in focus

An international perspective on biopesticide regulation

Navigating regulatory complexity for a streamlined and cost-effective route to market

tsg

a **science group** company

Global demand for plant protection products derived from natural materials continues to grow. However, complexities within markets and discrepancies between them can hinder biopesticides' registration and approval. In this paper, we consider the regulatory frameworks which affect biopesticides in the US, Canada, EU and UK, as well as specific data requirements for microbial pesticides. We also share expert insights that can result in a quicker, more cost-effective regulatory journey.

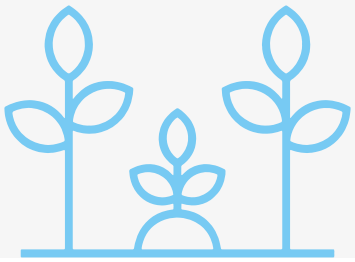
The demand for biopesticides in agriculture

Concerns about sustainability and the environmental impact of conventional pesticides continue to drive interest in biopesticides. However, manufacturers looking to meet this increased demand must navigate a complex regulatory landscape. In today's connected world, it's important to take a global perspective as well as focusing on individual target markets. Regulations evolve over time and can be influenced by wider trends in other parts of the world. With a well-informed regulatory strategy, it's possible to forge a more streamlined path that reduces time to market.

Here we consider regulatory frameworks in the United States (US), Canada, the European Union (EU) and the United Kingdom (UK) as principal markets of interest.

What are biopesticides?

Biopesticides are plant protection products derived from natural materials including plants, microbes and minerals. They include biochemical pesticides (naturally occurring substances) and microbial pesticides (microorganisms) as well as plant-incorporated protectants (PIPs). The latter definition is specific to the US Environmental Protection Agency (EPA) and refers to pesticidal substances produced by plants that contain added genetic material. Microbial products, which constitute the majority of the biopesticide market, are the main focus of this paper.



A diverse global picture

This snapshot of regulatory frameworks for biopesticides in the US, Canada, EU and UK highlights the complexity that exists within and between markets.

United States

The Biopesticides and Pollution Prevention Division (BPPD) of EPA's Office of Pesticide Programs (OPP) aims to facilitate the biopesticide registration process in the US. Data requirements for microbial and biochemical pesticide registration are listed in 40 CFR Part 158: Subpart V: Microbial Pesticides 158.2100 and Subpart U: Biochemical Pesticides 158.2000.

Data requirements for genetically modified microbial pesticides are determined on a case-by-case basis, depending on microorganism characteristics. PIPs fall under the remit of EPA, the US Department of Agriculture (USDA) and the Food and Drug Administration (FDA) as they're genetically modified crops with pesticidal traits. EPA outlines obligations for PIPs in 40 CFR Part 174.

Canada

In Canada, the Pest Control Products Act (PCPA), the Food and Drugs Act, and their associated regulations cover microbial pest control agents (MPCA) and end-use products (EPs).

PCPA is administered by the Pest Management Regulatory Agency (PMRA) of Health Canada and requires registration of all pest control products prior to import, sale or use. Pesticide registration categories cover the full spectrum of conventional, microbial and reduced risk, other biopesticides, non-conventionals and non-straight chain lepidopteran pheromone (NSCLP).

EU

The EU does not recognize biopesticides as a standalone regulatory category. They are regulated as plant protection products (PPPs), with the 'active substance' defined according to Regulation (EC) No 1107/2009, making use of data requirements in Part B of Commission Regulation (EU) No 283/2013 (for microbial active substances) and Regulation (EU) No 284/2013 (for microbial plant protection products).

Regulation (EC) No 1107/2009 includes 'basic substances' and 'low risk substances' categories for active substances and 'low risk products' for PPPs.

UK

Following its departure from the EU, the UK has established an independent regulatory regime. England, Scotland and Wales (and their associated islands) are governed by Great Britain (GB) regulations, whilst Northern Ireland (NI) remains within the jurisdiction of the EU under the Northern Ireland Protocol. Overseeing both the implementation of GB regulations and the required elements of EU regulations in NI is the Chemicals Regulation Division (CRD), part of the Health and Safety Executive (HSE).

GB regulation is closely aligned with EU Regulation (EC) No 1107/2009 and data requirements in Part B of Commission Regulation (EU) No 283/2013 (for microbial active substances) and No 284/2013 (for microbial plant protection products). However, divergence is likely over time.

