EBIC Environmental Biotechnology Innovation Centre



Guidance on Regulatory Approval of Genetically Modified Microorganisms (GMMs) for Environmental Applications

EBIC Partners:

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Disclaimer: This report has been developed with input and feedback from experts across academia, industry and regulatory organisations in the UK. These contributions have informed the guidance but should not be interpreted as formal endorsement of the report by the organisations represented. The report is provided for information purposes only and offers general guidance on the process of applying for and securing approval for the use of Genetically Modified Microorganisms (GMMs). It does not constitute regulatory or legal advice in relation to any specific case. Every effort has been made to ensure that the information is accurate and up to date at the time of publication. However, no warranty is given as to its accuracy or completeness, and no liability is accepted for any loss arising from reliance on its content.

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Executive Summary

Advances in engineering biology and the use of genetically modified microorganisms (GMMs) offers significant opportunities to deliver innovative environmental solutions, including the production of sustainable alternatives to conventional products, resource recovery, waste management, wastewater treatment, and pollution remediation. However, navigating the regulatory framework governing their use, particularly where activities may involve environmental release, can present challenges for researchers, developers, and start-up companies seeking to bring these technologies towards commercialisation and in practical applications.

This guidance document has been developed to provide a practical starting point for innovators, researchers, industry, and stakeholders to help understand the current UK regulatory landscape applicable to the development, use, and environmental application of GMMs. The guidance aims to clarify regulatory pathways, identify the questions that need to be addressed as technologies progress, and provide practical examples to help users identify and navigate the relevant regulatory requirements.

The guidance is structured in four sections:

- **Contained Use Regulations:** This section outlines the regulatory framework governing the contained use of GMMs. Detail can be found on the risk assessment methodology, including the identification and evaluation of potential risks to human health and the environment, the different classification levels, and the notification process.

- **Deliberate Release Regulations**: This section outlines the regulatory framework governing the intentional release of GMMs into the environment. Detail can be found on the preparation and submission of an application, the environmental risk assessment, and the evidence required to demonstrate safe release of GMMs under deliberate release activities. It also highlights the importance of considering the characteristics of the modified microorganism, its intended application, potential exposure pathways, environmental fate and persistence, and possible effects on non-target organisms and ecosystems.

- **GMM Inactivation and Waste Management:** This section highlights the safe management and inactivation of GMMs and associated waste materials. It details various inactivation methods, the importance of demonstrating effectiveness through validation, and the regulatory responsibilities with managing biological waste.

- **Practical Case Studies and Examples:** A series of case study examples mapping the regulatory requirements of GMM based solutions for different environmental applications. It details the regulatory pathway and evidence requirements for each example.

This document is not intended to replace formal regulatory advice or the requirements of the relevant competent authorities. Instead, the guidance seeks to improve awareness of the current regulatory pathways, support more informed decision-making from early research through to potential deployment, and encourage engagement between innovators, industry and regulators. By bringing together regulatory information and perspectives from industry and the engineering biology community, the aim is to help create greater clarity around the pathway to deployment of environmental biosolutions.

About the creation of the guidelines

Launched in March 2024, the Engineering Biology Innovation Centre (EBIC) is an Engineering Biology Mission Hub hosted, managed, and led by Cranfield University in collaboration with researchers from nine academic institutions - Bangor University, Cranfield University, Heriot-Watt University, Newcastle University, University of East Anglia, University of Edinburgh, University of Essex, University of Glasgow, and University of Southampton - and thirty associated partners. EBICs mission is to undertake innovative research to tackle pressing environmental challenges using synthetic biology, biotechnology, computational modelling, and engineering.

One of EBIC's core objectives is to support the translation of Engineering Biology solutions from the lab to market. In doing so it has engaged with stakeholders to better understand what can be done to advance, through good governance and regulation, the safe and responsible use of genetically modified organisms. These conversations exposed a need for 'light touch' advice for SMEs in particular regarding the requirements and process of regulatory approval for GMM based products and services. This challenge is particularly evident when it comes to environmental applications of EngBio where multiple regulators may be involved and specialised biocontainment techniques are required. Funded through an EBIC Flexifund award, the NAVIREG project has generated a series of guidance documents, collected here as a single volume, to help address this challenge.

We would take this opportunity to thank all those who have supported the production of these guidelines with their time and expertise. The various rounds of drafting and reviewing have added much clarity to the guidelines and improved readability for the target audience.

This report was produced with support from the Engineering Biology Innovation Centre (EBIC), funded by the Biotechnology and Biological Sciences Research Council (BBSRC), part of UK Research and Innovation (UKRI) through the Technology Missions Fund (TMF) (Grant reference BB/Y008332/1).

UKRI Biotechnology and Biological Sciences Research Council

For more information on EBIC, visit https://ebicentre.co.uk/

For more information on NAVIREG, visit https://ebicentre.co.uk/project-details-2/

Guideline for securing regulatory approval for the development and use of Genetically Modified Microorganisms –

Contained Use

Purpose of the Contained Use Guidance Document

This document provides guidance on the regulatory pathway governing the **Contained Use** of **Genetically Modified Microorganisms (GMMs) in the UK.** GMMs are a specific category of genetically modified organisms (GMOs) and therefore fall within the broader UK regulatory framework governing GMOs. However, the Contained Use Regulations specifically establish requirements for the contained use of genetically modified microorganisms. Background information on the regulatory framework, risk assessment methodology and a step-by-step regulatory approval pathway is outlined. The guide is intended for use by those developing Engineering Biology solutions targeted at solving environmental pollution or monitoring challenges but may be found helpful by those working in other sectors.

Definition of Contained Use

Genetically modified organisms (GMOs) are defined as organisms whose genes have been artificially altered to modify their characteristics in some way or another. Under the Genetically Modified Organisms (Contained Use) Regulations 2014, genetic modification means the alteration of the genetic material of an organism in a way that does not occur naturally by mating or natural recombination, subject to the techniques included and excluded under Schedule 2 of the Regulations**.** According to the Genetically Modified Organisms (Contained Use) Regulations 2014 administered by the **Health and Safety Executive (HSE)**, contained use covers any activities involving the **construction, culturing, storage, transportation, or otherwise use of GMOs** where control measures, such as physical, chemical or biological barriers are used to limit contact between GMOs and humans or the environment to provide a high level of safety. The Genetically Modified Organisms (Contained Use) Regulations 2014 implements EU Directive 2009/41/EC, which defines contained use as *any activity in which micro-organisms are genetically modified or in which such genetically modified micro-organisms (GMMs) are cultured, stored, transported, destroyed, disposed of or used in any other way, and for which specific containment measures are used to limit their contact with, and to provide a high level of safety for the general population and the environment*. Examples of contained use applications are shown in **Figure 1**.

What are GMOs? and GMOs and the law

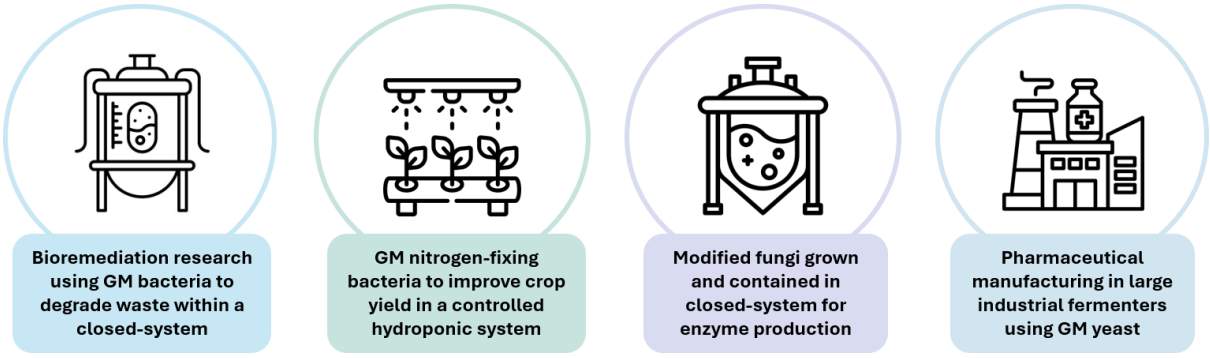


Figure 1. Examples of Contained Use GMM activities

The regulatory classification of activities involving a GMM depends on the nature of the activity and the controls applied, rather than solely on the purpose for which the GMM is supplied or applied. Where a GMM is constructed, stored or used under physical, chemical or biological containment, the activity may fall within the GMO (Contained Use) Regulations 2014. Where a GMM is intentionally released from containment into the environment, the activity may instead fall within the deliberate release regime. The supply or commercial sale of a GMM constructed under Contained Use may raise additional regulatory considerations that should be assessed separately. The Contained Use regulations do not cover GMOs as, or in, products which are placed on the market – i.e. making a GMO available to third parties, whether in return for payment or free of charge. These applications are covered by the regulations on Deliberate Release of GMOs.

UK Regulatory Framework on Contained Use

The primary legislation governing contained use of GMOs in Great Britain (England, Scotland, and Wales) is the **Genetically Modified Organisms (Contained Use) Regulations 2014 (SI 2014/1663)**. In Northern Ireland, the **Genetically Modified Organisms (Contained Use) (Northern Ireland) 2015** regulations apply.

- **In England and Wales**, the HSE and the Secretary of State for the Department for Environment, Food and Rural Affairs (DEFRA) acting jointly form the competent authority. Officials from the Welsh Government are included in matters relating to Wales, providing policy and risk oversight for Wales, while the HSE handles the administrative processing, statutory notifications, and facility inspections.
- **In Scotland**, the competent authority comprises Scottish Ministers and the HSE acting jointly. The Scottish Government are responsible for providing advice about the environmental risk of contained use GMO work carried out in Scotland, supported by the GM Team at Science and Advice for Scottish Agriculture (SASA). Under a formal Memorandum of Understanding (MoU), the HSE processes, administers, and manages the notification scheme on behalf of Scottish Ministers.
- **In Northern Ireland**, the competent authority is the Health and Safety Executive for Northern Ireland (HSENI) and the Department of the Environment (Northern Ireland) acting jointly.

Who is responsible for implementing the GMO (Contained Use) Regulations?

Scientific Advisory Committee on Genetic Modification (SACGM)

The **Scientific Advisory Committee on Genetic Modification (SACGM)** is a non-statutory scientific advisory committee that provides scientific advice to all the UK competent authorities on the contained use of GMOs, particularly on technical and scientific advice in respect of human and environmental risks. Their role is:

- To advise on the technical issues on individual activities notified under the Genetically Modified Organisms (Contained Use) Regulations 2014
- To provide advice on risk assessments for contained use activities involving GMOS
- To help develop and update guidance on all aspects of contained use of GMOs including the SACGM Compendium of Guidance

The SACGM provides a Compendium of Guidance which has been prepared in consultation with HSE and following the guidance is considered to be good practice by the members of the Committee.

The SACGM Compendium of Guidance

Classification and Notification

Classification

Under the Genetically Modified Organisms (Contained Use) Regulations 2014, genetically modified microorganisms (GMMs) are regulated as a category of genetically modified organisms (GMOs). For contained use, the proposed activity involving the GMO is subject to a risk assessment, which determines its classification as Class 1–4 and the corresponding containment level required to protect human health and the environment. The classification levels are outlined in **Table 1**.

Classification levels are based on the use of the GMM and the risk that the contained use presents to human health and the environment. It is not a classification of the organism as is the case in The Approved List of Biological Agents and Specified Pathogens Order

Table 1: Classification levels for activities involving GMOs under contained use conditions

Class	Level of Risk	Appropriate containment level required to protect human health and the environment
Class 1	No / negligible risk	Containment Level 1
Class 2	Low risk	Containment Level 2
Class 3	Moderate risk	Containment Level 3
Class 4	High risk	Containment Level 4

Premises notification

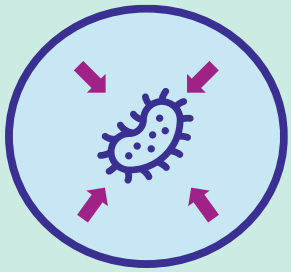


A **premises notification** is required for the creation or use of GMOs under contained use conditions if being conducted at the premises for the first time. Before beginning the activity, a premises notification must be submitted and paid for. HSE/HSENI will review the application and respond within 10 days to acknowledge receipt, at which point work can begin if the application is for Class 1 (low) contained use or involves larger GMOs. For Class 2 and above (medium to high), a further notification is required under Regulation 10, 11 or 12 (as appropriate) before the contained use activity can begin. Final clearance will be given within 45 days. Thereafter, only new Class 2 – 4 activities at the same site require additional notification / fees.

Check whether GMOs are already being used elsewhere in the building or premises as an existing premises notification may cover the new activity

Contained use notification

Whether or not a specific activity **requires a contained use notification in the UK depends on the risk classification of the work**. Classification (from Class 1 to Class 4) is based on a risk assessment (carried out by the applicant), which determines the containment measures required to adequately control the identified risks. The appropriate containment level to protect human health and the environment for each class is outlined in **Table 1 (above).**



To apply for Premises and Contained Use Notification, How do I notify?

Contained Use work that falls under Class 1 does not require **notification beyond the premises notification**, but any work considered to fall within Classes 2 - 4 must be notified (See **Notifying premises to be used for contained use and contained use notifications**). The Contained Use notification and consent requirements are outlined in **Table 2**.

Table 2: Contained Use notification requirements for relevant classification levels

Class	Notification of first Contained Use activity at relevant classification	Notification requirements for subsequent Contained Use activities
Class 1	Covered in premises notification. Work can begin once acknowledgement of premises notification is received.	Notification not required.
Class 2	Notification required. Consent not required. Work can begin 45 days after acknowledgement of notification has been received (unless consent explicitly refused).	Notification required. Consent not required. Work can begin once acknowledgement of notification has been received.
Class 3 & 4	Notification required. Consent required. HSE will grant or refuse consent within 90 days after acknowledgement of notification.	Notification required. Consent required. HSE will grant or refuse consent within 45 days after acknowledgement of notification.

Notification of work with larger GMOs (e.g. plants and animals) is only required where the genetic modification increases the risk of harm to human health as compared with the unmodified parental organism. Environmental risks for such larger organisms are separately assessed by DEFRA under the Environmental Protection Act 1990

For guidance on larger GMOs, see SACGM Guidance Part 4 for plants and Part 5 for animals

Biological Safety Officer (BSO) and Genetic Modification Safety Committee (GMSC)

Regulation 8 of the contained use regulations requires the person responsible for the contained use activity to ensure that expert advice on risk assessments is obtained. Class 1 risk assessments can be provided by a competent individual such as a **Biological Safety Officer (BSO).** Institutions and organisations conducting GMO work classified as Class 2 or above are required to establish, or have access to, a **Genetic Modification Safety Committee (GMSC)** under Regulation 16 of the Genetically Modified organisms (Contained Use) Regulation. The committee should include a BSO with GMO expertise, staff representatives with relevant scientific backgrounds, and an independent member familiar with regulatory requirements. The GMSC review proposed contained use activities, advise on classification and risk assessments, and provide competence advice as required by the regulations. Contained Use notification should contain detail on the GMO work being conducted, with necessary information on the genetic construct. This should describe the type of construct, explaining if and how the insertion of foreign DNA is expected to bring about significant alteration in the properties of the recipient organism. The GMSC should also provide advice on the notification application.

If there is no formal organisational structure to establish a BSO or GMSC e.g. in a biotech start up, this can be achieved by hiring an independent biosafety consultant, appointing a qualified scientific founder part-time, or contracting a local academic institution's safety officer to provide interim oversight and compliance setup

For more information, see guidance on regulations for the Genetically Modified Organisms (Contained Use) Regulations 2014 on Regulation 8

The overall regulatory consent pathway for GMOs under Contained Use is outlined in **Figure 2** from early planning to operation and compliance. The responsible person for each activity in the application process is outlined in **Figure 3**.

