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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Contact: Malcolm Burns
Email: Malcolm.Burns@lgcgroup.com

Prepared by: Malcolm Burns

Approved by: Alison Woolford

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Contents

Glossary

CRM - Certified Reference Material

Defra - Department for Environment, Food & Rural Affairs

DG SANTE - European Commission's Directorate-General for Health and Food Safety

DNA - Deoxyribonucleic acid

EFSA - European Food Safety Authority

ENGL - European Network of GMO Laboratories

EURL-GMFF - EU Reference Laboratory for GMOs in food and feed

FSA - Food Standards Agency

FSS – Food Standards Scotland

GeMMA – Genetically Modified Material Assessment Scheme

GMM - Genetically Modified Microorganisms

GMO - Genetically Modified Organism

JRC – Joint Research Centre

NMT - New Mutagenesis Techniques

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

PA - Public Analyst

PCR - Polymerase Chain Reaction

PT – Proficiency Testing

WG – Working Group

Role of the GMO Authorisations (Great Britain) position

The Food Standards Agency (FSA) and Food Standards Scotland (FSS) are the Competent Authority for the purpose of retained Regulation (EU) 2017/625 on Official Feed and Food Controls in the UK. To fulfil the FSA/FSS's obligation under Article 8 of Commission Implementing Regulation (EU) No 503/2013, LGC were appointed 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 Competent Authority. 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 Competent Authority
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 Competent Authority in August 2021 following open competitive tender. Pursuant to this role, LGC conducts the following activities, as specified in the contract:

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 (where applicable)
03/4 – Method validation through collaborative ring trials (where applicable)
03/5 – Reporting to the Competent Authority
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 2nd year of the GMO Authorisations (Great Britain) operation (April 2022-March 2023) in relation to the duties of the role.

Objective 01 – Infrastructure development

Tasks:

01/0 - Agree an operational protocol with the Competent Authority 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:
    - Four GMO Authorisation Quarterly Review Meetings were successfully held with the Competent Authority.

- Establishment of new quality procedures to ISO 9001 of the processes for quality control of method validation of new GMOs applications:
    - A copy of the draft reporting form for GMO renewals was uploaded to the FSA secure MS Teams site.
    - A copy of the draft document outlining the minimum performance requirements for analytical methods was uploaded to the FSA secure Microsoft Teams site.
    - LGC's ISO 17025 flexible scope of accreditation, which contributes towards the NRL function, was subject to a full audit by UKAS. Feedback received was very positive regarding the traceability and the quality of the records and results. No findings or recommendations for improvements were made.
    - Project work associated with the GMO NRL and Authorisation roles have been successfully migrated onto SharePoint in Microsoft Office 365. This is in line with migration of all government projects/contracts and data security compliance.

- Description of the method validation process:
    - 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.
        - This includes contributions payable for full novel (new) authorisations, renewals and pipeline applications. Costs for full authorisations (single GM events) are split into two payments, to cover the initial scientific dossier appraisal and related intralaboratory validation and then the follow on interlaboratory collaborative trial as appropriate. Cost models for different scenarios up to and inclusive of an application for a GMO consisting of six stacked events, covering all possible combinations of authorised/unauthorised GM events, were drafted. Details for payments of contributions and contact points for official correspondence were included.

- Initial maintenance activities:
    - Initial meetings were convened with IT experts and plans agreed to scope out preparing an online GB centric “GMO Compendium of Methods”, containing information and links for validated methods for the detection of GMOs approved for market placement in Great Britain. A proof of concept version was developed, tested and determined to be fit for purpose, and was demonstrated to the Competent Authority at the October quarterly meeting. This is ready to be soft-launched to the LGC live environment as an active document as and when required by the Competent Authority.

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 2022 to March 2023, providing a summary of the method validation service activities.
    - Four GMO Authorisation Quarterly Review Meetings were successfully held with the Competent Authority.
    - The last Quarterly Review Meeting was held as a hybrid event, with lab tours provided to staff members from the Competent Authority who attended the onsite meeting at LGC, focusing on the National Measurement Laboratory infrastructure (inclusive of Molecular Biology and the Office of the Government Chemist).
    - Copies of the Authorisation presentations from the NRL Quarterly review meetings were uploaded onto the FSA secure Microsoft Teams channel.
    - Monthly logs, providing detailed descriptions of all activities engaged in as part of the GMO Authorisations function, were provided on a monthly basis to the Competent Authority.