GB has indicated that it anticipates being able to reach approval decisions in approximately two years. This is considerably faster than the average EU equivalent time frame of four to five years.

Microbial biopesticide requirements

The four jurisdictions outlined above share many data requirements for microbial products. Requisites in the US and Canada are very similar, and those in the EU and GB are identical albeit regulated by different agencies. Nevertheless, there are certain variations related to active substances that need to be considered, as detailed in the following sections.

Identity of the active substance

Microorganism identification and characterization is critical to other aspects of biopesticide registration. The US EPA and Canada's PMRA expect accurate and current taxonomic information to verify the identity of microbial agents. Describing the manufacturing, fermentation or culturing method employed in production is equally important to demonstrate quality control. Regulators need enough information to understand how the product is made without overly constraining the production process.

For the most part, US and Canadian authorities' stipulations regarding identity of microbial pest control agents (MPCAs) are similar. However, PMRA requires the international regulatory status of the microorganism (DACO 1.3), a comprehensive data summary (DACO 12.7), and patent status (DACO 2.6). In the US, a sample of the MPCA must be provided (EPA Guideline 830.19). GB and EU data requirements in relation to the identity of the active substance are in alignment with EPA Guideline 830.19.

Biological properties

Regulatory agencies in the EU and GB require a description of the target organism and formation of toxic metabolites, as do EPA and PMRA.

Information on the source of the isolate, its natural occurrence and host specificity are also among EPA and PMRA data requirements. Variance between the two authorities is mainly due to PMRA's higher levels of specificity in relation to:

- Physiological properties, especially the effect of environmental parameters on growth, infectivity, dispersal and colonization ability (DACO 2.7.2 vi)
- Genetic stability and factors affecting this (DACO 2.7.1)
- Detailed discussion of microorganism relationships to any known human dermatophyte (DACO 2.7.2 x)
- Resistance/sensitivity to antibiotics or antimicrobial agents used in human or veterinary medicine (DACO 2.7.2 vi)

Function, MOA and handling

Data surrounding the function, mode of action (MOA) and handling of MPCAs is essential to regulatory agencies, providing further detail on use and longer-term effects. Again, EPA and PMRA requirements are very similar. Notable differences include PMRA's need for a statement of the MOA in terms of biochemical and physiological mechanism(s) and biochemical pathway(s) involved (DACO 10.2.1), as well as procedures for the decontamination of water in the event of an accident (DACO 8.4).

GB and EU active substance data requirements correlate with those of EPA and PMRA in relation to MOA, the development of resistance and associated management strategies.

Toxicology and exposure

Toxicology and exposure data provide regulators with insights on any harm a biopesticide may cause.

Toxicity testing explores a wide array of possible effects, ranging from cancer and neurotoxicity to birth defects. PMRA has several unique data requirements in this area. These include a summary of the MPCA's potential to be hazardous to humans with consideration of pathogenic potential, ability to infect and pattern of clearance, and toxicological effects (DACO 4.1). Proposed first aid measures and medical treatment (DACO 1.1) also need to be submitted.

EPA has one unique requirement, namely toxicity studies on metabolites (especially toxins) (EPA Guideline 885.355).

UK and EU requirements for typical acute toxicity information and demonstration of absence of risk to humans correlate with those of PMRA, as pathogenesis of the MPCA is of concern.

Ecotoxicological studies and non-target organisms

Ecotoxicological studies consider the various effects a pesticide can produce in an organism and how those effects change in line with exposure levels. They also deal with the potential exposure of plants, water resources and animals to pesticide residues in food, air and water.