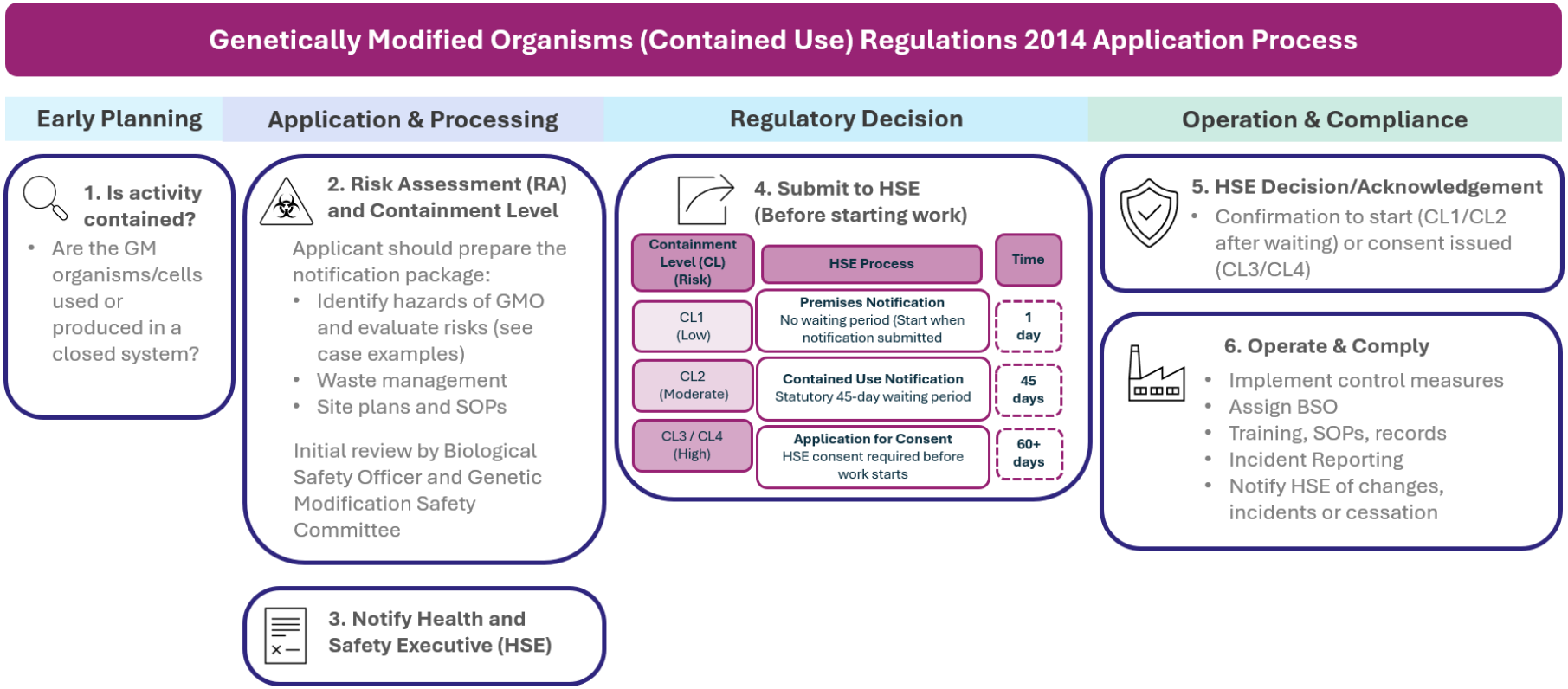


Figure 2. General notification process for GMOs in contained use application

Step 1: Early planning

Before submitting any notification, applicants should complete the following preparatory actions:

- **Determine if the GMO to be used or produced falls under the contained use regulations**
- **Early engagement with appropriate competent authority to better understand the regulatory approval process**
- **Characterise the GMO:** Fully establish the identity, form of genetic modification, and phenotypic characteristics of the organism
- **Conduct a literature and regulatory review:** Identify comparable organisms (See **HSE Public Register**), prior risk assessments, and relevant competent authority guidance documents
- **Establish or engage with a Genetic Modification Safety Committee (GMSC):** ensure committee and expertise are appropriate for the intended activities if they are Class 2 or above
- **Ensure facility readiness:** Confirm that laboratory or production facility infrastructure meets the containment requirements for the anticipated risk class

Step 2: Application and Notification

Prepare risk assessment: Include detail as described in **Risk Assessment Methodology** (Also see **Part II of the SACGM Guidance** for GMMs that are not associated with plants and **Part IV of the SACGM Guidance for GMMs** that are associated with plants)

A notification application containing the risk assessments, relevant Standard Operating Procedures, site plans and waste management procedures should be included. The general pathway for a new contained use activity at a new premises is:

i. **Premises notification (only if new premises):** Submit premises notification to the competent authority (see above) with the information required by Schedule 5 (**GMO Notification Forms**)**.** The competent authority will acknowledge receipt within 10 days for Class 1 activities and 45 days from acknowledgement of receipt for Class 2 activities. Work may begin on acknowledgement of receipt for Class 1 activities only.
ii. **Activity notification (Containment Class 2-4):** Submit activity-specific notification for all Class 2 – 4 contained use activities. Include risk assessment, classification rationale, and proposed containment measures.

Step 3: Regulatory Decision

i. **Regulatory Decision:** Await decision during time scale associated with each class's activities. For Classes 3 and 4, do not commence work until written consent is received (within 45 days of receipt of acknowledgement). Consent may be granted with or without conditions.

ii. **Emergency Planning (if risk assessment indicates an emergency plan is required):** Ensure plan is finalised and approved before consent is granted.

Step 4: Operation and Compliance

- **Commence Activities:** Class 1 and Class 2 activities can begin upon the expiry of the waiting period. For Class 3 and Class 4, activities may begin when consent is confirmed subject to compliance with any imposed conditions.
- **Ongoing Obligations:** Maintain robust records of the risk assessment and all relevant documentation. Review and update risk assessments when conditions change. Notify the competent authority of any incidents or accidents involving the GMO.

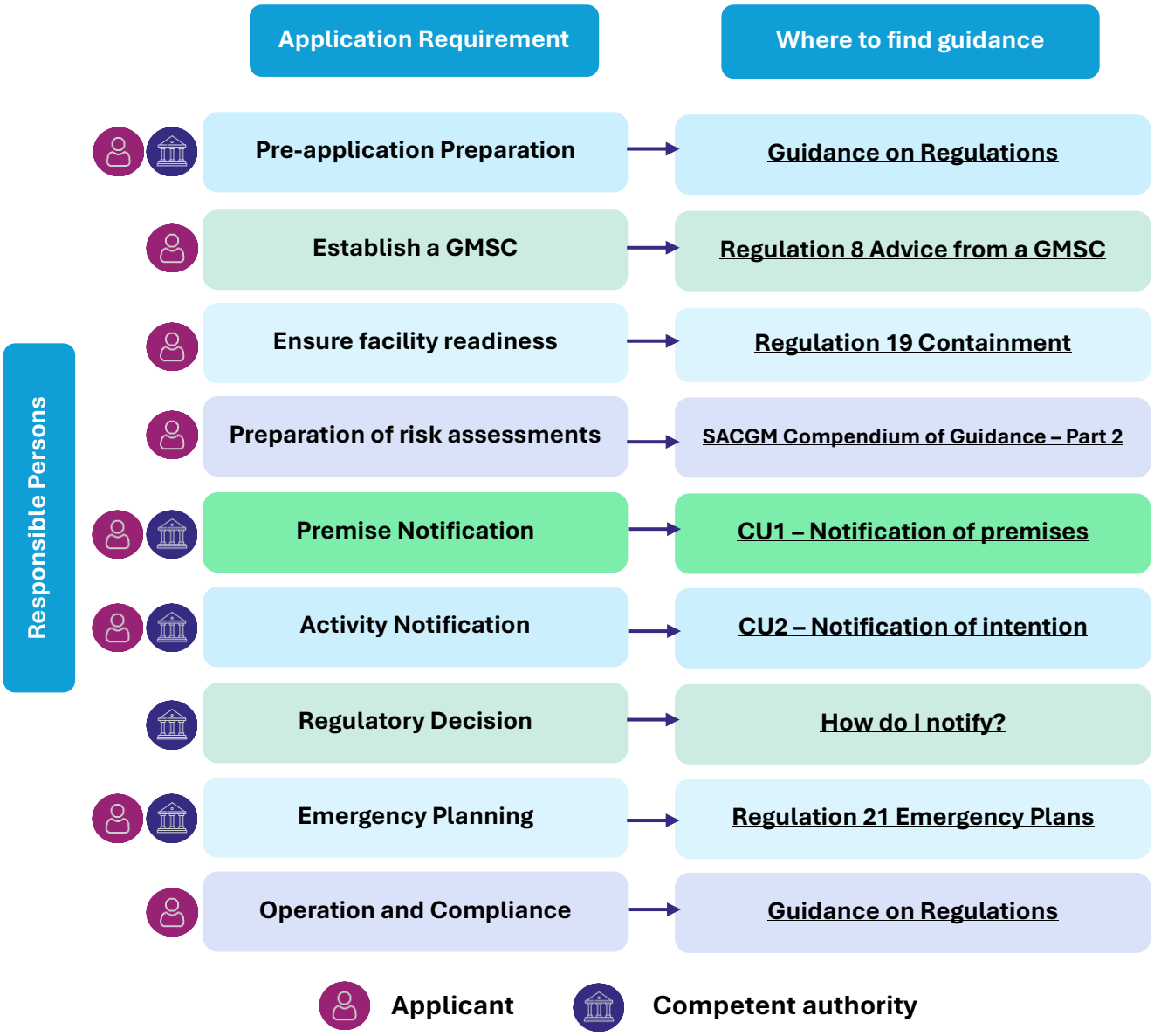


Figure 3. Responsible persons for GMO contained use application requirements and links to guidance

The risk assessment for GMOs under Contained Use conditions requires two procedures:

1. Identify potential harmful properties (hazard) of the GMM and allocate the GMM to an initial class (class 1 to class 4) taking into account the severity of the potential harmful effects.

   and

   Assessment of possibility of harmful effects occurring by consideration of exposure (both human and environmental) taking into account the nature and scale of the work, with containment measures appropriate to the initial class allocated.

2. Determination of final classification and containment measures required for the activity. Confirm final classification and containment measures are adequate by revisiting Procedure 1.

See guidance notes for risk assessment on the contained use of GMMs

Part I: Initial Classification - Hazards and Exposure Assessment

This component of the assessment requires the identification of the harmful properties (hazard) of the GMO due to genetic modifications or alteration of the recipient organism's existing properties resulting in its allocation to a risk category (Class 1 to Class 4) based on the severity of the potential hazards. Submissions should include analysis of potential for harm when the organism comes into contact with both human beings and the environment along with the nature and scale of work to be conducted as well as the nature and efficacy of containment measures appropriate to the initial allocated class.

Hazard Assessment

GMO Characteristics:

- Pathogenicity and virulence of the parental (recipient) organism
- Nature of the genetic modification and characteristics of the inserted or altered sequences
- Properties of the donor organism from which genetic material was derived
- Specific identity, source, location of insert and function of the insert (genes)
- Stability of the genetic modification
- Potential for gene transfer to other organisms
- Nature and source of the vector

Human health considerations (questions to be addressed):

- What are the hazards associated with the recipient strain?
  - Pathogenicity, and if it is pathogenic to humans who are immunocompetent
- Could the GMM establish an infection *in vivo* and how efficient would it be?
  - Diseases caused and mechanism of transmission including invasiveness and virulence
- Could the GMM or other organism acquire harmful sequences?
  - Possibility of survival outside of human host and biological stability
- What are the hazards associated with the inserted genetic material?
  - Expected toxic or allergenic effects of the GMO or its metabolic products

Environmental considerations (questions to be addressed):

- Has the stability or survivability of the recipient strain been altered?
  - Ecosystems which the GMO could be unintentionally released from Contained Use and the expected survivability
- Has the infectivity, pathogenicity or host-range of the recipient been altered?
- Does the inserted gene pose a risk to other organisms?
  - Known or predicted effects on plants and animals such as pathogenicity, toxicity, allergenicity, vector for a pathogen, altered antibiotic-resistance patterns, altered tropism or host specificity and colonisation
- Could the GMM or other organisms in the environment acquire harmful sequences?
  - Anticipated interaction of the modified GMO with other organisms and microorganisms
- Known or predicted involvement in biogeochemical processes

The Approved List of Biological Agents and Specified Pathogens Order provides a classification of biological agents approved by the Advisory Committee on Dangerous Pathogens (ACDP) and can be referred to in risk assessments

With these considerations and identification of hazards associated with the recipient and donor organism, vector and insert, the initial risk classification for the GMO is determined. **The severity of any possible harm is determined by considering what the result could be, not the likelihood of occurrence**. The next consideration for the initial classification is the **exposure assessment**. This stage assesses the likelihood and routes of human or environmental exposure to the GMO.

Exposure Assessment

Exposure considerations:

- Nature of the activity
- Scale and duration of the contained use activity
- Processes involving the organism (e.g. culture conditions, liquid handling, centrifugation) including containment and management of aerosols
- Effectiveness of proposed containment measures in reducing exposure
- Emergency procedures and incident response capacity
- Monitoring and management of GMM

Why does HSE require an initial classification?

The initial classification establishes the **baseline or inherent risk** of the activity. It answers the question:

If no specific containment or mitigation measures were applied, how hazardous would this work be?

By documenting the initial classification, HSE can understand the scientific basis for the assessment independently of the proposed containment measures.

Part II: Final classification

Following the Part I assessment of all potentially harmful characteristics for their severity and possibility of occurrence, with the effect of the containment and control measures in place as indicated by the initial classification, a **final classification** can be determined and relevant **containment measures** identified (**Table 3).** To determine the final classification, the applicant should revisit the initial classification to determine if it was correct given the intended activities to be conducted with the specified GM. By making a comparison of the initial classification against the final classification and associated containment measures, the final class and containment requirements should result in one of the following three conclusions:

Initial classification was correct and the outlined containment measures adequately prevent or minimise harm to human health and the environment

Initial classification is higher than the activity warrants and accordingly a lower classification with outlined containment conditions would be appropriate

Harmful effects have not been adequately considered in the initial classification and would not be adequately contained by the provisional containment considerations. Requires additional containment measures and possibly revision of the classification of the activity

Containment Levels

According to **Schedule 3 Part 2** of the Genetically Modified Organisms (Contained Use) Regulations 2014, to assign a contained use to the appropriate containment level, the person carrying out the risk assessment must:

a) First identify for each selected containment measure the column in the applicable table in Schedule 8 having the lowest number in which that selected containment measure is shown as being required, regardless of whether or not such requirement is subject to any qualification;
b) Then select the highest number of all the columns identified in accordance with (a); and
c) Then assign the contained use to the containment level of the highest number

The containment measures applicable to contained use involving micro-organisms in laboratories according to Schedule 8 Part 2 containment measures are outlined in **Table 1a** of Schedule 8 Part 2 of the Genetically Modified Organisms (Contained Use) Regulations 2014 and has been adapted in this guidance as **Table 3.** For containment measures applicable to contained use involving micro-organisms in plant growth facilities, see **Table 1b** in Schedule 8 Part 2 of the Genetically Modified Organisms (Contained Use) Regulations 2014 and for those involving micro-organisms in animal units see **Table 1c**. For containment measures applicable to contained use involving micro-organisms in premises other than those referred to in Tables 1a, 1b and 1c, see **Table 2** of Schedule 8.

Table 3: Containment measure applicable to contained use involving micro-organisms in laboratories as outlined in Schedule 8 of the Genetically Modified Organisms (Contained Use) Regulations

Containment Measures	Containment Level 1	Containment Level 2	Containment Level 3	Containment Level 4
Facilities				
Laboratory suite: isolation[1]	Not required	Not required	Required	Required
Laboratory: sealable for fumigation	Not required	Not required	Required	Required
Equipment				
Surfaces impervious to water, resistant to acids, alkalis, solvents, disinfectants and decontamination agents and easy to clean	Required for any bench	Required for any bench	Required for any bench and floor	Required for any bench, floor, ceiling and walls
Entry to laboratory via airlock[2]	Not required	Not required	Required where and to extent the risk assessment shows it is required	Required
Negative pressure relative to the pressure of the immediate surroundings	Not required	Not required	Required except for activities where transmission does not occur by the airborne route	Required

Extract and input air from the laboratory must be HEPA filtered	Not required	Not required	HEPA filters required for extract air except for activities where transmission does not occur by the airborne route	HEPA filters required for input and extract air[3]
Microbiological safety cabinet/enclosure	Not required	Required where and to extent the risk assessment shows it is required	Required, and all procedures with infective materials required to be contained within a cabinet/enclosure	Required, and all procedures with infective materials required to be contained within a cabinet/enclosure
Autoclave	Required on site	Required in the building	Required in the laboratory suite[4]	Double Ended autoclave required in laboratory
Systems of work				
Access restricted to authorised personnel only	Not required	Required	Required	Required (via airlock key procedure)
Biohazard sign on door **Specific measures to control aerosol dissemination**	Not required Not required	Required Required so as to minimise	Required Required so as to prevent	Required Required so as to prevent
Shower	Not required	Not required	Required where and to extent the risk assessment shows it is required	Required

Protective clothing	Suitable protective clothing required	Suitable protective clothing required	Suitable protective clothing required; footwear required where and to extent the risk assessment shows it is required	Complete change of clothing and footwear required before entry and exit
Gloves	Not required	required where and to extent the risk assessment shows they are required	Required	Required
Efficient control of disease vectors (e.g. rodents and insects) which could disseminate GMMs	Required where and to extent the risk assessment shows it is required	Required	Required	Required
Waste				
Inactivation of GMMs in effluent from hand-washing sinks and showers and similar effluents	Not required	Not required	Required where and to extent the risk assessment shows it is required	Required

Inactivation of GMMs in contaminated material and waste	Required by validated means where and to extent the risk assessment shows it is required	Required by validated means	Required by validated means, with waste inactivated within the laboratory suite	Required by validated means, with waste inactivated within the laboratory
Other measures				
Laboratory to contain its own equipment	Not required	Not required	Required, so far as is reasonably practicable	Required
An observation window or alternative is to be present so that occupants can be seen	Required where and to extent the risk assessment shows it is required	Required where and to extent the risk assessment shows it is required	Required where and to extent the risk assessment shows it is required	Required
Safe storage of GMMs	Required where and to extent the risk assessment shows it is required	Required	Required	Secure storage required
Written records of staff training	Not required	Required where and to extent the risk assessment shows it is required	Required	Required

[1] “isolation” means, in relation to a laboratory, separation of the laboratory from other areas in the same building, or being in a separate building.

[2] Entry must be through an airlock which is a chamber isolated from the laboratory. The clean side of the airlock must be separated from the restricted side by changing or showering facilities and preferably by interlocking doors.

[3] Where viruses are not retained by the HEPA filters, extra requirements will be necessary for extract air.

[4] Where the autoclave is outside the laboratory in which the contained use is being undertaken, but within the laboratory suite, there must be validated procedures for the safe transfer of material into that autoclave, which provide a level of protection equivalent to that which would be achieved by having an autoclave in that laboratory.

For more information on containment recommendations:
Schedule 8: Part 2 Containment measures
SACGM Part 3: Containment and control of activities involving genetically modified microorganisms

Once the final classification and containment conditions have been determined, the level of human and environmental exposure should be reassessed (as in Part I). The possibility of any harmful effects occurring should be acceptably low. When the risk assessment process has been completed by the applicant, this can be reviewed and approved by the appropriate competent authority.

Why does HSE require a final classification?

Once hazards have been identified, applicants must determine whether the proposed control measures reduce the risk sufficiently. It answers the question:

Given the containment measures proposed, what is the residual level of risk?

For example, an initial classification may require higher containment because it involves an organism capable of surviving outside the laboratory. The residual risk may be reduced to justify a lower contained use class by actions such as the use of closed bioreactors, validated sterilisation of waste, restricted laboratory access, appropriate microbiological practices, and effective monitoring. Alternatively, if the control measures are inadequate, the final classification may remain high or require additional containment.

