for service delivery as an agreement between LGC and the applicant were drafted;
    - The GMO Authorisations (GB) position attended a live European Food Safety Authority (EFSA) webinar entitled "Webinar on application procedure for GMO". This webinar explained the current GMO application process in the EU, including: lifecycle of the application; account creation and management; applications and modifications of authorisation; a demo of the e-submission system; dossier intake and portal updates; confidentiality assessment of requests submitted; public consultations; risk assessment; and adoption and publication of the authorisation https://www.efsa.europa.eu/en/events/webinar-application-procedure-gmo

- Establishment of new quality procedures to ISO 9001 of the processes for quality control of method validation of new GMOs applications:

- Reporting forms are being drafted, which will be used to communicate to the FSA summaries of the pertinent information and recommendations associated with each stage of the (scientific method validation appraisal part) authorisation process;
- Initial drafts of the following reporting forms have been started:
    - Scientific Dossier appraisal;
    - DNA extraction method report;
    - In-house detection method verification;
    - Method validation collaborative trial report;
    - Application summary report;
    - GMO renewals.
- A copy of the draft reporting form for GMO renewals was uploaded to the FSA secure MS Teams site for the GMO authorisations function;
- A copy of the draft document outlining the minimum performance requirements for analytical methods was uploaded to the FSA secure MS Teams site for the GMO authorisations function.

- Guidance notes for applicants are being drafted, the purpose of which is to provide published advice to applicants on the process of the (scientific method validation appraisal) authorisation process, inclusive of costs, time-frames and how information should be supplied;
- Initial drafts of the following guidance notes have been started:
    - Financial Contributions;
    - Provision of control samples;
    - CRM sample workflow;
    - CRM acceptance criteria;
    - Validation guidance.
- A copy of the draft guidance document outlining Financial Contributions from Applicants was uploaded to the FSA secure MS Teams site for the GMO Authorisations function.

- Description of the method validation process:
    - Preliminary guidance notes for applicants for the envisaged fee structure have been drafted and are subject to agreement with the FSA and relevant stakeholders.

- Guidance on the submission process and expected timeframes:
    - The FSA held a meeting with stakeholders from industry, representing potential applicants for authorisation of GMOs in Great Britain. Following a request from the FSA GM Policy team, LGC provided a list of current EU literature available as guidance for GMO applications, suggesting that the industry members could be invited to comment on these from a GB perspective, providing any suggestions how these could be further streamlined and optimised for their use for a GB centric market;

- Explanatory note for applicants regarding practical instructions on the method validation task of the authorisation laboratory is being drafted.

- Explanatory note for applicants regarding payment of financial contributions for method validation process:
  - Advised the FSA in relation to providing estimates for the costs to applicants for GMO authorisations, as requested by Defra for information on costs to businesses for GMO authorisations to support an impact assessment (IA) Defra were drafting.

- Initial maintenance activities:
  - A shared e-mail inbox for communications with applicants as part of the GB GMO Authorisation function has been established. The e-mail address is GMO@lgcgroup.com
  - Key members of the GMO Authorisations (GB) function have confirmed secure access to the FSA dedicated MS Teams Channel for GMOs;
  - A meeting was held with the FSA to discuss the authorisation processes (external and internal), fee structure, control materials, publication of guidance notes, webpages, Compendium of Methods, and anticipated number of applications;
  - An initial SharePoint site had been set-up for beta testing for storage of relevant data/files for the GMO National Reference Laboratory (NRL) and Authorisation functions;
  - The migration of the above two functions from the secure Share Drive structure at LGC to the online SharePoint structure has commenced. The transition period needs to progress at a measured pace due to the amount of information that needs to be migrated, coupled with testing of the new SharePoint structure and familiarization of users with the infrastructure and processes of the new system;
  - Example but functional webpages have been drafted to represent revised and updated webpages to house important information pertaining to the GMO NRL and GMO Authorisations (GB) positions;
  - Approval has been given to place the GMO Authorisation webpages alongside the GMO NRL webpages, to be accessible via the main LGC website. Draft pages are under construction for a main webpage with links through to dedicated pages for guidance notes, the GMO Compendium of Methods, and other related material;
  - Throughout the first year of operation, initial maintenance activities (e.g., contract support, project planning, establishment of service delivery, etc.) have been delivered by the Project Management team.

Objective 02 – Core support activities

Tasks:

02/1 - Production of an annual report
02/2 - Review and maintain a list of validated reagents
02/3 - Maintain a list of reputable suppliers
02/4 - Maintain appropriate storage facilities to house materials
02/5 - Maintenance of support for ISO/IEC 17025:2017 accreditation
02/6 - Report PT round results to the FSA as part of recognised external quality assessment exercises
02/7 - Maintain a national GMO Compendium ("database") containing lists of control materials and methods
02/8 - Continue international stakeholder engagement
02/9 - Establish a process for setup costs and overhead costs associated with each GB centric authorisation
02/10 - Maintenance of storage and distribution service
02/11 - Continuous improvement activities
02/12 - Contract management

Example activities in relation to these Tasks:

- Production of the GMO Authorisations (Great Britain) annual report:
    - The current document represents the GMO Authorisations (Great Britain) annual report for the operational period April 2021 to March 2022, providing a summary of the method validation service activities.