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

- Maintain a list of reputable suppliers:
    - In conjunction with the GMO NRL position, draft lists of reagents and suppliers have been prepared, maintained and updated.

- Maintain appropriate storage facilities to house materials:
    - Throughout the second year of operation, LGC has continued 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.
    - LGC's ISO 17025 flexible scope of accreditation was subject to a full audit by UKAS during 2022. Feedback received was very positive regarding the traceability and the quality of the records and results. No findings or recommendations for improvements were made.

- 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.
    - GeMMA U97: the GMO Authorisation function participates in this as part of a mandatory requirement for ISO 17025 flexible scope of accreditation, and to demonstrate continued competency in this area. Two results were submitted to provide evidence of capability, one for manual/overnight CTAB DNA extraction, and one for automated Maxwell DNA extraction. Z-scores of -0.3 and -0.1 respectively provide evidence of the GMO Authorisation function's continued fitness for purpose in this area.
    - GeMMA "Challenge round" C09: This GMO proficiency test round included qualitative/quantitative determination of two GM soya events in two challenging sample matrices (mixed flours and a processed matrix). The GMO Authorisation function successfully detected, identified and quantified the two GMO events (soya MON89788 and 40-3-2) in the two test materials, receiving Z-scores of -0.2 and -0.6.
    - GeMMA U105: Results for this GeMMA round have been submitted and the final report by the scheme organisers will be published in due course.

- Maintain a national GMO Compendium ("database") containing lists of control materials and methods:
    - Initial meetings were convened with IT experts and plans agreed to scope out preparing an online GB centric "GMO Compendium of Methods", containing information and links for validated methods for the detection of GMOs approved for market placement in Great Britain. A proof of concept version was developed, tested

and determined to be fit for purpose, and was demonstrated to the Competent Authority at the October quarterly meeting. This is ready to be soft-launched to the LGC live environment to enable a go-live as and when required by the Competent Authority.

- GB GMO register and GMO Compendium of Methods: At the request of the FSA, provided feedback on the user interface and content of the "GB GMO register" (Register of regulated food and feed products for Great Britain - GMO authorisations) at https://data.food.gov.uk/regulated-products/landing .

- Continue international stakeholder engagement
  - The International Conference on GMO Analysis and New Genomic Techniques was a three day event held in Berlin (Germany) on the 14th to 16th March 2023. The conference provided a forum to promote broad technical and scientific exchange between scientists worldwide on the status and challenges for traceability, detection and identification of GMOs, with an emphasis on the fast evolving DNA-based detection methods. A focus was provided on detecting products as a result of New Genomic Techniques (gene editing), which are currently classified as GMOs. The conference was held to contribute to capacity building for experts and laboratories involved in the detection and identification of GMOs and served as platform of networking among regions as well as at global level. LGC was invited to provide the first technical presentation on the opening day of the conference, outlining the current status and challenges associated with detecting both conventional GMOs and products as a result of New Genomic Techniques. LGC was also part of a panel discussion as well as co-chairing the final expert panel discussion session on the last day of the conference, the latter aimed at identifying common issues and potential solutions for GMO analysis on a global scale.
  - Following discussions with the Head of the EURL-GMFF, a key member of the GMO Authorisations staff was invited to participate in a new ENGL Working Group on New Mutagenesis Techniques, as well as attending an ENGL plenary meeting. It was made explicit that the attendance was on the basis of being a recognised independent international scientific expert in GMO analysis.
  - Kept the FSA informed regarding three new GM events authorised in the EU on the 4th April 2022: Decision 2022/529: Genetically modified oilseed rape 73496 (DP-Ø73496-4); Decision 2022/530: Genetically modified cotton GHB811 (BCS-GH811-4); and Decision 2022/531: Genetically modified soybean GMB151 (BCS-GM151-6). All three are single GM events and reference materials and reference samples were made available.
  - Alerted the FSA to the approval by the European Commission of two new GMOs (maize and soya stacked events) for authorisation on 19th/20th May 2022. These were genetically modified maize NK603 × T25 × DAS-40278-9 and its sub-combination T25 × DAS-40278-9, as well as soybean MON 87769 × MON 89788.
  - Brought to the attention of the FSA that the European Commission approved the use of a new GM maize stacked event (and its constituent stacks) on 29th June 2022: Decision (EU) 2022/1094: maize stacked event DP4114 × MON 810 × MIR604 × NK603 and genetically modified maize combining two or three of the single events DP4114, MON 810, MIR604 and NK603. Further details can be found in the Official Journal of the EU: https://eur-lex.europa.eu/eli/dec_impl/2022/1094/oj
  - Validation of a ddPCR method for GMO detection: A scientific paper was published, describing the development and successful validation of a ddPCR method for the detection of the GMO maize event MON810. As part of the official authorisation