The two-stage process allows inspectors to:

- evaluate whether the applicant has identified all relevant hazards
- assess whether the proposed containment measures are proportionate
- ensure consistency in classification across different facilities and applicants
- verify that containment is based on evidence rather than assumptions
- provide a transparent audit trail showing how the final containment class was reached

This approach distinguishes between a **hazard** and a **managed risk** and ensures containment measures are evidence based and proportionate to the actual level of risk posed by the activity.

Guideline for securing regulatory approval for the development and use of Genetically Modified Microorganisms –

Deliberate Release

Purpose of the Deliberate Release Guidance Document

This document provides guidance on the regulatory pathway governing the **Deliberate Release** of **Genetically Modified Microorganisms (GMMs).** The Genetically Modified Organism (GMO) deliberate release regulations apply to both GMMs and other organisms. However, GMMs have different regulatory guidance due to their microbiological properties and relevant containment measures, which are not typical for GM plants or animals. Background information on the regulatory framework, risk assessment methodology and a step-by-step regulatory approval pathway is outlined below. Thorough understanding of the regulatory pathway is essential for those developing environmental solutions using GMMs who intend to conduct field trials for research and development, commercial GMM cultivation, and the placing of GMM derived products on the market.

Definition of Deliberate Release

Genetically modified organisms (GMOs) are defined as organisms whose genes have been artificially altered to modify their characteristics in some way or another. According to the Genetically Modified Organisms (Deliberate Release) Regulations 2002 (as amended), the definition of deliberate release follows the operative definition under the European Commission's Council Directive 90/220/EEC (subsequently revoked and replaced by Directive 2001/18/EC) where deliberate release of a GMO is defined **as intentionally introducing GMOs into the environment without containment measures** designed to limit their contact with the public and the environment. The subsequent directive, Directive 2001/18/EC, governs both the deliberate release into the environment and the commercial placing on the market of GMOs. Whilst contained use employs specific containment measures (physical barriers, inactivation techniques, engineering controls) to prevent or minimise environmental exposure, deliberate release involves intentional environmental contact and therefore carries inherently higher potential for human and ecosystem interaction and irreversibility. Examples of deliberate release applications using GMMs are shown in **Figure 4.**

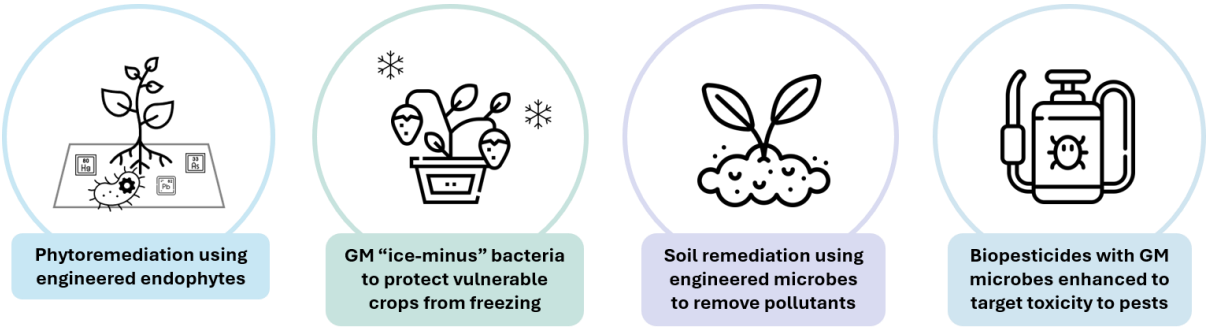


Figure 4. Examples of GMM activities intended for Deliberate Release

What are GMOs? and **GMOs and the law**

UK Regulatory Framework

Legislative Basis

England

The primary legislation governing deliberate release of GMOs in Great Britain (England, Scotland, and Wales) is the **Genetically Modified Organisms (Deliberate Release) Regulations 2002 (SI 2002/2443)** and **Part VI** of the **Environmental Protection Act 1990 (EPA 1990)**. In England, the **Department for Environment, Food and Rural Affairs (DEFRA)** are the competent authority for deliberate release. The 2002 regulations were amended by the Genetically Modified Organisms (Deliberate Release) (Amendment) (England) Regulations 2022 to introduce new clauses relating to qualifying higher plants which, in turn was revoked and replaced by the Genetic Technologies (Precision Breeding) Regulations 2025.

England - Genetic Modification Inspectorate: deliberate release inspection programme

Scotland

In Scotland, the competent authority is the Scottish Government with the GM Inspectorate and **Science and Advice for Scottish Agriculture (SASA)** being responsible for ensuring compliance with the regulations. The primary legislation governing deliberate release for research is Part II of The Genetically Modified Organisms (Deliberate Release) (Scotland) Regulations 2002 and for commercial releases it is Part III.

Scotland – Science and Advice for Scottish Agriculture (SASA) GM Services

Wales

The regulatory basis for Wales is similar to that for England and Scotland and the **Welsh Government** serve as the competent authority for deliberate release of GMOs into the environment in Wales.

Wales – Environmental regulators operating in Wales: signposting guide

Northern Ireland

In Northern Ireland, GMO deliberate release regulations are governed under a separate regulatory framework, the **Genetically Modified Organisms (Deliberate Release) Regulations (Northern Ireland) 2003 (amended by the 2019 regulations)**. The competent authority for Northern Ireland is the **Department of Agriculture, Environment and Rural Affairs (DAERA)** which administers and implements regulations concerning the deliberate release of GMOs into the environment (such as research trials or marketing approvals).

Northern Ireland – Department of Agriculture, Environment and Rural Affairs

The Advisory Committee on Releases to the Environment (ACRE)

ACRE is a statutory independent advisory committee appointed under Section 124 of the Environmental Protection Act 1990. It advises the Secretary of State on risks to human health and the environment from the release of GMOs / GMMs and works within the legislative framework of the GMO (Deliberate Release) Regulations 2002 (which implement the retained EU Directive 2001/18/EC). ACRE undertakes a review of all Deliberate Release applications and provide advice on:

- the risks posed to human health and the environment by the release or marketing of GMOs and any conditions which should be attached to consents
- the limitations and conditions of consents issued to released or marketed GMOs
- charges relating to the cost of issuing consents and in respect of maintaining inspection and enforcement regimes
- making of regulations under Part VI of the Environmental Protection Act 1990
- evaluation of new GM research findings
- any science-based GM matter
- research needs for risk assessment of GMOs
- releases into the environment of non-indigenous animals and plants

Advisory Committee on Releases to the Environment

Notice of application for Deliberate Release

Advertisement in a national newspaper and notice to genetic modification safety committee (GMSC)

Regulation 12 (4c) of the GMO Deliberate Release Regulations requires the person responsible for the deliberate release activity applied for to advertise certain information relating to the intended release in a national newspaper. Following submission of an application for consent to deliberately release a GMO, the applicant must within 10 days, give written **notice of application for Deliberate Release** is given to a number of persons. This includes any person, or member of a **genetic modification safety committee (GMSC),** from whom advice must be obtained under **Regulation 8** of the Genetically Modified Organisms (Contained Use) Regulations 2014. The notice must contain the information specified in **Regulation 12 (1)**. Advice given by the appointed GMSC is **not** required in a deliberate release application, and the **Health and Safety Executive (HSE)** fulfils any such function.

For more information on appointing a BSO and establishing a GMSC, see the EBIC Guidance on Genetically Modified Microorganisms for Contained Use Approval in the UK

How does the applicant navigate the two regulatory pathways concerning a GMSC/BSO?

The requirement to notify a GMSC/BSO of a GMM deliberate release activity does not mean that the GMSC approves the deliberate release application. The purpose is to ensure that the person or GMSC who has responsibility for providing advice on the applicant's contained use risk assessment is made aware that an application for deliberate release has been submitted. The construction and initial characterisation of the GMM will normally be undertaken as a contained use activity where advice must be obtained from a GMSC if the use is Class 2 or above. Data generated during a contained use activity can be used to inform a deliberate release application. However, the deliberate release application itself must include both an environmental risk assessment prepared in accordance with Regulation 6 and the information required by Regulation 11. The precise regulatory requirements will depend on the proposed activity and the measures used to control exposure, since the same GMM may be subject to different regulatory requirements depending on context and application.

If there are no formal organisational structures available to appoint a BSO or establish a GMSC (e.g. a biotech start up), advice can be sought by hiring an independent biosafety consultant, appointing a qualified scientific employee, or contracting a local academic institution's safety officer to provide interim oversight and compliance setup

To apply for consent to release a GMM in the UK, a formal notification and technical dossier must be submitted to the relevant competent authority (see **Guidance for Developing Genetically Modified Organisms)**. The application requires two components:

- Part A: A1 Form (General Information) and A2 to A6 (the Technical Dossier)
- Part B which provides information for the public register

The overall regulatory approval pathway for GMOs under the deliberate release legislation is outlined in **Figure 5** covering from early planning to operation and compliance.

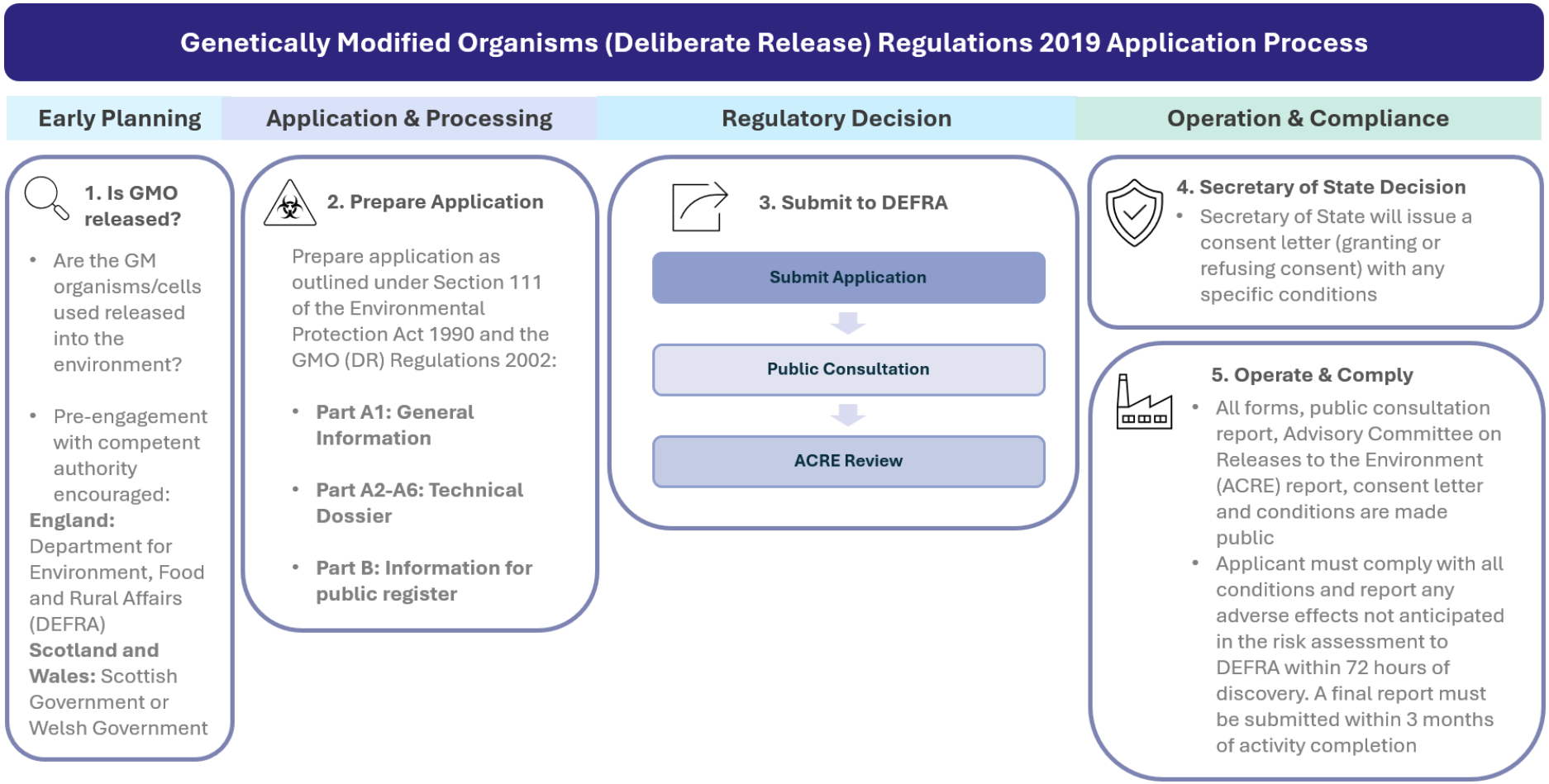


Figure 5. General application process for approved use of GMOs in Deliberate Release applications

The responsible person for each activity in the application process is outlined in **Figure 6**. The application undergoes public consultation and is reviewed by ACRE for DEFRA and the Devolved Administrations. If the application is approved, all forms, the consent letter and any conditions of approval are made public.

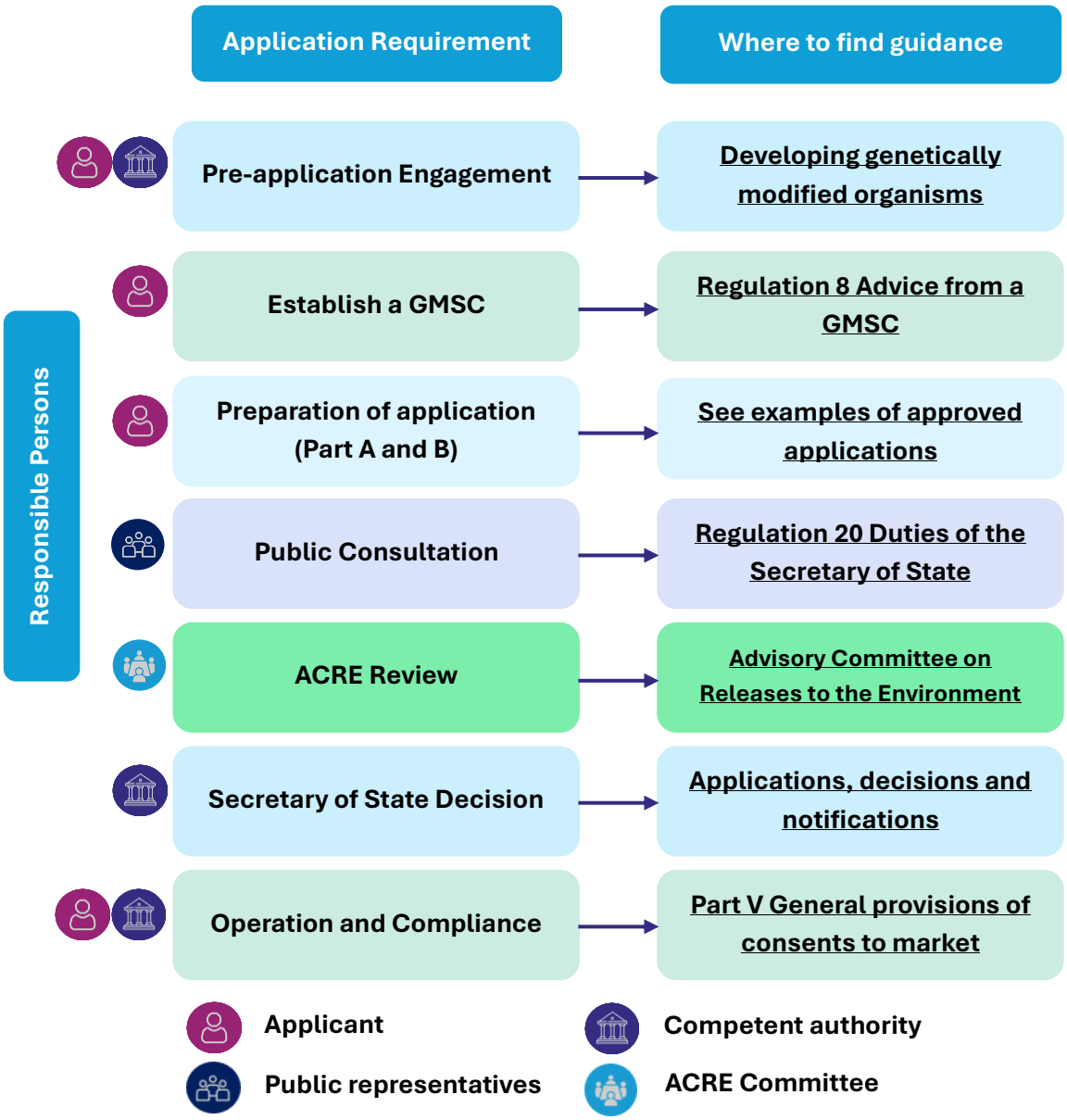


Figure 6. Responsible persons for GMO deliberate release application requirements and links to guidance

(I) Pre-Application Engagement

Before conducting any GMO work, applicants should engage with their relevant competent authority to discuss:

- The nature and form of the proposed release
- Environmental Risk Assessment (ERA) approach (See **Risk Assessment Methodology** section)
- Notification requirements before submitting a formal application

Competent Authority Contacts:

- England – gm-regulation@defra.gov.uk
- Northern Ireland - biodiversity.policy@daera-ni.gov.uk
- Scotland - GMInspectorate@sasa.gov.scot
- Wales - plant.health@gov.wales

(II) Prepare Application

Compile the application as outlined under Section 111 of the Environmental Protection Act 1990 and the GMO (Deliberate Release) Regulations 2002.

(III) Submit Application

Submit application including Part A and Part B to relevant competent authority who place it on the public register.

(IV) Public Consultation

The Secretary of State places the application on the public register and invites public representations for a set period of 60 days. This period allows for 12 days placement on the register (and for the applicant to advertise this in a national newspaper) and only after the 60 days from initial receipt of the application can a decision be made. Any member of the public or organisation may submit representations.

(V) ACRE Review

ACRE independently reviews the risk assessment and any public representations, then provides its advice to DEFRA. ACRE's assessment is published alongside the application.

(VI) Secretary of State Decision

DEFRA considers ACRE's recommendations along with public representations and advise the Secretary of State on issuance of a consent letter (granting or refusing consent) together with any conditions. HSE confirms agreement with the risk assessment regarding human health.