- Review and maintain a list of validated reagents:
    - In conjunction with the GMO NRL position, draft lists of reagents and suppliers have been prepared. Laboratories associated with the GMO Authorisations (Great Britain) and GMO NRL positions are in frequent contact with LGC, who are able to provide updated advice on the current availability of validated reagents and reputable suppliers.

- Maintain a list of reputable suppliers:
    - In conjunction with the GMO NRL position, draft lists of reagents and suppliers have been prepared. Laboratories associated with the GMO Authorisations (Great Britain) and GMO NRL positions are in frequent contact with LGC, who are able to provide updated advise on the availability of validated reagents and appropriate suppliers

- Maintain appropriate storage facilities to house materials:
    - Throughout the first year of operation, LGC has developed and continues to maintain space within dedicated secure walk-in cold room facilities for the storage of any control materials on behalf of the GMO Authorisation (GB) function.

- Maintenance of support for ISO/IEC 17025:2017 accreditation

- Activities related to the use of validated methods of detection for GMOs is governed by LGC's ISO/IEC 17025:2017 flexible scope of accreditation. LGC has participated in over 50 external quality assessment proficiency test (PT) rounds since 2000, being a mixture of both EURL Comparative Tests and GeMMA proficiency test rounds. In all proficiency test rounds, LGC has received satisfactory (z<[2]) scores.

- Report proficiency test (PT) round results to the FSA as part of recognised external quality assessment exercises:
  - LGC has participated in over 50 PT rounds since 2000, being a mixture of both EURL Comparative Tests and GeMMA proficiency test rounds. In all proficiency test rounds, LGC has received satisfactory (z<[2]) scores based on over 90 different GM targets analysed;
  - PT round results are regularly communicated to the FSA as part of the NRL function, and this activity will continue as part of future work.

- Maintain a national GMO Compendium ("database") containing lists of control materials and methods:
  - Further discussions with IT experts were held in order to provide a draft outline for the envisaged "GMO Compendium of Methods" as well as the linked list of GMO Control materials;
  - The Project Management team have provided consistent and continued support for Website development, and maintenance and development of the GMO Compendium throughout the first year of operation of the GMO Authorisation (GB) position.

- Continue international stakeholder engagement
  - With the withdrawal of access to services formerly provided by the EURL, UK based laboratories have had to make alternative arrangements for continued international networking;
  - Communications have been held with the National Biosafety Authority (NBA) of Kenya, regarding networking and sharing best practice guidance on GMO sampling and controls. The National Biosafety Authority (NBA) is a state corporation in Kenya mandated to ensure safety of human and animal health and provide adequate protection of the environment from harmful effects that may result from GMOs. The Authority was established by the Biosafety Act (2009) to regulate all activities involving GMOs in food, feed, research, industry, trade and environmental release and it fulfils its mandate by ensuring and assuring safe development, transfer, handling and use of GMOs.

- Establish a process for setup costs and overhead costs associated with each GB centric authorisation:
  - Consultation with Food Standards Scotland (FSS), regarding views associated with the appraisal of the FSA document entitled "Consultation on applications for nine genetically modified organisms for food and feed uses". LGC provided comments and experiences on the resistances conferred by specific GM events (e.g. herbicide, pest and drought resistance) as well as the text formatting and inference from some of the claims associated with the applications from stacked events.

- Maintenance of storage and distribution service:
    - Throughout the first year of operation, LGC has developed and continued to maintain capability for storage and distribution facilities on behalf of the GMO Authorisation (GB) function.

- Continuous improvement activities:
    - Throughout the first year of operation of the GMO Authorisations position, regular contact between the FSA and LGC has been augmented through the LGC Key Account Manager, who has also facilitated support for continuous improvement activities (e.g., monthly report structure).

- Contract management:
    - Throughout the first year of operation of the GMO Authorisations position, the Project Management team have provided consistent and continued support for all Contract management related activities;
    - Two GMO Authorisation (GB) quarterly reviews with the FSA (October 2021 and January 2022) were attended, to discuss progress and activities in the previous quarter, as well as planned activities for the next quarter;
    - As part of the GMO Authorisations (GB) position, an advertisement was published regarding a job position for a Research Analyst to help contribute towards delivery of the function. Shortlisted candidates were invited to two interviews. The position was filled by a suitably qualified individual in November 2021.