process for placing on the market of GMOs, applicants need to propose a method for detection of those GMOs for control purposes. Digital PCR is gaining increasing favour as a reliable, accurate and sensitive method for detection of GMOs. The study was an original example of multi-lab validation of a digital PCR method for GMOs, serving also as a model for future regulatory dPCR validations. LGC is cited and thanked for its input into the study. The full paper can be found here: https://doi.org/10.1016/j.foodcont.2022.109117

- Contacted by BELAC (Belgian Accreditation Body) to ask to confirm approval of membership on their list of GMO analytical experts, to be called upon to act as auditor to ISO 17025 and ISO 17034 for GMO analysis and reference material production.
- HORIZON-CL6-2023-FARM2FORK: New detection methods on products derived from new genomic techniques to enable safe innovation in the food system. Following a series of meetings, the manager to the GMO Authorisation function has been asked to consider joining the official Scientific Advisory Board, for a consortium proposal in response to the above tender invitation.
- ENGL Working Group on “Detection of food and feed plant products obtained by new mutagenesis techniques” (ENGL WG NMT): active contribution and involvement in this Working Group, with a focus on reviewing the original ENGL (2019) report “Detection of food and feed plant products obtained by targeted mutagenesis techniques”, in line with recent developments and current analytical best measurement practice guidance.
- Made the FSA/Defra aware that EFSA released an important FAQ regarding the risk assessment of plants produced by New Genomic Techniques, entitled "Criteria for risk assessment of plants produced by targeted mutagenesis, cisgenesis and intragenesis”. Intragenesis, where there was previous ambiguity, has now been included in the definition of a New Genomic Technique (previously only qualified by targeted mutagenesis and cisgenesis).

- Establish a process for setup costs and overhead costs associated with each GB centric authorisation:
  - A copy of the draft guidance document outlining Financial Contributions from Applicants was uploaded to the FSA secure Microsoft Teams site.

- Maintenance of storage and distribution service:
  - Throughout the second 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 second 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).
  - Held discussions with the FSA regarding the current status of Roundup Ready soya (40-3-2) in the UK (first authorised in the EU in February 2012), as this was the model GM event being used to demonstrate fitness for purpose as part of the FSA GMO analytical capability building exercise.

- Provided advice into the Defra Impact Assessment of the Genetic Technology (Precision Breeding) Bill.
- The report entitled "*(EC) Legislation for plants produced by certain new genomic techniques - Public Consultation Factual Summary Report*", alongside a summary of the pertinent key-points for traceability of NGT products in the food/feed supply chain, was sent to the FSA.

- Contract management:
  - Throughout the second year of operation of the GMO Authorisations position, the Project Management team have provided consistent and continued support for all Contract management related activities.
  - Four GMO Authorisation (GB) quarterly reviews with the Competent Authority were attended, to present and discuss progress and activities in the previous quarter, as well as planned activities for the next quarter.
  - All project work associated with the GMO NRL and Authorisation roles have been successfully migrated onto SharePoint in MS Office 365. This is in line with migration of all government projects/contracts and data security compliance.

- Meetings:
  - The Joint NRL (Feed Additives and GMOs) Network Meeting was held as a virtual event. The meeting provided both NRL functions the opportunity to communicate relevant updates on methods, enforcement, training and other applicable activities, as well as providing a suitable forum for exchanging information and for participants to raise any further training needs and support requirements. An update was also provided on the GMO Authorisations position, inclusive of 24 applications that had been received by the FSA. In addition, the FSA provided an update on relevant scientific and policy areas. Sixteen staff from eight Official Laboratories attended the event, as well as ten representatives from the Competent Authority.