(VII) Operation and Compliance

The applicant must comply with any and all conditions issued with the consent letter. Any adverse effects not anticipated in the ERA must be reported to DEFRA within 72 hours of discovery. A final report must be submitted within three months of activity completion.

Information Required for Consent to Release a GMO – organisms other than higher plants

To apply for consent to release a genetically modified organism (GMO) other than a higher plant (e.g., microorganisms, animals, or insects) in the UK, you must submit a formal notification and technical dossier to the relevant competent authority. The application requires:

- a completed **Part A1 Form** (General Information)
- a completed **Part A2 to A6 Form** (Technical Dossier)
- a completed **Part B form**

Once submitted, the competent authority consults with ACRE during the review period. Each consent granted is published publicly including the application forms as well as a consent letter confirming consent and outlining any conditions and ACRE advice on DEFRAs **Genetically modified organisms: applications, decisions and notifications** page. Applicants are strongly **encouraged** to **consult with the appropriate national competent authority before completing an application** to ensure that necessary requirements are met before formal submission.

Part A1:

Part I: General Information

1. The name and address of the applicant and the name, qualifications, and experience of the scientist and of every other person who will be responsible for planning and carrying out the release of the organisms and for the supervision, monitoring and safety of the release (**following GDPR requirements on the public register**)
2. Title of the project

Part II: Information relating to the organisms

Characteristics of the donor, parental and recipient organisms

3. Scientific name and taxonomy
4. Usual strain, cultivar or other name
5. Phenotypic and genetic markers
6. The degree of relatedness between the donor and recipient or between parental organisms.
7. A description of identification and detection techniques.
8. The sensitivity, reliability (in quantitative terms) and specificity of detection and identification techniques.
9. A description of the geographic distribution and of the natural habitat of the organisms including information on natural predators, prey, parasites and competitors, symbionts and hosts.
10. The organisms with which transfer of genetic material is known to occur under natural conditions.
11. Verification of the genetic stability of the organisms and factors affecting that stability.

12. The following pathological, ecological and physiological traits:
    a. the classification of hazard according to existing Community rules concerning the protection of human health and the environment
    b. the generation time in natural ecosystems, and the sexual and asexual reproductive cycle
    c. information on survivability, including seasonability and the ability to form survival structures, including seeds, spores and sclerotia
    d. pathogenicity, including infectivity, toxigenicity, virulence, allergenicity, carrier (vector) of pathogen, possible vectors, host range including non-target organisms and possible activation of latent viruses (proviruses) and ability to colonise other organisms
    e. antibiotic resistance, and potential use of these antibiotics in humans and domestic organisms for prophylaxis and therapy
    f. involvement in environmental processes including primary production, nutrient turnover, decomposition of organic matter and respiration

13. The sequence, frequency of mobilisation and specificity of indigenous vectors and the presence in those vectors of genes which confer resistance to environmental stresses.
14. The history of previous genetic modifications.

Characteristics of the vector

15. The nature and source of the vector
16. The sequence of transposons, vectors and other non-coding genetic segments used to construct the genetically modified organisms and to make the introduced vector and insert function in those organisms.
17. The frequency of mobilisation, genetic transfer capabilities and/or methods of determination of the inserted vector.
18. The degree to which the vector is limited to the DNA required to perform the intended function.

Characteristics of the modified organisms

19. The methods used for the modification.
20. The methods used:
    a. to construct inserts and introduce them into the recipient organism Parent strain
    b. to delete a sequence
21. A description of any insert and/or vector construction
22. The purity of the insert from any unknown sequence and information on the degree to which the inserted sequence is limited to the DNA required to perform the intended function.
23. The methods and criteria used for selection
24. The sequence, functional identity and location of the altered, inserted or deleted nucleic acid segments in question and, in particular, any known harmful sequence.

Characteristics of the genetically modified organisms in their final form

25. A description of genetic traits or phenotypic characteristics and in particular any new traits and characteristics which may be expressed or no longer expressed
26. The structure and amount of any vector or donor nucleic acid remaining in the final construction of the modified organisms
27. The stability of the organism in terms of genetic traits
28. The rate and level of expression of the new genetic material in the organisms and the method and sensitivity of measurement of that rate and level
29. The activity of the gene product.
30. A description of identification and detection techniques, including techniques for the identification and detection of the inserted sequence and vector.
31. The sensitivity, reliability (in quantitative terms) and specificity of detection and identification techniques.
32. The history of previous releases or uses of the organisms.

33. In relation to human health, animal health and plant health:
    a. the toxic or allergenic effects of the non-viable organisms and/or their metabolic products
    b. the comparison of the organisms to the donor, recipient or (where appropriate) parental organism regarding pathogenicity
    c. the capacity of the organisms for colonization
    d. if the organisms are pathogenic to humans who are immunocompetent:
        i. diseases caused and mechanisms of pathogenicity including invasiveness and virulence
        ii. communicability
        iii. infective dose
        iv. host range and possibility of alteration
        v. possibility of survival outside of human host
        vi. presence of vectors or means of dissemination
        vii. biological stability
        viii. antibiotic-resistance patterns
        ix. allergenicity and x. availability of appropriate therapies
    e. Other product hazards

Part III: Information relating to the conditions of release

The release

34. A description of the proposed deliberate release, including the initial purpose or purposes of the release and any intention to use the genetically modified organisms as or in a product in the future
35. The intended dates of the release and time planning of the experiment including frequency and duration of releases.
36. The preparation of the site before the release
37. The size of the site.
38. The method or methods to be used for the release.
39. The quantity of organisms to be released.
40. The disturbance of the site, including the type and method of cultivation, mining, irrigation, or other activities.
41. Worker protection measures taken during the release.
42. Post-release treatment of the site
43. The techniques foreseen for elimination or inactivation of the organisms at the end of the experiment or other purposes of the release.
44. Information on, and the results of, previous releases of the organisms and in particular, releases on a different scale or into different ecosystems

The environment (both on the site and in the wider environment)

45. The geographical location and national grid reference of the site or sites onto which the release will be made, or the foreseen areas of use of the product.
46. The physical or biological proximity of the site to humans and other significant biota.
47. The proximity to significant biotopes, protected areas or drinking water supplies.
48. The climatic characteristics of the region or regions likely to be affected
49. The geographical, geological and pedological characteristics.
50. The flora and fauna, including crops, livestock and migratory species.
51. The description of target and non-target ecosystems likely to be affected.
52. A comparison of the natural habitat of the recipient organisms with the proposed site or sites of release.
53. Any known planned developments or changes in land use in the region which could influence the environmental impact of the release.

Part IV: Information relating to the interactions between the organisms and the environment

Characteristics affecting survival, multiplication and dissemination

54. The biological features which affect survival, multiplication and dispersal.
55. Known or predicted environmental conditions which may affect survival, multiplication and dissemination, including wind, water, soil, temperature and pH.
56. Sensitivity to specific agents.

Interactions with the environment

57. The predicted habitat of the organism.
58. Studies of the behaviour and characteristics of the organisms and their ecological impact carried out in simulated natural environments, such as microcosms, growth rooms and greenhouses.
59. The capability of post-release transfer of genetic material:
    a. from the genetically modified organisms into organisms in affected ecosystems
    b. from indigenous organisms to the genetically modified organisms
60. The likelihood of post-release selection leading to the expression of unexpected or undesirable traits in the genetically modified organisms.
61. The measures employed to ensure and to verify genetic stability, the description of genetic traits which may prevent or minimise dispersal of genetic material and methods to verify genetic stability.
62. The routes of biological dispersal, known or potential modes of interaction with the disseminating agent, including inhalation, ingestion, surface contact and burrowing.
63. A description of ecosystems to which the organisms could be disseminated.
64. The potential for excessive population increase of the organisms in the environment.
65. The competitive advantage of the organisms in relation to the unmodified recipient or parental organism or organisms.
66. The identification and description of the target organisms if applicable

67. The anticipated mechanism and result of interaction between the released organisms and the target organisms if applicable.
68. The identification and description of non-target organisms which may be adversely affected by the release of the genetically modified organisms, and the anticipated mechanisms of any identified adverse reaction.
69. The likelihood of post-release shifts in biological interactions or in the host range.
70. The known or predicted interactions with non-target organisms in the environment, including competitors, prey, hosts, symbionts, predators, parasites and pathogens.
71. The known or predicted involvement in biogeochemical processes.
72. Any other potentially significant interactions with the environment.

Part V: Information on monitoring, control, waste treatment and emergency response plans

Monitoring techniques

73. Methods for tracing the organisms and for monitoring their effects.
74. Specificity (to identify the organisms and to distinguish them from the donor, recipient or, where appropriate, the parental organisms), sensitivity and reliability of the monitoring techniques.
75. Techniques for detecting transfer of the donated genetic material to other organisms.
76. Duration and frequency of the monitoring.

Control of the release

77. Methods and procedures to avoid and/or minimise the spread of the organisms beyond the site of release or the designated area for use.
78. Methods and procedures to protect the site from intrusion by unauthorised individuals.
79. Methods and procedures to prevent other organisms from entering the site.

Waste treatment

80. Type of waste generated.
81. Expected amount of waste.
82. Description of treatment envisaged.

Emergency response plans

83. Methods and procedures for controlling the organisms in case of unexpected spread.
84. Methods, such as eradication of the organisms, for decontamination of the areas affected.
85. Methods for disposal or sanitation of plants, animals, soils and any other thing exposed during or after the spread.
86. Methods for the isolation of the areas affected by the spread.

87. Plans for protecting human health and the environment in case of the occurrence of an undesirable effect.

Part VI: A description of the methods used or a reference to standardised or internationally recognised methods used to compile the information required by this schedule, and the name of the body or bodies responsible for carrying out the studies

Parts A2–A6: Technical Dossier

Part A2: Data or results from any previous releases of the GMO

Provide information on data or results from any previous releases of this GMO by you either inside or outside the European Community (especially the results of monitoring and the effectiveness of any risk management procedures).

Part A3: Details of previous applications for release

Give details of any previous applications to release the GMO made to the Secretary of State under the 2002 Regulations or to another Member State under the Deliberate Release Directive 2001/18/EC

Part A4: Risk assessment and a statement on risk evaluation

Risk assessments on:

- Environmental impact of the release of the GMOs
- Factors affecting dissemination
- Human health impact
- Monitoring the GMO
- Emergency response

Risk evaluations on:

- Pathogenicity
- Production of biologically active/toxic products
- Genetic stability; reversion to virulence; or recombination with other pneumonoviruses
- Survival/dissemination

Part A5: Assessment of commercial or confidentiality of information contained in this application

Identify clearly any information that is considered to be commercially confidential. A clear justification for keeping information confidential must be given.

Part A6: Statement on whether detailed information on the description of the GMO and the purpose of release has been published

Make a clear statement on whether a detailed description of the GMO and the purpose of the release have been published, and the bibliographic reference for any information so published (included to assist with protection of the applicant's intellectual property rights, which may be affected by the prior publication of certain detailed information e.g. by its inclusion on the public register).

Part B: Information about the release application to be included on the public register

- B1: The name and address of the applicant
- B2: A general description of the genetically modified organisms in relation to which the application is being made
- B3: The location at which the genetically modified organisms are proposed to be released
- B4: The purpose for which the genetically modified organisms are proposed to be released (including any future use to which they are intended to be put)
- B5: The intended dates of the release
- B6: The environmental risk assessment
- B7: The methods and plans for monitoring the genetically modified organisms and for responding to an emergency

Risk Assessment Methodology

In the UK, the Environmental Risk Assessment (ERA) principles and methodology for GMOs follows those outlined in Annex II of the Deliberate Release Directive (Directive 2001/18/EC). It establishes a case-by-case evaluation of potential direct, indirect, immediate, or delayed adverse effects on human health and the environment. The six steps of the ERA process are:

Step 1: Problem formulation including identification of hazard and exposure pathways

Defines the scope and objectives of the ERA and identifies potential hazards. It involves characterising the GMO (phenotypic and genomic characteristics); describing the environment of the proposed release; and provide a **problem formulation**.

Step 2: Hazard Characterisation:

Hazard characterisation identifies and evaluates the potential adverse effects of the GMO.

Major hazards will include:

- Persistence and invasiveness, including gene flow
- Effects on target and non-target organisms
- Effects on specific habitats and ecosystem
- Impacts on human and animal health

Step 3: Exposure Characterisation

Exposure characterisation assesses the likelihood, scale, and route by which the identified hazard could come into contact with the identified target as determined in Step 1 - the problem formulation.

Step 4: Risk Characterisation

Risk characterisation integrates the outputs of hazard and exposure characterisation to estimate the magnitude, probability, and reversibility of potential adverse effects. Risk characterisation takes explicit account of uncertainty and precautions, and can be characterised as:

- Negligible risk
- Potential risk subject to risk management
- Unacceptable risk

Step 5: Risk Management Strategies

Risk management strategies must be proposed to reduce or eliminate potential adverse effects, where risks are not negligible. Strategies include for example: isolating a site from non-GM crops or ecologically sensitive habitats, refuge requirements, monitoring obligations, and geographic restrictions.

Step 6: Overall Risk Evaluation and Conclusions

The overall risk evaluation integrates all ERA outputs into a coherent conclusion on whether the GMO in its intended use and receiving environment can be considered safe.

Guidance on Inactivation Techniques for Genetically Modified Microorganism (GMM) and Disposal of Associated Waste

Purpose of the Inactivation Techniques Guidance

Under the UK Genetically Modified Organisms (Contained Use) Regulations 2014, all facilities working with genetically modified microorganisms (GMMs) must ensure that contaminated material and waste are managed to prevent exposure to humans and the environment. This guidance document outlines suggested inactivation techniques and disposal methods for waste arising from work with GMMs, specifically for Class 1 and Class 2 GMMs under Contained Use activities. It also offers guidance on managing the persistence, spread, and environmental fate of the organisms intended for Deliberate Release.

Regulatory Guidance on Waste Inactivation for Contained Use Activities

For GMMs deployed under the Genetically Modified Organisms (Contained Use) Regulations 2014, risk assessments must consider the exposure of humans and the environment and determine appropriate containment measures. The Health and Safety Executive (HSE) guidance specifically treats waste and effluent as potential routes of exposure. For Contained Use, the regulations are **risk-based** rather than prescribing one universal inactivation technology. The appropriate inactivation technique depends on the containment classification, organism, activity and waste stream. The chosen containment measure needs to be demonstrated as being effective for the specific GMM being used. As part of Regulation 5 risk assessment of contained use involving micro-organisms, the risk assessment must take full account of all aspects of the planned work, including handling, transport, work area decontamination, inactivation of GMMs, disposal and waste management including where waste contractors are used. The HSE should be notified of all work including waste disposal and management. The general approach for waste inactivation of GMMs under Contained Use is outlined in **Figure 7**.

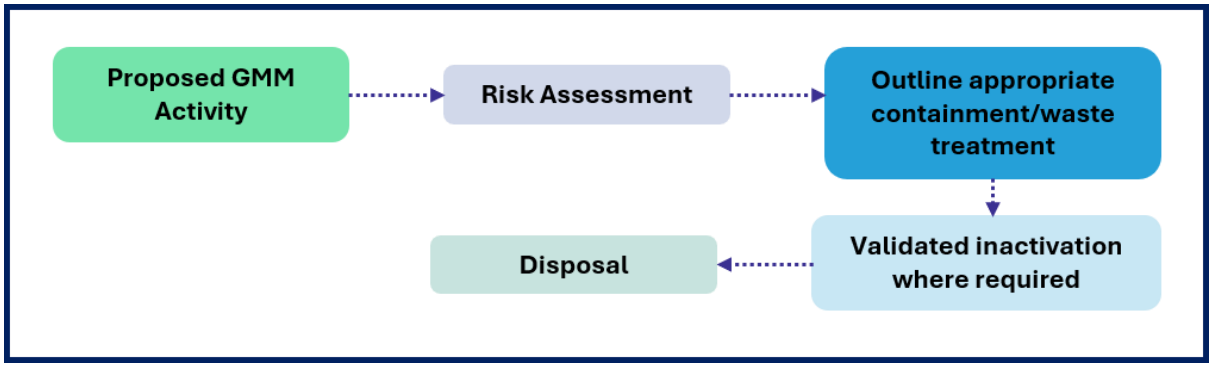


Figure 7. General regulatory approach for waste inactivation of GMMs used under Contained Use

For regulatory guidance on waste inactivation and management, see guidance on Regulations Schedule 8 and SACGM Compendium of guidance – Part 3

When must GM waste be inactivated?

For Contained Use activities, there are variations in the requirements for inactivation depending on the class of the Contained Use activity as summarised in **Table 4**.

Table 4: Requirements for inactivation of genetically modified microorganisms in contaminated material and waste by containment class

Contained Use class	Waste Inactivation Requirement
Class 1	Required by validated means where and to the extent the risk assessment shows it is required
Class 2	Required by validated means
Class 3	Required by validated means, with waste inactivated within the laboratory suite
Class 4	Required by validated means, with waste inactivated within the laboratory

Class 1 Contained Use

For Class 1 activities, waste does not automatically require inactivation; however, the risk assessment should determine and document whether it is necessary. Inactivation may be omitted **only if all** the following conditions are met:

The GM organism has no potential to cause harm to human health or the environment

The GM organism is biologically contained e.g. multiple disabling mutations or auxotrophy as restrictive nutrient requirements cannot be met outside the laboratory

It cannot establish or multiply outside the laboratory

It cannot transfer its genetic material to other microorganisms e.g. non-mobilisable plasmids

For more information see guidance on Regulation 19 of the Contained Use Guidance

If **all four conditions are met**, the GM waste can be removed directly off site and does not require inactivation. If any of these conditions are not met, waste should be inactivated before disposal.

Class 2, 3 and 4 Contained Use

For all Class 2-4 activities, contaminated waste **must be inactivated using a validated method** before disposal. Validated techniques include autoclaving, chemical disinfection and off-site treatment which are further discussed in the validated inactivation section below. The types of waste that require inactivation are outlined in **Figure 8**.