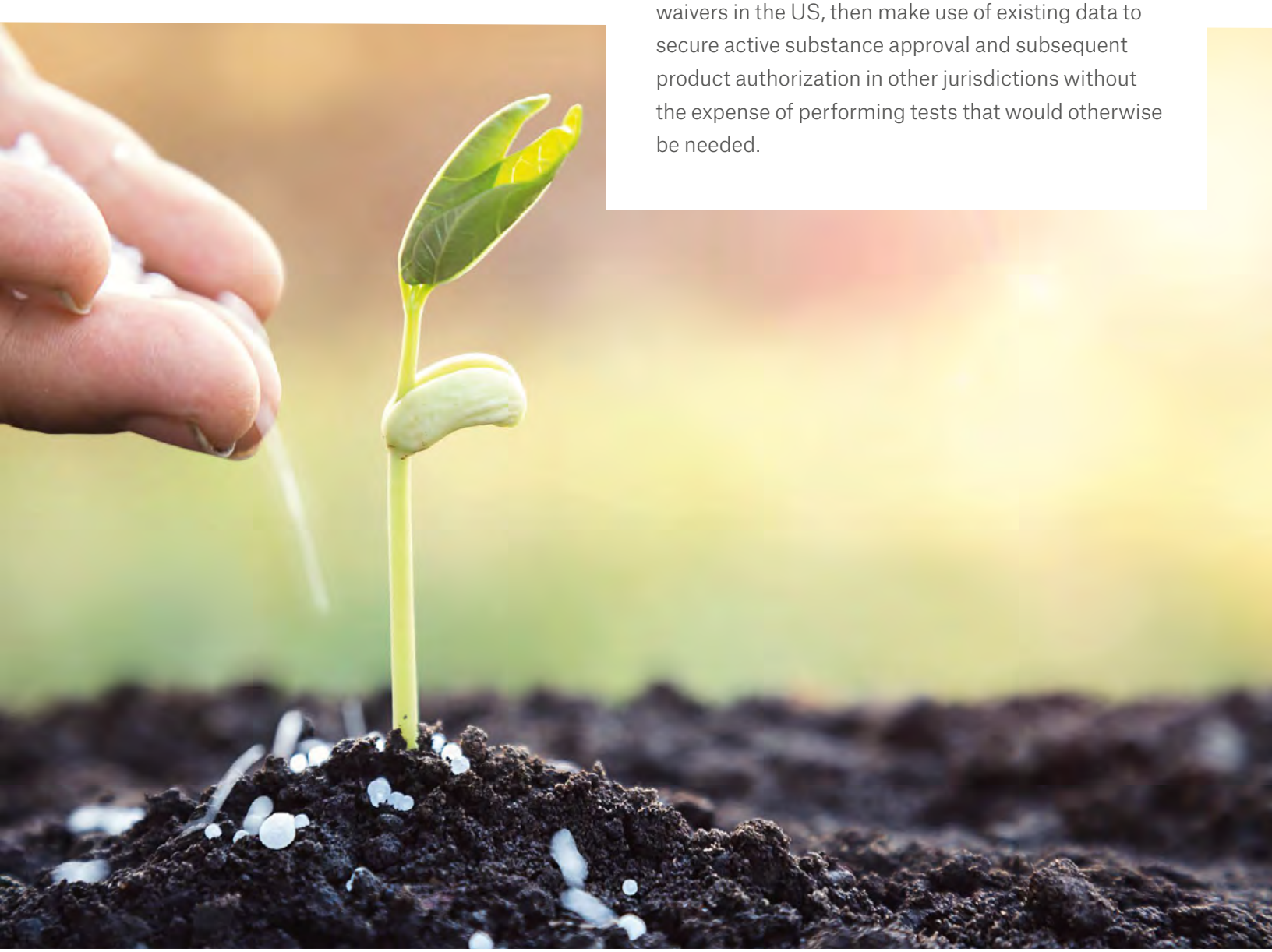
EPA requires effects on non-target organisms (EPA Guideline 885.4050 / 850.4000 / 885.4100) to be established, as does the EU (Commission Regulation (EU) No. 283/2013, Annex II, Part B, 8). However, Canada's PMRA asks for a summary and evaluation of environmental impact (DACO 9.1/12.7) of the MPCA. GB and the EU also require data on non-target organisms (EU Annex IIB 8.4 / 8.6).

Strategies for approval and registration

While there is much complexity in the legislative frameworks that cover biopesticides, understanding similarities between markets can help streamline global strategies. Taking advantage of data waivers and internationally agreed guidelines also improves cost-efficiency and simplifies the regulatory process.

Data waivers

In the US, the OPP has issued memoranda and other documents which indicate that applicants can present data which support a waiver for certain requirements. These include mammalian acute toxicity data for pesticide technical active substance and pesticide end use formulations. It's possible to invoke these waivers in the US, then make use of existing data to secure active substance approval and subsequent product authorization in other jurisdictions without the expense of performing tests that would otherwise be needed.