Objective 03 – Core authorisation activities

Task:

03/1 - Reception of the application
03/2 - Scientific assessment of dossiers and data
03/2.1 - Scientific assessment of documentation
03/2.2 - Scientific assessment of data
03/2.3 - Report and recommendation
03/3 - Experimental testing of samples and methods
03/3.1 - Sample and reagent prep
03/3.2 - DNA extraction method verification (yield, integrity and purity)
03/3.3 - Experimental design for assessment of key metrics and performance characteristics
03/3.4 - PCR quality metrics (Dilution series, dynamic range, r-squared, PCR eff. and ΔCt)
03/3.5 - Trueness and RSD_r
03/3.6 - LOD/LOQ
03/3.7 - Detection method comparison to dossier
03/3.8 - In-silico specificity tests
03/3.9 - Final report on in-house verification
03/4 - Method validation through collaborative ring trials
03/4.1 - Optimise/adjust experimental design for collaborative trial
03/4.2 - Recruitment of participating laboratories
03/4.3 - Data collation and analysis
03/4.4 - Arrange payment of participating laboratories
03/5 - Reporting to the Authority (FSA)
03/5.1 - Summary reports in standard format (validation trial, validated method. DNA extraction method)
03/5.2 - Publication of method validation results
03/6 - Control materials housing
03/6.1 - Reception and storage

Example activities in relation to these Tasks:

Please note: No official GB based applications which were required to be processed for the method validation part of the authorisation procedure were received by LGC in the first reporting year of operation of the GMO Authorisations (GB) function. This included no applications for new GM events (single or stacked), GMO renewals (coming up towards their 10 year renewal date) or GMO pipeline applications (part way through the EU authorisation process on the 1st January 2021, at the end of the transition period of the UK away from the EU).
Nevertheless, for completeness, the following sections have been included in this annual report of activities.

- Scientific assessment of dossiers and data:
    - The FSA forwarded to LGC an example “Pipeline Application Exercise”, in order to check that all pertinent information for the (technical method validation) assessment of an authorisation would be submitted by the applicant;
    - The example provided was a GM stacked event (test application RP1180), comprising six separate single maize events. The scientific dossier and associated files supplied for the appraisal consisted of 888 files split across 51 folders (approx. 500MB data);

- Four main questions were posed. Please see below for these as well as the summary responses:
- *Was the correct information supplied as part of the application?*
    - It was clear that some critical information on the method and its performance were only accessible by following a link to a third-party website. This would create an issue for assessment of the application, should GB stakeholders not be able to access the website in the future (e.g. the weblink becomes inactive, the webpage is moved, or access is otherwise denied);
- *Qualify and categorise any missing information*
    - Validated event specific methods for detection of the individual single events that comprised the stacked event example were missing with the application. This made any evaluation, based on the documentation supplied with the application alone, very challenging;
- *What files are necessary for future applications for the (analytical) assessment?*
    - The necessity to provide all relevant information at the point of submission of the application was further supported;
- *Was the data provided sufficient for all types of applications?*
    - LGC advised that the data supplied with the current example was bespoke to a stacked event only, and additional information would need to be supplied when considering the authorisation of a new GM event, or for the application for a renewal of a GMO.
- LGC provided detailed feedback on all of the above queries. A meeting was held to clarify the queries and the initial responses;
- A "Summary Note" to the above exercise was written and provided by LGC and subsequently uploaded to the FSA secure MS Teams site for the GMO Authorisation function. This document, consisting of an Executive Summary, introduction and advice on the four questions, provided an itemised response to the four queries.
- Key recommendations from the exercise included:
    - The need for applicants to include and disclose all relevant information for effective appraisal of the application (including full disclosure on separate methods for single events comprising the stacked events) as part of the application, and not to refer to information only available on third-party websites;
    - The need to provide clear guidance notes to the applicant optimising the type and amount of information submitted with the dossier;
    - The requirement for the GMO Authorisation (GB) function to appraise the method for detection for any application prior to authorisation;
    - Bespoke information may be needed for the categories of single and stacked GMOs, as well as GMO renewal applications.

- Recruitment of participating laboratories:
    - Alongside the current expertise and capability offered by UK Official Laboratories, two previous ENGL members based in the UK were approached regarding their

potential inclusion as UK based expert industry labs for GMO testing as part of any inter-laboratory based trials for GMO authorisations.

- Summary reports in standard format (validation trial, validated method, DNA extraction method):
    - A standard style of formatting for reporting forms (to be sent back to the FSA summarising pertinent information and recommendations from each stage of the method validation process of the GMO authorisation) has been formalised;
    - A first drafting of a full Summary Report for GMO Applications has been written. This includes the appraisal of the scientific dossier, experimental testing of the DNA extraction method, intra-laboratory trail of the detection method, inter-laboratory trial of the detection method, and a GMO renewals summary.