See Schedule 8 Tables 1a and 2 of the Contained Use 2014 Regulations

Types of waste requiring consideration

Contained Use risk assessments should address all waste streams generated by the Contained Use activity. Examples of the types of waste requiring inactivation consideration are shown in **Figure 8**.

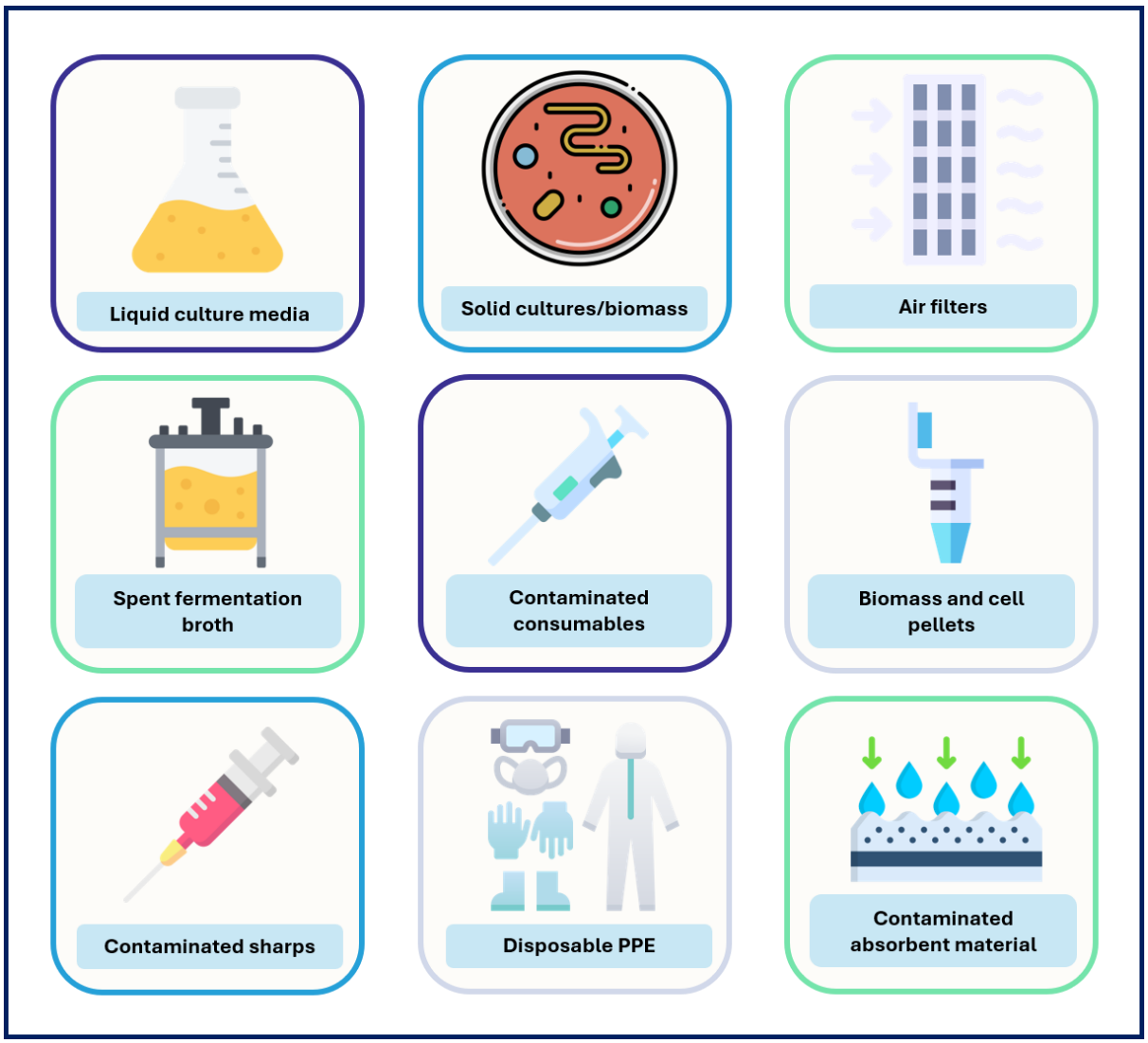


Figure 8. Examples of GM waste streams requiring assessment for inactivation

Inactivation techniques

Where required, GMM waste must be inactivated before disposal. Various inactivation techniques have been tested by researchers as summarised in **Figure 9**. There are no approved techniques, only validated techniques based on evidence. The chosen technique should be suitable for the GMM and the activity.

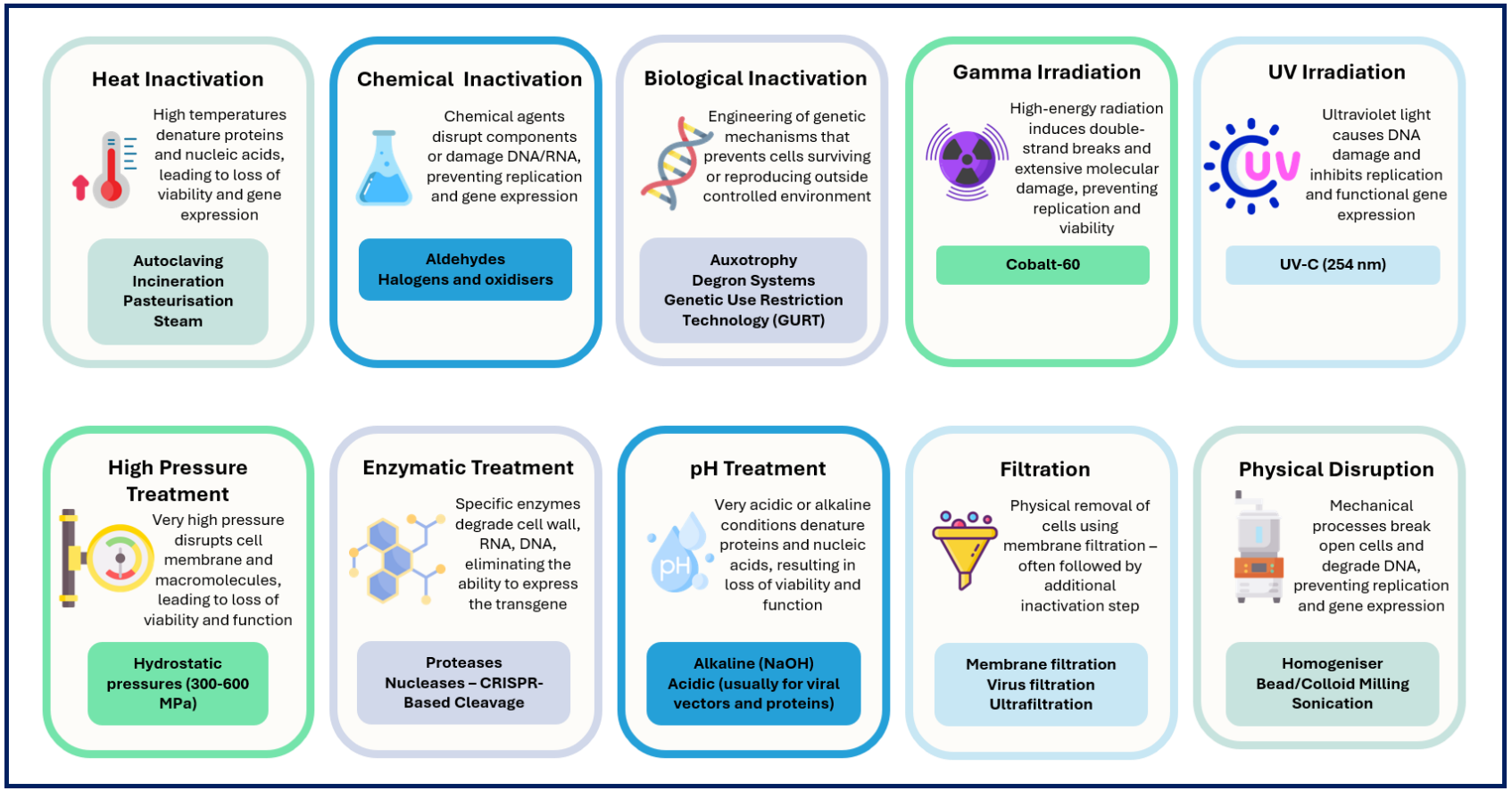


Figure 9. Different GMM inactivation techniques

Selection of an inactivation method should be based on factors including the **characteristics of the GMM**, the **nature and volume of the waste**, the **composition of the waste matrix**, the **proposed treatment process** and the **potential consequences of treatment failur**e. The selected method should be demonstrated to be effective under the conditions in which it will be applied. Validation should take account of relevant worst-case conditions, including the characteristics and concentration of the GMM and factors within the waste matrix that could reduce treatment efficacy. Critical treatment parameters should be defined and routinely monitored, with appropriate procedures in place for treatment failure or deviation from validated conditions. The factors to consider are summarised in **Table 5.**

Table 5: Key factors to consider when selecting a GMM inactivation method

Factor	What should be considered?
Properties of the GMM	Susceptibility to heat, chemicals, radiation or other treatment; ability to survive outside its host/environment; presence of spores or other resistant forms; environmental persistence
Nature of the genetic modification	Whether the modification could alter survival, environmental persistence, pathogenicity, toxin production, host range or susceptibility to the proposed treatment
Type of waste	Liquid culture, wastewater, sludge, biomass, solid waste, contaminated PPE, filters, sharps, equipment, etc.
Concentration and quantity of GMM	Initial viable cell concentration and total volume/mass to be treated. High biomass loads may require different treatment conditions from small laboratory volumes
Composition of the waste	Organic material, proteins, suspended solids, salts, detergents, buffers and other components can interfere with chemical or thermal inactivation
Scale	A method validated at laboratory scale may not automatically be effective at pilot or industrial scale
Downstream disposal	Treatment should be considered together with what happens afterwards. Inactivation may need to occur before discharge, transport or disposal

Practical and occupational considerations	Worker exposure, chemical hazards, heat/pressure hazards, compatibility with equipment and materials, and the feasibility of implementing the procedure consistently

Validated inactivation

The Health and Safety Executive (HSE) does not explicitly require a specific inactivation technique but instead requires that the chosen method for inactivation must be a validated technique that has been demonstrated to consistently achieve the required level of inactivation for the organism and waste stream concerned. A single technique may be sufficient where the required outcome has been demonstrated. The following approaches may provide validated inactivation when their efficacy for the intended use has been demonstrated **(HSE L29, paragraph 135)**:



Steam sterilisation (autoclave)

Applications: Solid waste, culture media, glassware

Validation: Biological indicators, temperature/time records, routine performance testing



Chemical disinfection

Applications: Liquid cultures, equipment surfaces

Validation: Appropriate disinfectant concentration, contact time and compatibility with organism



Off-site treatment (e.g. removal to an incinerator)

Applications: Clinical waste, contaminated disposables

Validation: Licensed contractor, documented treatment efficacy, and compliance with waste legislation

Validation requirements

Validation should demonstrate that the selected treatment:

- Is effective for the specific GMM
- Works across the waste matrix (liquid, sludge, solids, filters etc.)
- Is reproducible
- Is routinely monitored

Validation evidence includes:

- Autoclave cycle validation using biological indicators
- Routine temperature and pressure logging
- Disinfectant efficacy studies
- Documented standard operating procedures (SOPs)
- Maintenance and calibration records

The SACGM Compendium of Guidance defines validation as:

Establishing documented evidence that a disinfection process will consistently inactivate target organisms under defined conditions of use

The HSE specifically notes that disposal of **waste and effluents** should be considered during preparation of the risk assessment because they may provide routes for environmental exposure. For a regulatory application, evidence should be provided to cover various requirements as outlined in **Table 6**.

Table 6: Evidence requirements to demonstrate validated inactivation of GMM

Requirement	What you should demonstrate
Target organism	The treatment is effective against the specific GMM
Waste matrix	Treatment works in the actual waste
Treatment parameters	Define temperature/time, chemical concentration/contact time

Validation	Evidence that the process reliably achieves the required level of inactivation
Monitoring	Parameters monitored during routine operation
Failure detection	How treatment failure is identified
Contingency	What happens to untreated waste following failure
Records	Treatment, maintenance, and validation records retained
Revalidation	Triggered following significant changes to equipment/process

These requirements are particularly important for large-scale GMM processes, as the same treatment at lab scale may not work reliably for large volumes.

Autoclave

An autoclave does not have to be the method of inactivation used; however, access to an autoclave is **required** as part of the notification process. The specific requirement to ensure an autoclave is available is because it provides absolute physical sterilisation through validated steam under pressure and provides a suitable alternative should the chosen inactivation method is unavailable or unfit for purpose. Different containment levels require different autoclave arrangements **(Table 7)**. If an autoclave is not present in the building or laboratory, a derogation must be sought from the HSE to allow Class 2-4 work to continue.

Table 7: Autoclave requirements for different laboratory containment levels

Containment Level (CL)	Autoclave requirement
CL1	Required on site
CL2	Required in the building
CL3	Required in the laboratory suite
CL4	Double-ended autoclave required in the laboratory

Chemical disinfection

Chemical disinfection can provide validated inactivation when efficacy for the intended use has been demonstrated and has the advantage of not requiring the use of a pressure vessel such as an autoclave. There are several factors to consider when planning to use disinfection for inactivation of GMMs. These include:

- Nature of the microorganism(s)
- Nature of the material being disinfected
- The presence/quantity of organic material
- Concentration of the disinfectant and contact time
- Circumstances under which disinfection is required (e.g. spillages or waste inactivation)
- Health hazards presented by the disinfectant

Commonly used chemical disinfectants include:

- Alcohols e.g. ethyl alcohol and isopropyl alcohol
- Chlorine compounds e.g. sodium hypochlorite (household bleach)
- Quaternary ammonium compounds ("Quats") e.g. benzalkonium chloride
- Oxidising agents e.g. hydrogen peroxide and peracetic acid
- Aldehydes e.g. glutaraldehyde and formaldehyde

Off-site disposal

Off-site disposal of GM waste by a licenced contractor is a validated option for inactivation. If removing waste directly for incineration without inactivation on site, arrangements should be well documented in a risk assessment outlining measures to reduce accidental spillages and indicating what class the waste before incineration. Class 1 waste would generally be treated as **offensive waste** and class 2 waste would be classified as **infectious waste.**

The site of disposal must also comply with the Contained Use Regulations for the handling of GMMs that have not been inactivated. Agreement for the disposal of waste by a third party must be obtained from the competent authority

If the GM waste has been inactivated through a validated technique on site before off-site disposal, it is no longer regulated under the GMO (Contained Use) Regulations and is subject to general waste legislation. However, the risk assessment should consider the most appropriate waste route following on site inactivation (if used). The user has a Duty of Care for their waste up until final destruction.

If renting lab space e.g. biotech start-up, consult with the host lab to discuss requirements with the waste contractor. In the case of multiple occupancies, each applicant responsible for the contained use carried out in each organisation will need to notify separately

Regulatory Guidance on Waste Inactivation for Deliberate Release Activities

For GMMs deployed under the Genetically Modified Organisms (Deliberate Release) Regulations 2002, which apply in England, Scotland, and Wales under separate competent authorities (Northern Ireland is governed under a separate regulatory framework, the Genetically Modified Organisms (Deliberate Release) Regulations (Northern Ireland) 2003 (amended by the 2019 regulations), there isn't a general provision regarding inactivation since Deliberate Release involves intentional environmental release. Therefore, regulation focuses on managing the persistence, spread, and environmental fate of the organism, rather than requiring universal sterilisation of all GM waste before disposal. Deliberate Release activities require prior approval from the relevant UK competent authority (see EBIC Guidance on Deliberate Release) and are assessed on a case-by-case basis through an **environmental risk assessment (ERA)**. The competent authority may impose **consent conditions** requiring specific waste treatment or decontamination measures where these are necessary to protect human health or the environment. For a Deliberate Release activity, waste management considerations should include:

- What GMM-containing waste is generated?
- Where can viable GMM enter the environment?
- What is the concentration/quantity of viable GMM?
- What happens to the GMM during the proposed waste-treatment process?
- What evidence demonstrates effective inactivation?
- What happens if the treatment system fails?
- How are residual biomass, sludge, filters, equipment and wastewater managed?
- How is the site decommissioned at the end of the trial?

For a Deliberate Release involving GMMs, the ERA should evaluate all materials that could contain viable GM organisms including those outlined earlier in **Figure 8** and additional materials that could be used in a Deliberate Release activity such as those in **Figure 10.**

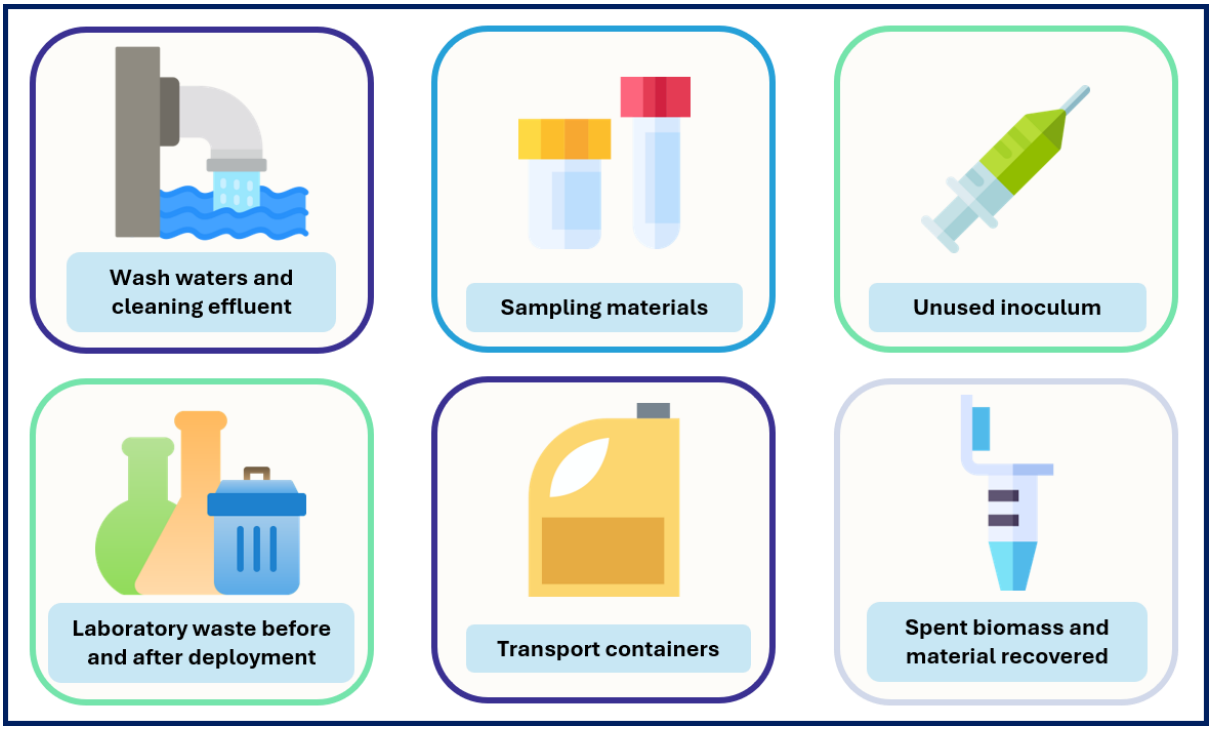


Figure 10. Examples of additional waste streams to consider in the environmental risk assessment for Deliberate Release activities

Although no specific techniques are recommended in the Deliberate Release regulations, the applicant should inactivate GM waste as outlined in the section above on **Inactivation Techniques** for each waste stream. Inactivation of GM waste is used to prevent **unintentional secondary releases** outside the authorised release area, rather than because the Deliberate Release regulations mandate a specific inactivation method.