Guideline-based development

The Organization for Economic Co-operation and Development (OECD) has developed guidelines to make the testing of chemicals less onerous. It's compiled a collection of the most relevant internationally agreed testing methods used by government, industry and independent laboratories to assess the safety of chemicals.

Since the US, Canada, UK and EU are all OECD member countries they benefit from the Mutual Acceptance of Data (MAD) system. This means that a safety test carried out in accordance with the OECD Test Guidelines and Principles of Good Laboratory Practice in one OECD country must be accepted by other OECD countries for assessment purposes. The system eradicates the time and expense that would be involved in performing multiple studies.

The EU has also published guidance on how data requirements for metabolites can be applied to EU-level approval of microorganisms as active substances, and Member State level authorization of plant protection products. This guidance addresses metabolites present in the active substance and the plant protection product as well as those produced by the microorganism after application (in situ production). The document's approach is based on a consensus reached by the EU Working Group on Biopesticides and endorsed by the Standing Committee on Plants, Animals, Food and Feed (SANCO/2020/12258 of 23/10/2020).

TSG outsourcing benefits

TSG Consulting is uniquely placed to execute international development projects. This reduces the need for clients to engage with multiple contractors across jurisdictions to achieve market entry for a new microbial plant protection product. We can also support activity surrounding existing MPCAs/MPCPs that are already registered in specific territories.

- TSG handles all necessary regulatory and management activities under one organizational structure across teams in Europe and North America. We employ project and regulatory management specialists and regulatory scientists in each required discipline. This ensures we deliver a focussed program to achieve project objectives.
- Our proactive approach means studies at contract research organizations (CROs) are initiated and completed in a coordinated and timely manner. The same is true of regulatory and scientific resource management.
- We have many years of experience and a proven track record dealing with microbial (and traditional) plant protection products. We fully understand the technical challenges faced in their approval in North America and Europe.
- TSG has an in-depth knowledge of the US EPA, California Department of Pesticide Regulation (DPR) and Canada's Pest Management Regulatory Agency (PMRA). We also hold detailed knowledge of the various regulatory authorities in Europe, developed through valuable working relationships and recruitment of staff from those authorities.
- The study monitoring and commissioning experience at TSG is manifest in our effective working relationships with CROs and Study Directors. Importantly, we understand which CROs are reliable and have specific areas of relevant expertise.
- In the US, TSG is also well equipped to assist clients in the process of market entry (or rounding out a biochemical/microbial portfolio) via supplemental distribution. This is achieved via competitive research to assess the current technical grade of the active ingredient (TGAI) registered by EPA followed by discussion of possible next steps in relation to product registration.

Interested in learning more?

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About TSG Consulting

TSG Consulting provides companies with high quality regulatory and scientific consulting services.

We help clients worldwide address the technical and regulatory issues in taking their products to market in multiple jurisdictions. Our scientific expertise, regulatory knowledge and understanding of local nuances enable our clients to navigate the complex and ever-changing regulatory landscape across the globe.

We serve a number of key markets and industry sectors including agricultural, industrial, consumer, food and beverage, animal health, and medical. Our teams comprise scientists and regulatory experts – many of whom have previously held positions at regulatory agencies, departments, and in industry.

This combination of science, regulatory expertise and knowledge of how institutions and industry operate provides our clients with superior and well-rounded guidance. TSG Consulting has offices in France, Germany, Spain, UK, USA and Canada. TSG is a Science Group (London listed) company.

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About Science Group plc

Science Group plc (AIM:SAG) is a science-led advisory and product development organization. The Group has three divisions:

- R&D Consultancy: providing advisory, applied science and product development services cross sector helping clients derive maximum return on their R&D investments.
- Regulatory & Compliance: helping clients in highly regulated markets to launch, market and defend products internationally, navigating the frequently complex and fragmented regulatory ecosystems.
- Frontier Smart Technologies: designing and manufacturing chips and modules for the DAB/DAB+ radio markets with 80% market share (excluding the automotive market).

With more than 400 employees worldwide, primarily scientists and engineers, and speaking more than 30 languages collectively, the Group has R&D centers in Cambridge and Epsom with more than ten additional offices in Europe, Asia and North America.

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