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 Competent Authority
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 requiring processing for method validation services as part of the authorisation procedure were received by LGC in the second reporting year of operation of the GMO Authorisations (GB) function. This included no full applications for new GM events (single or stacked), full 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:
    - Received a request from the FSA for the GMO Authorisation function to appraise the scientific documentation associated with GMO renewals (past their 10 year authorisation status in the EU/UK) for authorisation in Great Britain. The findings from the appraisal of the GMO renewals were further examined, independently checked, verified and revised by a second member of the GMO Authorisations staff, both as a training exercise and as an opportunity to further review, revise, refine/develop the reporting sheets and mechanism for the infrastructure of the Authorisations role.

- Bespoke advice provided to the FSA regarding GMO authorisations:
    - Provided advice regarding the use of a genetically modified microorganism used in the production of novel protein. Based on the adopted EU legislation, it was highly likely that the presence of any recombinant DNA in a food/feed product would be considered non-compliant unless authorised, and that this applied equally to living GMOs and products/DNA derived from these. The presence of any unauthorised GMOs/GMMs was considered non-compliant with UK legislation, irrespective of the amount.
    - Assisted the FSA in relation to advice regarding the use of a genetically modified microorganism (GMM) for Food Enzyme production. The advice concerned the need for labelling and a detection method. The GMO Authorisation position advised that if the GMO is subject to the relevant UK GMO legislation, then the provision of a suitable method for its detection was a requirement. The GMO Authorisation position also stated that their records indicated that DG SANTE, supported by a number of other EU NRL's and CA's, have stated that the presence of any recombinant DNA in a product means that the product is considered non-compliant with EU legislation, unless authorised.
    - Held discussions with the FSA regarding the current status of Roundup Ready soya (40-3-2) in the UK (first authorised in the EU in February 2012), as this was the model GM event being used to demonstrate fitness for purpose as part of the FSA GMO analytical capability building exercise.
    - A request from the FSA was received regarding the costs for the renewal process. LGC responded stating that there would be an upfront cost to the applicant to cover the appraisal. Should minor issues be found, the initial fee should also cover the appraisal of additional information requested from the applicant, should this be proportionate to the amount of effort involved. Should the appraisal of the renewal reveal major findings, these would be reported back to the Competent Authority as part of the review process alongside recommendations on how to proceed. Should these recommendations include additional intra-laboratory and/or inter-laboratory validation trials, these will be costed as per the Authorisations contract.

- Experimental testing of sample and methods:
    - Staff from the GMO Authorisations function were involved in helping characterise the homogeneity, stability, confirmation and purity of candidate European reference materials (ERM-BF446, MIR162 maize)
        - https://crm.jrc.ec.europa.eu/p/g/BF446/ERM-BF446d-MIR162-Maize-nominal-1/ERM-BF446d

- Detection method comparison to dossier:
    - As part of the FSA's Regulated Product Register, the FSA provided a list of current and anticipated GMO applications in GB and requested that the GMO Authorisation function provide advice on availability and practical implementation of methods. The GMO Authorisation position provided a Microsoft Excel workbook summary as a response, itemising each of the individual GM events/methods referred to in the FSA Regulated Product Register, along with details of the current availability of methods on the EURL website, details on the probes and also on the practical implementation of the methods based on the availability of current PCR reagents.

- Recruitment of participating laboratories:
    - Alongside the current expertise and capability offered by specific UK Official Laboratories and two previous ENGL member based laboratories in the UK, the GMO NRL function is working closely with several other UK Official Laboratories in support of the FSA initiative on GMO analytical capability building.

- Summary reports in standard format (validation trial, validated method, DNA extraction method):
    - A standard style of formatting for reporting forms (to be supplied back to the FSA summarising pertinent information and recommendations from each stage of the method validation process of the GMO authorisation) have been formalised and agreed with the FSA.
    - A first drafting of a full Summary Report for GMO Applications has been provided. 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.