For Deliberate Release applications, it is important to note that whilst the authorised environmental release involves the intentional release of the GMM into a receiving environment, the management of associated waste and materials must comply with the consent conditions and environmental risk assessment. All other materials, waste and equipment that are not intended for environmental exposure are expected to be subject to inactivation, so they do not create uncontrolled releases beyond those covered in the consent.

See Schedule 2 Part V of the Deliberate Release Regulations 2002

Decommissioning at the End of Deliberate Release activity

Most Deliberate Release consents include provisions for managing the site after the Deliberate Release activity. Depending on the organism and application, these may include:

- Removal and treatment of remaining cultures or biomass
- Decontamination of equipment
- Monitoring for persistence of the GMO
- Management of contaminated soils, sediments or sludge where relevant
- Post-release surveillance to verify that the organism behaves as predicted in the ERA

Guidance Case Studies

EBIC Case Study Examples

Purpose of the Case Studies

Various practical case study examples are presented to illustrate the types of regulatory considerations that may arise for the use of GMMs for different environmental applications. The case studies cover a range of potential regulatory pathways that fall under either Contained Use and Deliberate Release. Applications range from biobased chemical production to wastewater treatment.

Each case study details the environmental problem being addressed; the engineering biology solution, case study assumptions; the regulatory pathway mapped and evidence required; other regulatory requirements; and examples of companies with similar technologies for comparison.

The EBIC Case Studies are as follows:

- Case Study 1: Biobased Products from Waste
- Case Study 2: Sustainable Chemicals
- Case Study 3: Environmental Biosensors
- Case Study 4: Phytoremediation of Contaminated Soils
- Case Study 5: Wastewater Treatment
- Case Study 6: Biofuel Production

The case study examples are not intended to represent an exhaustive or fully representative list of GMMs for environmental solutions, but as examples of how different GMM environmental solutions have different regulatory pathways and to emphasise there is not a single one-size-fits all regulatory pathways for all GMM technologies under the current Regulations.

Case Study 1: Production of Biobased Products from Mixed Waste Streams

The Problem

Various chemical products are used in our day-to-day lives, from pharmaceuticals to household cleaning products. The chemical industry relies heavily on processing fossil-fuel derived feedstocks to produce these chemicals, **with approximately 95% of feedstocks derived from oil, gas, and coal**. The finite nature of fossil fuels coupled with significant greenhouse gas emissions from their processing and the geopolitical uncertainties that increasingly compromise supply chains has triggered a desire to find sustainable biobased alternatives.

Alternative feedstocks for chemical production are required to replace our dependency on fossil fuels. One source being explored is plastic waste, which constitutes both an alternative feedstock and a circular feedstock as it addresses another key environmental issue. Global plastic waste generation is projected to reach **approximately 225 million tonnes annually.** Plastic pollution is a global problem, with **19-23 million tonnes** of plastic waste leaking into aquatic ecosystems, polluting lakes, rivers, and seas which ultimately threatens wildlife and human health. Global awareness of plastic waste and the environmental problems associated with it has increased in recent years. Due to the properties of synthetic polymers, they are highly resistant to degradation, resulting in ineffective end-of-life management. Conventional recycling involves mechanical and chemical recovery, which are not only energy-intensive and selective for material types, but also only recover **less than 10% of end-of-life plastics**. As a result, effective plastic recycling or upcycling technologies are required to tackle the problem.

The EngBio Solution

An upcoming approach that tackles both problems outlined above is the use of Engineering Biology to valorise plastic waste streams into bio-based chemicals and materials **(Figure 11)**. Biological valorisation using specific catalytic enzymes and engineered microorganisms offers an alternative route to convert these waste streams into value-added outputs, providing closed-loop recycling for plastic waste under a more sustainable and efficient process, with low energy inputs and lower greenhouse gas emissions. Typically, microbial plastic upcycling approaches are target a plastic polymer from one specific waste stream; e.g. nylon from textiles only instead of from various waste streams. However, post-consumer plastic waste streams are inherently variable at large scale, and the use of plastic waste feedstocks will likely be from mixed streams. The bioprocessing of plastic waste into high-value chemicals operates at lower temperatures and therefore lower CO_2 emissions, reducing the environmental impact associated with the production of these common chemicals. The overall goal of this platform supports the core principles of green chemistry, to replace synthetic chemicals with bio-based alternatives and addresses several critical environmental challenges – plastic pollution, rising CO_2 levels, and reliance on fossil fuels, while generating commercially valuable outputs and creating a circular economy.

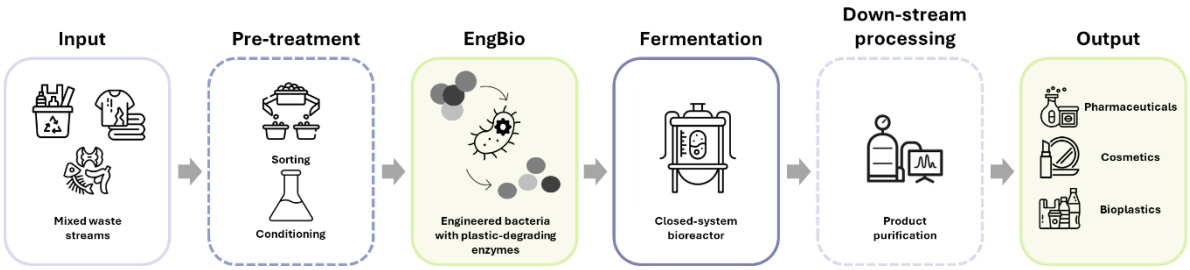


Figure 11. *General process of microbial waste valorisation into value-added products*

Case Assumptions

Several naturally occurring microorganisms have been discovered with the ability to degrade plastic into an energy source due to specific enzymes that alter long hydrocarbon chains typical of many types of plastics. The process involves the excretion of extracellular enzymes which attach to the surface of the plastic and **hydrolyse it into short polymer intermediates** which are assimilated by the microbes as a carbon source. Most reported enzymes degrade hydrolysable plastics such as polyesters, polyamides, and polyurethanes. These enzymes include PETase, MHETase, cutinase, and nylonase. Initial research focused on describing the biodegradation of plastics and monomer recovery, but **recent advancements** have explored the valorisation of plastics using enzymatic biocatalysis into the production of value-added products. For this case study, it is assumed that a company is using an engineered PETase expressed in *Pseudomonas putida* (*P. putida*) KT2440 to valorise PET waste into the metabolic intermediate terephthalic acid (TA) that is further processed into adipic acid, a precursor for nylon production.

Regulatory Pathway and Evidence Requirements

This case study involves the use of a closed-system bioreactor under conditions designed to prevent contact of the GMO with humans and the environment. Therefore, the case study falls under **The Genetically Modified Organisms (Contained Use) Regulations 2014.** A work through of risk assessment considerations associated to the engineering of *P. putida* to valorise PET waste is outlined along with evidence requirements to support the risk assessment approval pathway **(Figure 12)**.



Figure 12. *Example walkthrough of risk assessment and evidence requirements associated with engineered P. putida for PET waste valorisation into value-added products*

Other Regulatory Requirements

Environment Agency (Environmental Permit)

- Environment Permit application for waste treatment will be required as it involves the use of plastic waste as a feedstock
- Ensure consideration of industrial emissions & waste management, processes, feedstock type and quantity, evidence of monitoring and reporting

UK REACH (HSE Chemicals Regulation Division)

- If producing ≥ 1 tonne per year legal entity, submit a dossier (IUCLID) to UK REACH and provide evidence of physico-chemical properties, human health data, environmental data, and exposure scenarios

Similar Cases

For comparison:

Carbios (France) has demonstrated successful scaling-up of enzymatic hydrolysis of PET. The bioprocesses developed by CARBIOS requires the use of GMOs, which are used for the process itself or for the production of enzymes. In accordance with Directive 2009/41/EC of May 6, 2009, GMOs used required a Class 1 confined environment. To minimise risks of releasing the GMOs into the natural environment, they demonstrated the GMOs are destroyed at the end of the production phase by thermochemical means.

Epoch Biodesign (UK) have developed a solution to tackle the recycling of waste plastic through innovative enzyme engineering. The company uses AI to engineer and optimise enzymes involved in depolymerising nylon into its initial monomers for nylon recycling. The optimised enzymes are likely to be expressed into a microbial chassis. Based on current information, Epoch Biodesign are at TRL4-6 and would be considering market regulatory pathways.

For contrast:

Blue Cycle (Netherlands) aimed to convert plastic waste into oil. The company went bankrupt in 2024 due to high costs but also community backlash as residents residing near the plant filed numerous environmental complaints over odours. Environmental compliance and emission management was not well established, leading to the community and environmental scrutiny.

The Problem

The chemical industry is involved in **nearly every aspect of the modern-day life**. The industry relies heavily on processing fossil-fuel derived feedstocks to produce synthetic chemical products, and as such, these processes lead to the release of billions of tonnes of carbon dioxide (CO_2). Chemicals produced from oil and gas make up 90% of all raw materials, with the largest consumers of petrochemicals being fertilisers, plastics and textiles which make up **70% of the total demand**. Given that fossil fuels are a finite resource, and with rapid population growth, increasing industrialisation, and rising geo-political uncertainty, there is considerable pressure on finite resources including fossil fuels. Additionally, the increasing scale of industrial activities, scientists have seen an increase in detection of chemical signatures in various extreme environments from the **highest mountains** to the **deepest oceans**, as well as in the human food chain. Many synthetic chemicals are non-biodegradable and persist in the environment for a long time. There is an urgent need to find **sustainable alternatives** that reduce environmental pollution and are suitable alternatives to industrial chemicals.

The EngBio Solution

Biomanufacturing using microorganisms to transform **low-cost carbon feedstocks into cleaner alternatives to synthetic chemicals** has become a promising approach to replace traditional, inefficient and unsustainable manufacturing of various fossil-fuel based products (**Figure 13**). Fossil-based feedstocks are no longer considered the sole foundation of the chemical industry as the shift to alternative feedstocks become increasingly appealing as a renewable and environmentally friendly alternative. For example, biosurfactants are a biodegradable surface-active alternative to chemical surfactants. Bioplastics are produced from renewable feedstocks and are designed as a bio-based alternative to synthetic plastics. Bio-based dyes offer a cleaner alternative to synthetic-coloured dyes in the textile industry, which often uses large amounts of toxic chemicals. In the past, sustainable feedstocks included plant-derived sugars such as sugarcane. However, with the increasing demand for food production and limited agricultural land, the use of plant-derived sugars restricts scaling up these processes. Instead, alternative feedstocks such as utilising the agricultural residues i.e. the organic by-products from plant matter and gas feedstocks e.g. CO_2 and methane, are becoming emerging renewable feedstocks in EB.

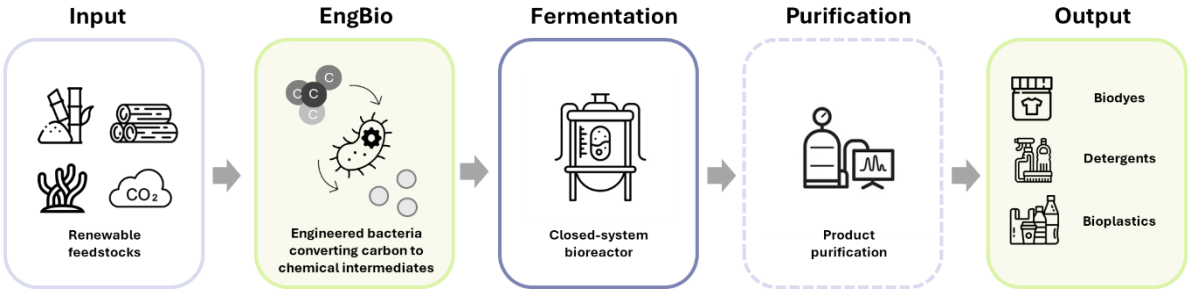


Figure 13. *General process of the biomanufacturing of sustainable chemical alternatives*

Case Assumptions

Most examples follow a similar framework, where genes involved in the expression of the specific protein to produce the compound of interest is identified from a specific organism and engineered into a microorganism to produce the compound of interest at larger scale using renewable feedstocks as a carbon source. Naturally, the bacterial species that produce these biobased compounds are environmental bacteria such as *Cupriavidus necator* which produce PHAs or *Streptomyces coelicolor* which produce natural pigments. Microbial chassis such as *Escherichia coli*, *Bacillus* species, and *Pseudomonas* species are often genetically engineered for this technology. For CO_2 capture, cyanobacteria are commonly used due to their natural ability to capture carbon. In the case of cyanobacteria where it already has the natural ability to capture CO_2, gene editing techniques such as CRISPR-Cas systems are commonly used to edit the genes involved in carbon-fixing pathways to convert CO_2 into biobased compounds. For this case study, the technology involves using engineered cyanobacteria *Synechococcus elongatus* UTEX 2973 to convert CO2 feedstock into biobased compounds under contained-use conditions to produce products such as hyaluronic acid for personal care.

Regulatory Pathway and Evidence Requirements

This case study involves the use of a closed-system bioreactor under conditions that limit contact of the GMO with humans and the environment. Therefore, the case study falls under **The Genetically Modified Organisms (Contained Use) Regulations 2014.** A work through of the risk assessment considerations associated to the engineering of a Cyanobacteria to convert CO_2 into sustainable chemical alternatives is outlined along with evidence requirements to support the risk assessment approval pathway **(Figure 14).**



Figure 14. *Example walkthrough of risk assessment and evidence requirements associated to engineered Synechococcus for converting CO_2 into sustainable chemicals*

Other Regulatory Requirements

Environment Agency

- If using CO_2 as a feedstock, the technology falls under Carbon Capture, Usage, and Storage (CCUS)
- Obtain environmental permit for this technology
- See Post-combustion carbon dioxide capture: emerging techniques - GOV.UK for more information

UK REACH (HSE Chemicals Regulation Division)

- If producing ≥ 1 tonne per year legal entity, submit a dossier (IUCLID) to UK REACH and provide evidence of physico-chemical properties, human health data, environmental data, and exposure scenarios

Similar Cases

For comparison

Deep Blue Biotech (UK) have engineered cyanobacteria to capture CO_2 to produce high-value molecules using water, light, and CO_2 and have demonstrated this with hyaluronic acid. The engineered cyanobacteria are cultured in a water-based photo bioreactor which is exposed to light and CO_2 and the cells break down CO_2 into valuable chemicals by photosynthesis.

neo-fossil (UK) have developed a carbon-negative technology that takes up CO_2 to convert into chemical compounds. The technology involves identifying genes from ancient plants that absorb CO_2 and engineer the pathway into bacteria with these genes along with the genes involved in converting CO_2 into precursors of the compound of interest. The compounds are then extracted and sold as carbon-negative products to be used in products such as concrete aggregates and insulation.

Colorifix (UK) have developed a technology to produce biobased coloured dyes for the textile industry. Different organisms are identified for their ability to produce a particular pigment and the genes involved in the production of that pigment are identified. The genes of interest are then heterologously expressed in a recombinant chassis. Colorifix provide the GMO as a freeze-dried sample and sell this to the customer, e.g. a textiles company, where they will be grown in bioreactors. The subsequent culture is then pumped directly into standard dye machines along with the yarn, fabric, or garment to be dyed.

For contrast

Amyris (USA) is a biotechnology company regarded as a pioneer in the industrialisation of synthetic biology that applied engineering biology techniques to produce sustainable chemicals for cosmetics, fragrance, and pharmaceuticals using plant-derived sugars. The company filed for bankruptcy in August 2023 due to high-profile financial failure and failure to efficiently scale-up.

Case Study 3: Environmental Biosensors for the Detection of Pollutants, Pathogens, and Contaminants

The Problem

Soil contamination poses a significant threat to human health, agriculture, and the environment due to the presence of toxic pollutants at levels that are at risk to humans and the environment. Various activities contribute to soil contamination, with **industrial activities being the biggest contributor** followed by agricultural practices, poor waste disposal, accidental spills and leaks, construction and urbanisation, and untreated wastewater. **Contaminants in the soil are detrimental** in various ways such as reducing biodiversity, passing contaminants to higher trophic levels including humans, and contaminating drinking water. A pollutant causing serious concerns are **PFAS** (Per- and polyfluoroalkyl Substances) which are termed "forever chemicals" since they have carbon-fluorine bonds, making them virtually indestructible. They have been associated to increased risk of certain cancers, reproductive effects, developmental effects in children and increased interference with natural hormones.

Clean-up and restoration of already contaminated soils require accurate assessment of the type and level of contamination. Monitoring soil quality to get an accurate understanding and distribution of the contaminants present as well as having **quality monitoring data is important**. Current techniques to monitor soil contaminants include **spectroscopic techniques** such as Visible Near-Infrared Spectroscopy (Vis-NIR) and Laser-Induced Breakdown Spectroscopy (LIBS) which allows for rapid, chemical-free screening *in situ*. Alternatively, highly sensitive, laboratory-based techniques such as inductively coupled plasma-mass spectrometry (ICP-MS) and inductively coupled plasma-optical emission spectrometry (ICP-OES), provide precision and trace-level quantification. However, all these techniques lack real-time, on-site, and cost-effective analysis and often require technical expertise which are associated to high costs.

The EngBio Solution

A monitoring technique that is easy to use, cheap, accessible, that can be used in real-time and on-site are biosensors (**Figure 15**). They have become a useful analytical tool for detecting pollutants by utilising biotechnology techniques coupled with a signal transducer to detect and quantifiably measure signals. Due to the modularity of the technology, various types of biosensors have been developed including cell-free and whole-cell based biosensors, and specific and nonspecific ones. A target analyte is identified e.g. pesticide, heavy metals, pathogens, pharmaceuticals and is sensed by a bioreceptor. For cell-free biosensors, sensing elements include DNA, proteins, and aptamers. Depending on the type of target analyte, different sensing elements are more suitable. **Whole-cell based biosensors** can be either specific where it is based on the metabolism or detoxification genes in microorganisms or non-specific based on stress responsive genetic regulation. When the bioreceptor interacts with the analyte, a physical or chemical change occurs, which is then detected by a transducer to produce a signal e.g. electrochemical, optical, piezoelectric. The signal is often weak with

background noise so the electronics in the biosensor is often **optimised to amplify and filter the signal**. The signals are then processed and displayed in a readable format to be analysed.

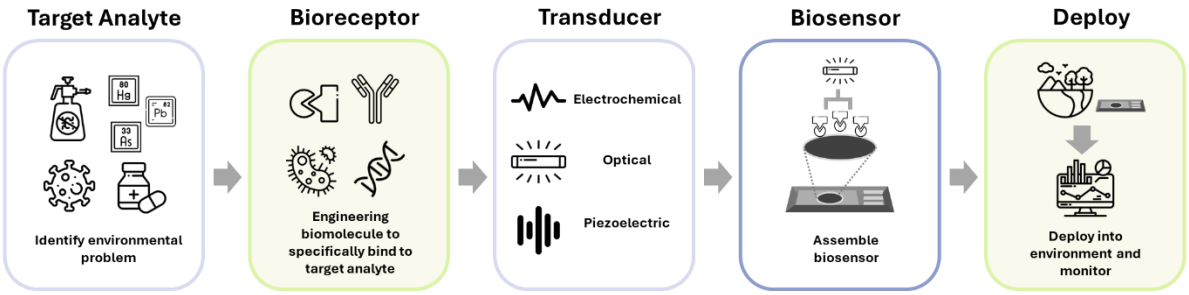


Figure 15. *General process of microbial waste valorisation into value-added products*

Case Assumptions

Advances in biotechnology allows **engineering of whole-cell biosensors** based on metabolic genes as sensing elements. Microbial whole-cell biosensors detect concentrations based on the genetic elements that respond to the target analyte, which are controlled under the promoters of the reporter genes to convert the biological response into a detectable signal such as fluorescence. Whole-cell based biosensors are more advantageous than cell-free biosensors because they are suitable for assessing the bioavailability and toxic effects. For this case study, the technology involves the development of a whole-cell biosensor by genetically engineering *Rhodococcus jostii* RHA1 to detect PFAS in the soil which produces a fluorescent response upon detection of PFAS.

Regulatory Pathway and Evidence Requirements

This case study only focuses on the development and production of the whole-cell biosensor, and not the deployment of environmental applications. Therefore, the case study falls under **The Genetically Modified Organisms (Contained Use) Regulations 2014**. A work through of risk assessment considerations associated to the engineering of a whole cell biosensor using *Rhodococcus jostii* to detect PFAS and produce a fluorescent signal is outlined along with evidence requirements to support the risk assessment approval pathway **(Figure 16)**.



Figure 16. *Example walkthrough of risk assessment and evidence requirements associated with engineered R. jostii for the production of whole-cell based biosensors for the detection of PFAS*

Other Regulatory Requirements

Department for Environment, Food & Rural Affairs (DEFRA)

- **If biosensor is then to be deployed outside contained conditions:**
  - The GMO (Deliberate Release) Regulations 2002 (SI 2002/2443) applies
  - Consent from the Secretary of State (via DEFRA) will be required
- **Advisory Committee on Releases to the Environment (ACRE)** provides statutory advice to DEFRA on the potential risks to human health and the environment from the release of GMOs

Similar Cases

For comparison

Oxford Molecular Biosensors (UK) have developed whole-cell biosensors using engineered bacteria to produce an optical signal which changes in the presence of toxic compounds, and changes and intensity of the light signal is relative to the overall toxicity of the sample. The company is currently developing specific biosensors to detect individual elements based on a switch-on light system using synthetic biology to increase sensitivity. The company are at TRL 7 and have demonstrated a functional prototype in an operational environment. However, the biosensors are not deployed in the environment as they operate from a molecular microbiology laboratory and test water samples within a contained laboratory to overcome hurdles associated to deliberate release regulations.

FREDsense (Canada) is a biosensor company to detect water contaminants, particularly PFAS using a bacteria-based biosensor. The genetically engineered bacteria can detect contaminants and when the target analyte is present, it binds to the biosensor and generates an electrochemical signal. The company offers a service to test PFAS in their lab, which bypasses the regulatory hurdles associated with the deployment of the biosensor in the environment.

For contrast

Arsenic Biosensor Collaboration (UK) was a project based at Cambridge University in collaboration with colleagues from the University of Edinburgh developed a whole-cell arsenic biosensor using a strain of *Bacillus subtilis* which is non-hazardous to humans or the environment to detect arsenic. Genes that produce coloured pigments are engineered into the bacteria and the modified bacteria turns green when arsenic levels are safe and purple when arsenic levels are unsafe. The team proposed that the biosensor falls under "contained release" as the biosensor featured multiple physical and genetic containment measures to ensure that deployment of the biosensor in the environment would still contain the GMO. However, at the time the project faced **a large degree of uncertainty regarding regulatory approval pathways**

as neither HSE nor DEFRA were able to make a decision on regulatory approvals related to the project.

CEXAL Ltd (UK) are a biotech company producing DNA biosensors for bacterial detection. They are developing a cell-free biosensing system to rapidly detect microorganisms in water samples. Using engineering biology, they developed oligo constructs that detects microbial DNA to produce a quantifiable signal in the presence of pathogens. By using a cell-free platform, the deployment of environmental biosensors would not fall under regulations associated to contained use and deliberate release as no living organisms are involved.

Case Study 4: Phytoremediation of Contaminated Soils using Engineered Plants

The Problem

Globally, over 10 million contaminated soil sites have been identified, of which 50% are affected by metal and metalloid pollution. Rapid industrialisation, urbanisation, and poor waste disposal are **contributing to soil pollution**. Soil pollution poses a significant threat to human health, agriculture, and the environment due to the presence of toxic pollutants. Heavy metals including lead (Pb), cadmium (Cd), arsenic (As), mercury (Hg), nickel (Ni), cobalt (Co), manganese (Mn), and aluminium (Al) are commonly present in soils, of which **As, Pb, Cd and Hg are included in the top 20 Hazardous Substances of the Agency for Toxic Substances and Disease Registry**, **posing serious threats to the environment and human health**. Contaminated soil decreases soil fertility, which puts pressure on food production as vast areas of land are unusable. When crops are grown on contaminated soil, research has shown that these contaminants enter the food chain and pass contaminants to higher trophic levels from plants to humans, **posing a long-term risk to human health**.

Conventional soil purification methods include mining, chemical stabilisation, soil washing, and thermal processes. Whilst the methods are effective, they are **extremely expensive, labour-intensive, time-consuming**, and are **highly disruptive to the local ecosystem**. Another alternative is microbial remediation however, it is **limited by large-scale application** and exhibits **instability**. Therefore, a suitable alternative is needed to effectively address contaminated soil whilst being cheap and accessible.

The EngBio Solution

Phytoremediation is an innovative solution that is gaining prominence as a solution to soil contamination (**Figure 17)**. **Phytoremediation uses the natural capacity of different plants to remove or reduce soil pollution in various ways**. Phytoextraction involves absorbing the contaminants from the soil and storing them in the plants tissue, which in turn stabilises the contaminants inside the soil, which is referred to as phytostabilisation. Some plants can absorb contaminants in the water through roots by rhizofiltration or transform some contaminants into the form of flying by phytovolatilisation. The advantage of phytoremediation over conventional methods is that it is solar-driven and requires less use of chemicals, which is much **cheaper and is more ecologically friendly**. However, **traditional phytoremediation techniques are not effective** particularly in the presence of co-contaminants, low pollutant bioavailability, and limited plant adaptation to stressed environments. **Engineering biology has been used to enhance phytoremediation**, including **genetically modifying the plant** to enhance tolerance to pollutants and **engineering the microbial consortia** for enhanced pollutant degradation.

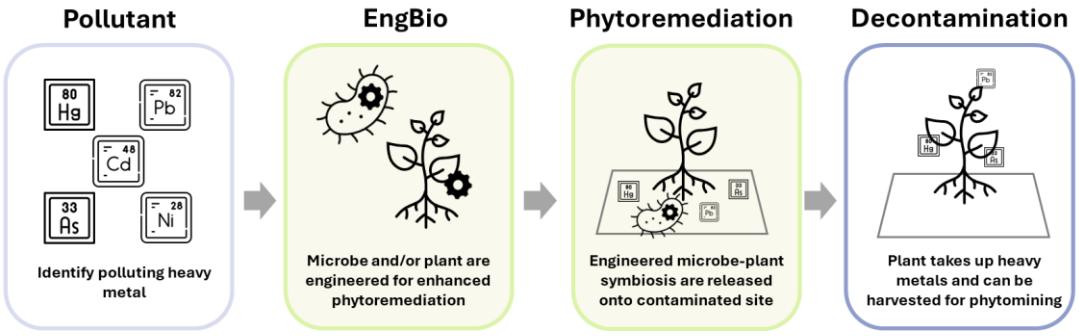


Figure 17. *General process of phytoremediation of heavy metal pollutants using engineered plant and microbe symbiosis*

Case Assumptions

Engineering biology has been used to improve phytoremediation. This can be achieved by **genetic engineering of plants** which involves the introduction of metabolic pathway genes or genes from microbial detoxification pathways to enhance phytoremediation potential of plants. Alternatively, **engineering the microbes that are symbiotic with the plants** can assist the plants phytoremediation potential by maintaining soil fertility, regulate nutrient cycling and enhancing the availability of soil nutrients. Genetic modification of endophytes in particular can substantially improve remediation efficiency of phytoremediation of heavy metal pollution. For this case study, endophytic bacteria from the genus *Enterobacteriaceae* are engineered with enhanced ability to improve phytoremediation of Cd and Pb in *Brassica juncea* by the introduction of glutathione (GSH) synthase gene *gcsgs*.

Regulatory Pathway and Evidence Requirements

This case study involves the genetic modification of endophytic bacteria which would be produced under Contained Use conditions. However, the implementation of the engineered endophyte as a phytoremediation tool involves the release of the engineered microbe in the environment. For this case study, the regulatory pathway is mapped for the release of the engineered microbe in a contaminated field so therefore, this case study falls under **The Genetically Modified Organisms (Deliberate Release) Regulations 2019**. A work through of risk assessment considerations associated to the phytoremediation of Cd and Pb using engineered endophyte grown with *Brassica juncea* is outlined along with evidence requirements to support the risk assessment approval pathway **(Figure 18)**.

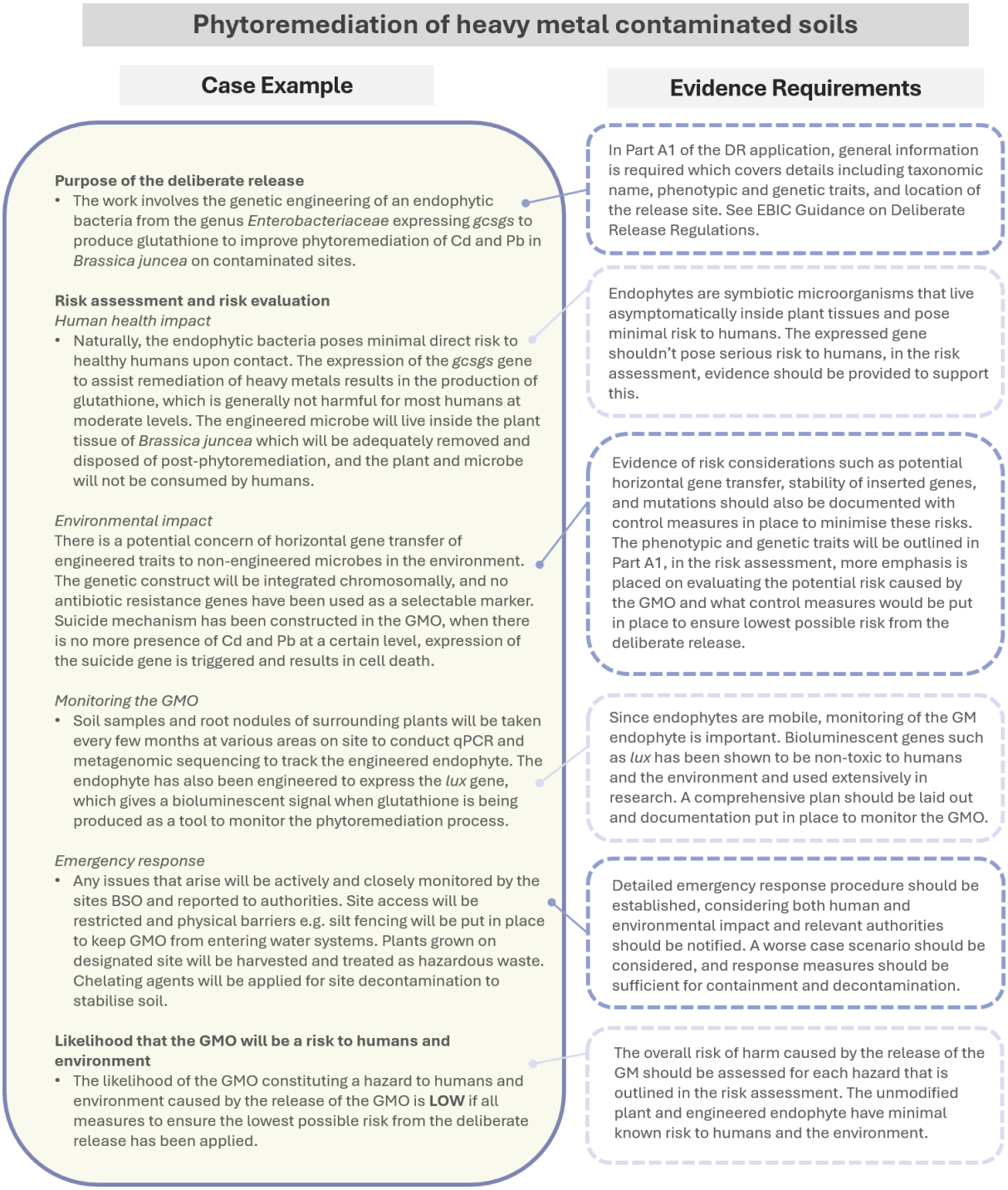


Figure 18. *Example walkthrough of risk assessment and evidence requirements associated with engineered endophyte from the genus Enterobacteriaceae for assisting phytoremediation of heavy metals Cd and Pb in Brassica juncea*

Other Regulatory Requirements

Environmental Protection Act 1990

- Part VI: Governing of GMOs, with established legal framework for risk assessments, public notifications, and consents required to import, acquire, release or market GMOs, ensuring that human-controlled organisms do not escape or cause damage to the environment
- Part IIA: Contaminated land legislation is required for working on a contaminated site

Environment Agency (Environmental Permit)

- Environment Permit application for remediating contaminated land - Environment Agency (England), Scottish Environment Protection Agency (SEPA), Natural Resources Wales (Wales)
- Ensure consideration of industrial emissions & waste management, processes, feedstock type and quantity, evidence of monitoring and reporting

Similar Cases

For comparison

Remephy (UK) is a phytoremediation company utilising the symbiotic relationship between plants and bacteria. They have engineered naturally occurring bacteria which allows the selected plants to extract heavy metals more efficiently than the non-engineered bacteria. The plants are then harvested and processed to extract the metals to be recycled back into clean energy supplies. Based on available information, Remephy are positioned at TRL 3-4 as they have validated their prototype in laboratory soil samples.

Deeproot Biolabs (USA) is using plant-based solutions to extract and clean up pollutants and contaminants from soil. They are developing engineering endophytes that live in the plant roots to enhance phytoremediation and phytomining. The company was founded in 2025, so it is in the early stages of development.

For contrast

Intrinsyx Bio (USA) are a biotech company offering phytoremediation as a service to boost crop yields using naturally occurring endophytes, which increase nutrient uptake, enhance stress tolerance, and improve overall plant health. They have tested their technology in the lab and on fields and have proven the technology to be effective. However, they do not integrate engineering biology and avoid GM hurdles.

Edenspace Systems Corporation (USA) are a crop biotechnology company that used brake fern to extract arsenic from the soil (marketed as Edenfern). Although proven to be successful commercially, interest in the technology became stagnant due to the time-intensive nature of the technology. In addition, the cost of handling hazardous waste generated by the harvested fronds is high. The company decided to transition their focus to specialised agricultural biotechnology.

Case Study 5: Wastewater Treatment Using Engineered Microbes

The Problem

Water is an indispensable resource, supporting lives and livelihoods as well as ecosystems. **Contamination of natural water bodies is a global issue**, driven by the rapid growth of economies, unrestrained pollution discharge, the manufacturing and use of hazardous chemicals, as well as microbiological and viral infectious agents. Efforts to mitigate the impact of contaminated waters involve efforts to both prevent pollutants from entering the natural water environment and adequately treat water for societal use - be that municipal, recreational, industrial, or agricultural.

Wastewater treatment plants (WWTP) are designed to **remove pollutants from industrial or municipal sources before they can enter natural water bodies**. WWTPs involve **three main types of process**: primary treatment involving screening and settling of solids, secondary treatment involving biological breakdown, and tertiary treatment involving final processing. However, the need for more efficient and sustainable treatment processes coupled with tighter limits on discharged water quality mean that **traditional wastewater treatment methods struggle to achieve the pollution** removal levels required. Many of the novel chemical and physical methods involved in wastewater treatment are expensive, complicated to set up, and require high maintenance. In addition, the **increased use of chemicals creates significant sludge management challenges**. Many industrial manufacturing sites will operate their own wastewater treatment plan in order to pre-treat effluent prior to discharge into the public sewer system.

The EngBio Solution

Microbes have been used as a biological treatment to remove contaminants from wastewater, either as a pure or mixed microbial culture, for many years. The most common biological treatment process is **activated sludge**, which consists of bacteria and protozoa under aerobic conditions which use organic material in the sludge as food. However, traditional biological methods are struggling to completely break down organic pollutants and have limited suitability for some contaminants. Researchers have investigated using **engineering biology to produce tailored microbes that efficiently remove pollutants** like microplastics, hydrocarbons, metals and oils from water as an innovative solution to reduce the need for chemical dosing at WWTPs (**Figure 19**). Whilst traditional chemical and physical treatment methods are a one-size-fits-all approach, using engineering biology to produce a **consortium of tailored microbes**, the **bioremediation of wastewater can be tailored for each WWTP** since each plant site displays unique chemical profiles. As such, the use of engineered microbes is a cheaper, eco-friendly, and highly specific method for addressing water contamination.

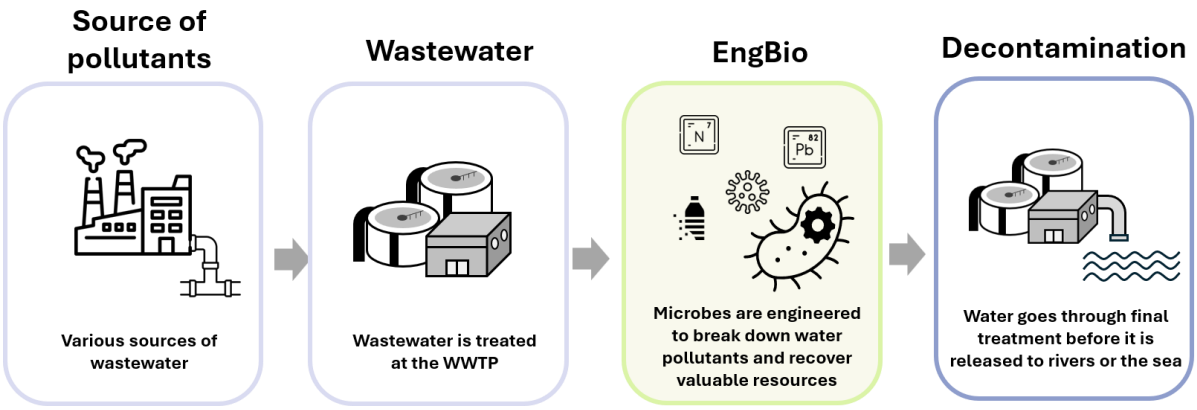


Figure 19. *General process of wastewater treatment using engineered microbes for pollutant removal and resource recovery*

Case Assumptions

Engineering biology to improve wastewater treatment can be achieved by genetic engineering of microbes with specific genes involved in breaking down certain pollutants found in wastewater, which can be introduced from another species or enhanced in existing bacteria. ***Bacillus subtilis*** has become a popular choice as a microbial chassis for bioremediation solutions. For this case study, *Bacillus subtilis* H1 is engineered overexpressing the endogenous genes *nar, nir, nas, gln,* and *glt* involved in nitrogen metabolism. The engineered microbes adhere to a **moving bed biofilm reactor (MBBR)** to form a biofilm to actively degrade nitrile - an organic chemical compound containing a carbon-nitrogen triple bond commonly used to manufacture synthetic rubber gloves, adhesives (e.g. super glue), and automotive seals.

Regulatory Pathway and Evidence Requirements

This case study involves the genetic modification of an engineered bacteria which would be produced under Contained Use conditions (e.g. in a laboratory or biomanufacturing setting). However, the use of the engineered bacteria for pollutant removal in a WWTP involves the bacteria being encapsulated on a membrane at a WWTP and the treated water released into the environment (e.g. a river). The engineered bacteria are thereby in direct contact with a medium which is not contained and the appropriate regulatory pathway is therefore **The Genetically Modified Organisms (Deliberate Release) Regulations 2019**. A work through of risk assessment considerations associated to the remediation of nitrile from wastewater using an engineered *Bacillus* species is outlined along with evidence requirements to support the risk assessment approval pathway **(Figure 20)**.



Figure 20. *Example walkthrough of risk assessment and evidence requirements associated with engineered Bacillus subtilis to remove nitrile from wastewater at a wastewater treatment plant.*

Other Regulatory Requirements

Environmental Protection Act 1990

- Part VI: Governing of GMOs, with established legal framework for risk assessments, public notifications, and consents required to import, acquire, release or market GMOs, ensuring that human-controlled organisms do not escape or cause damage to the environment

Environment Agency

- **The Environmental Permitting (England and Wales) Regulations 2016:** a discharge permit may need to be varied or amended to account for the GMO, depending on how the organism is used and whether it can be discharged with the effluent
- **The Water Environment (Water Framework Directive) (England and Wales) Regulations 2017:** protects receiving waters and requires evidence that discharges will not adversely affect aquatic ecosystems

Similar Cases

For comparison

Microvi (USA) have developed an encapsulated platform which uses both natural and engineered nitrifying microbes that are encapsulated inside a proprietary structure which can be deployed in WWTP reactors to remove various pollutants including ammonia.

For contrast

Bio2pure (UK) is a biotechnology company that produces a "starter strain" for wastewater treatment. They use naturally occurring probiotic bacteria which they grow under conditions that allow the bacteria to adapt to the pollutant and use the pollutant as a carbon source. Since the microbes they use in their technology are naturally occurring, they are able to avoid the GMO approval route.

Case Study 6: Biofuel Production

The Problem

Fossil fuels still meet approximately **80% of the world energy needs**. The continued reliance on fuels such as coal, oil and natural gas is a major contributor to environmental pollution and climate change. Fossil fuels are finite resources, and their extraction, processing and combustion generate significant greenhouse gas emissions, particularly carbon dioxide, which contributes to global warming. Their use also contributes to air pollution through the release of particulate matter, nitrogen oxides, sulphur oxides and other pollutants, which can adversely affect human health and ecosystems. Fossil fuel combustion was projected at **38.1 billion tonnes of fossil CO2 emissions in 2025** and it is projected that CO_2 emissions from **petroleum fuels could rise by 80% by 2030**.

Increasing global energy demand, driven by population growth and industrialisation, is placing further pressure on finite fossil fuel resources and highlighting the need for alternative, more sustainable sources of energy and fuels. **Biofuels produced from biological resources** provide one potential alternative, offering opportunities to reduce dependence on fossil-derived fuels while potentially lowering lifecycle greenhouse gas emissions and contributing to a **more circular and sustainable energy system**. Emissions from burning biofuels also contain **less net CO_2 due to the carbon sequestration** that occurs during biomass maturation. There have been increased efforts to move towards the production of biofuels. **Four distinct generations of biofuel production** have emerged each characterised by a specific feedstock type. First generation biofuels were produced from food crops e.g. sugarcane, corn, and vegetable oils. However, this production method was often criticised due to conflict with land allocation and food production problems. As a result, a second generation of biofuels used microbes and non-edible crops as a more environmentally friendly approach and has been shown to outperform traditional biofuel production in terms of environmental impact. The third generation of biofuels used microalgae as they generate more biomass and oil content than conventional crops. This generation of biofuels is considered to resolve the dilemma of food versus fuel as it does not rely on agricultural land use. The fourth generation of biofuels uses genetically engineered microorganisms, plants, and advanced synthetic biology systems. Genetic modification enhances organisms' biofuel production potential **by improving sugar utilisation, higher lipid synthesis, and increased photosynthesis**.

The EngBio Solution

Constraints on land use for biofuel production have made fourth generation biofuels utilising engineering biology techniques a promising alternative to fossil fuels **(Figure 21)**. It encompasses genetic engineering to increase desired traits of organisms used in biofuel production. This can be achieved by either engineering pathways in native producers or reconstructing pathways from natural producers into model organisms including bacteria, yeast, and algae. Engineering biology allows metabolic pathways to be improved to produce next generation biofuels including butanol, isopropanol, and hydrocarbons that are typically

liquid fuel so **are similar to petroleum products, which are better fit with existing fuel systems and networks** than first and second generation biofuels.

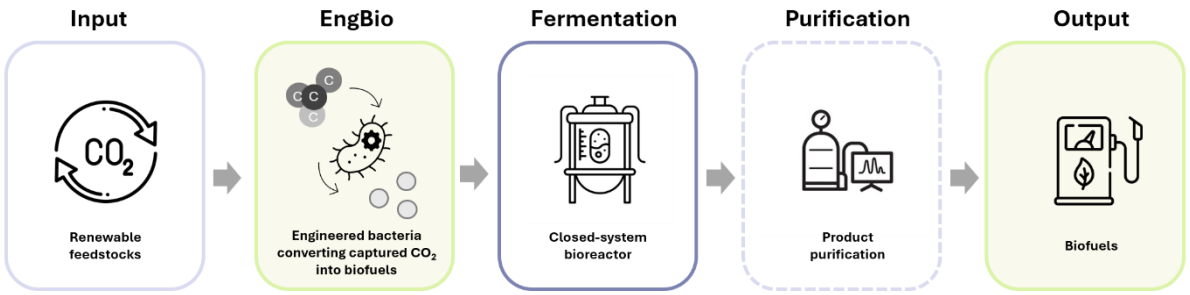


Figure 21. *Fourth-generation biofuel production using engineered bacteria*

Case Assumptions

Using microalgae for biofuel production combines concepts from third and fourth generation biofuel developments. Microalgae has low input and high yield prospects, a smaller carbon footprint than first-generation energy crops and a fast growth rate whilst having high lipid accumulation rates and low carbon dioxide emissions. Microalgae can also grow in wastewater, meaning they can be used to treat effluent whilst simultaneously producing biofuels. Genetic engineering of microalgae by overexpression of enzymes involved in lipid synthesis and storage have been explored to improve biofuel production. Overexpression of acetyl-CoA carboxylase (ACCase) which is involved in fatty acid synthesis and knockout of genes involved in fatty acid oxidation e.g. acyl CoA oxidase and acyl CoA synthase, can increase lipid synthesis. For this case study, the technology involves engineering the microalgae *Chlamydomonas reinhardtii* for biodiesel production by overexpression on the triacylglycerols (TAGs) metabolic gene type 2 diacylglycerol acyltransferases (DGATs) to increase lipid content.

Regulatory Pathway and Evidence Requirements

This case study involves the use of a closed-system photobioreactor under conditions that limit contact of the GMO with humans and the environment. Therefore, the case study falls under **The Genetically Modified Organisms (Contained Use) Regulations 2014.** A work through of the risk assessment considerations associated with the engineering of a microalgae to enhance production of biofuels is outlined with evidence requirements to support the risk assessment approval pathway **(Figure 22)**.

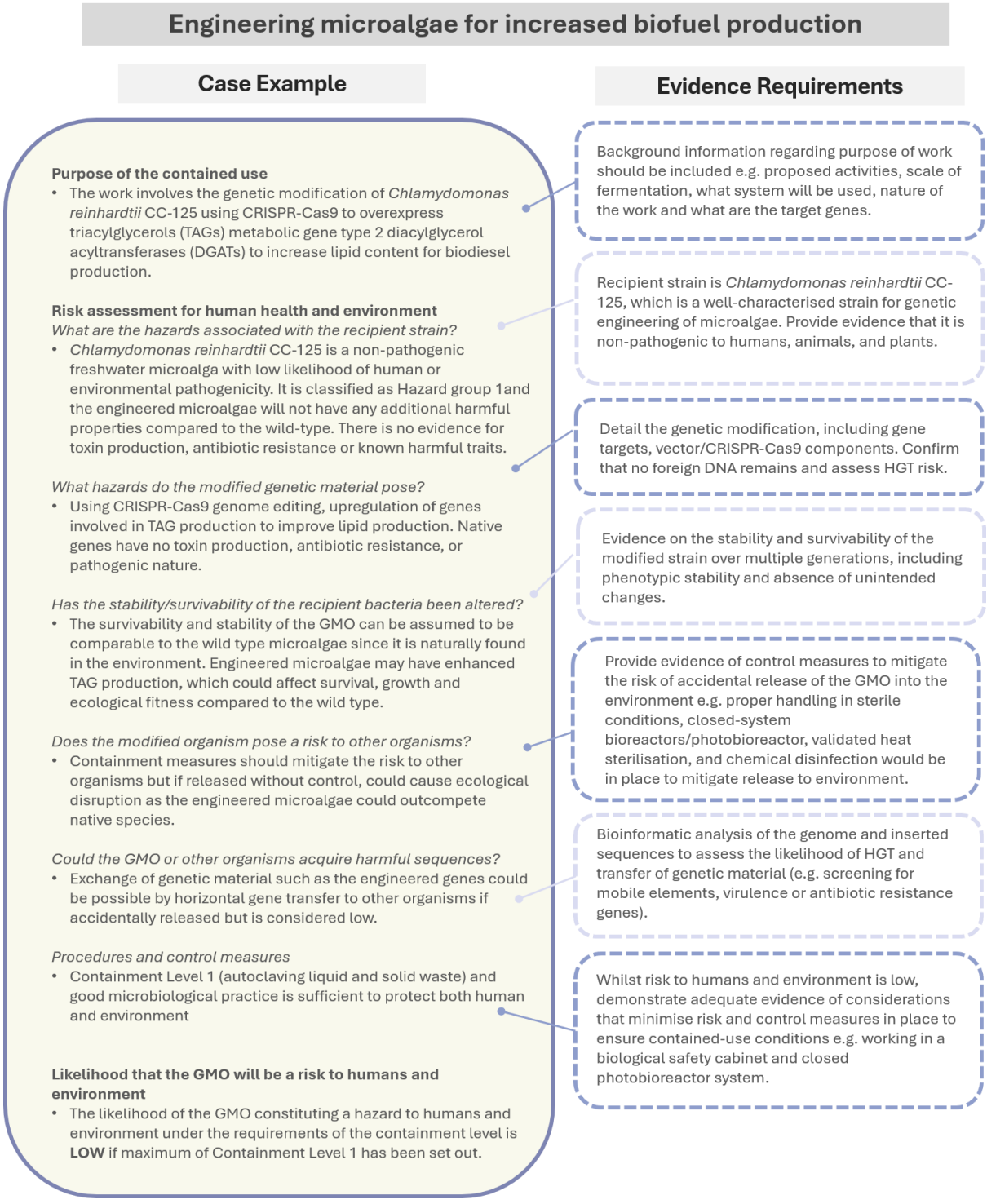


Figure 22. *Example walkthrough of risk assessment and evidence requirements associated with engineered C. reinhardtii CC-125 for the production of biodiesel*

Other Regulatory Requirements

Environment Agency

- If using CO_2 as a feedstock, the technology falls under Carbon Capture, Usage, and Storage (CCUS)
- Obtain environmental permit for this technology
- See Post-combustion carbon dioxide capture: emerging techniques - GOV.UK for more information

UK REACH (HSE Chemicals Regulation Division)

- If producing ≥ 1 tonne per year legal entity, submit a dossier (IUCLID) to UK REACH and provide evidence of physico-chemical properties, human health data, environmental data, and exposure scenarios

Similar Cases

For comparison

Phycobloom (UK) are genetically engineering algae to produce oil, as a cheap, carbon-neutral bio-oil to replace petrochemicals, particularly those used in aviation and maritime shipping. Their technology is different to other biofuel companies as the engineered algae can continuously secrete oil outside of their cells, which eliminates the need to extract the oil from inside the cell which is expensive and energy intensive, reducing their overall CAPEX. As the algae does not have to be killed to harvest the oil, the engineered algae can be kept alive and continuously reused, reducing the overall cost.

LanzaTech (UK) are converting industrial emissions, carbon dioxide, and gasified waste into ethanol. They have engineered *Clostridium autoethanogenum* to convert carbon oxide gases into ethanol. The company are developing new microbial strains to convert carbon gases into other critical molecules to expand their product portfolio, which has led to their success commercially and technologically. Although the company have been successful in securing funding from worldwide investors, high costs associated to scaling up may result in some drawback.

For contrast

TMO Renewables (UK) engineered a thermo-tolerant bacteria that can digest plant sugars rapidly at high temperatures. They engineered it to convert household waste and cellulosic material into ethanol. The process involved a pre-treatment to break down non-food organic waste into separate cellulose fibres. The treated material was then converted into simple sugars

using enzymes that can be consumed by the engineered microbe to convert the sugar into alcohol. In 2010, they won a $500 million contract with the US firm Fibernight. However, in December 2013 they entered administration due to cash shortages and scaling hurdles, which required immense capital that outpaced their incoming revenue and investor support.

Documents Reviewed in Preparation of Guidance

1. Legislation and statutory instruments

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Great Britain (2019) The Genetically Modified Organisms (Deliberate Release) (Amendment) (England) Regulations 2019, SI 2019/1252. Available at: https://www.legislation.gov.uk/uksi/2019/1252/made

Great Britain (2023) Genetic Technology (Precision Breeding) Act 2023. Available at: https://www.legislation.gov.uk/ukpga/2023/6/contents

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2. Regulatory guidance and technical resources

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