Regulatory Frameworks for Biopesticides and Biostimulants: A Comparative Analysis of the EU, US, India and Japan

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TRENDS AND DEVELOPMENTS FOR BIOPESTICIDES AND BIOSTIMULANTS IN EU

In the EU, the last months have seen significant changes in regard to the current as well as the future regulations for biopesticides and biostimulants. One of the key issues of course is the step from national biostimulant regulations to EU harmonised rules under a fertiliser framework. Entry into force of the new EU fertiliser Regulation 2019/1009 has brought on several changes. For one, the new regulation will significantly simplify market entry for biostimulant products from its applicability in 2022 onwards, provided that they are compliant to the new regulation, as there will be harmonised rules and procedures applicable for all EU Member States. However, by including biostimulant products and explicitly excluding them from EU plant protection products Regulation 1107/2009, the new fertiliser regulation not only closes a regulatory gap through bringing biostimulants under harmonised rules from June 2022 onwards, but opens up another one. This is mainly due to the fact that the official definition of biostimulants, eligible for registration under the EU framework in future, is mainly a legal and regulatory, not a scientific one. According to Regulation 2019/1009 biostimulants are defined as products 'stimulating plant nutrition processes independently of the product's nutrient content with the sole aim of improving one or more of the following characteristics of the plant or the plant rhizosphere: (a) nutrient use efficiency, (b) tolerance to abiotic stress, (c) quality traits, [or] d) availability of confined nutrients in soil or rhizosphere'. However, plants normally do not adhere to regulatory definition and thus do not differentiate between abiotic and biotic stress. Many of the plants' stress defence systems are involved in both, abiotic and biotic stress response. Thus, differentiation between the legal frameworks in which a product is to be registered may become difficult for many products, especially in case of closely related substances (e.g. certain botanicals). The sole claim of abiotic functions for a product in order to fall under the fertiliser/biostimulant framework may not be sufficient, considering the vast amount of scientific literature and public information on functions of many substances available, the competitive position between biostimulant and plant protection product manufacturers and distributors, etc. This could lead, for example, to the requirement to register products under the plant protection product framework which previously have been marketed under the national fertiliser laws as 'biostimulants'. One, almost historical, example are Trichoderma species which, at least in many countries, where brought onto the market as biostimulant, plant or soil aid products for decades, but which more and more have to be approved/authorised as plant protection products due to their fungicidal potential. As the last months indicate, the 'dual use' potential of a substance or product harbours many possibilities for interpretations and possible problems. According to current ongoing discussions in the Standing Committee on Plants, Animals, Food and Feed, the regulatory status of some active substances are already under discussion. In the specific case, the plant protection product framework for an existing and approved chemical active substance is challenged by some Member States. The Member States consider the substance as plant biostimulant according to the new definition and thus falling outside the scope of the plant protection products regulation. In this context it is important to note that the new fertiliser regulation does not allow for products to have biotic stress action. On the other hand, if a product is effective only against abiotic stress it does not fulfil the criteria of the plant protection regulation. However, in case a product has dual action against abiotic and biotic stress it is absolutely eligible for registration under the plant protection framework as respective substance/product categories such as 'elicitor' or 'plant activator' are already included and covered by Regulation 1107/2009.

Other practical examples highlight that changes in the legal and regulatory procedures for plant protection products are ongoing on many levels and that efforts to implement EU's Green Deal, Farm to Fork, Biodiversity and Sustainability goals as well as the General Food Law are rapidly increasing. This is not only due on EU, but also on

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national levels in the individual Member State as foreseen by several legislative acts, e.g. the SUD (Sustainable Use Directive 128/2009) and the respective National Action Plans. According to the Sustainable Use Directive, for example 'Member States shall take all necessary measures to promote low pesticide-input pest management, giving wherever possible priority to non-chemical methods, so that professional users of pesticides switch to practices and products with the lowest risk to human health and the environment among those available for the same pest problem'. Based on this argumentation, the Swedish authority rejected an application for re-authorisation of a chemical insecticidal plant protection product used in silviculture against beetles, arguing that widely-used non-chemical methods are available and non-authorisation of the chemical product therefore does not cause any significant economic or practical disadvantages for the forest owners. The decision for non-authorisation was confirmed by law courts in the meantime. The Swedish decision is one of the first in the EU substituting chemical plant protection products based on the availability of more environmental friendly alternatives. In addition, the Swedish government decided to completely ban the use of plant protection products in certain areas, such as public areas, parks or gardens. Exemptions from the ban are only foreseen for plant protection products that are deemed to pose a limited risk to human health and the environment, that is mainly products containing active substances classified as low risk according to Regulation 1107/2009 and thus, biorational products.

The examples of the recent Swedish decisions are a good indication for possible upcoming changes triggered by the new EU's Green Deal, a "roadmap for making the EU's economy sustainable by turning climate and environmental challenges into opportunities across all policy areas" (EU COM 11 December 2019). In regard to agriculture in general and the use of plant protection products in particular, the most important components of the Green Deal are the so-called Farm to Fork (F2F) Strategy and the Biodiversity strategy. Key actions are for example:

- Reduction of the use and risk of chemical pesticides by 50% by 2030
- Reduction of the use of more hazardous pesticides by 50% by 2030
- Revision of the Sustainable Use Directive (for pesticides; SUD) to significantly reduce use and risk and dependency on pesticides and enhance Integrated Pest Management and to improve the link between the objectives of the SUD and other legislation linked to their implementation, such as the Common Agricultural Policy (CAP) and Water Framework Directive
- Boost the development of EU organic farming area, with the aim to achieve 25% of total farmland under organic farming by 2030
- Revision of the EU Thematic Strategy for Soil Protection by 2021

With the Green Deal being in place in the EU since December 2019 only, the implementation of most of the actions and initiatives of the F2F and Biodiversity strategies will take some time. However, the Directive 128/2009 on the sustainable use of pesticides as underlying legal basis for many of the Green Deal targets – often neglected for many years – is already available and allows for direct action. Based on these already available prerequisites, in March 2021 a six month foresight study was launched to assure that by 2030 the pesticide use and risk reduction targets announced in the Farm to Fork and Biodiversity Strategies can be fulfilled. Also in regard to other Green Deal targets several tangible actions are already taken. The European Commission published the basics for an action plan for the development of future organic production in March 2021. The action plan builds up on the upcoming new legislation on organic farming (Regulation 2020/1693) of November 2020 amending Regulation 2018/848 on organic production and labelling of organic products, which enters into force on 1 January 2022. Already designed to boost the organic farming sector, the new regulation in any case includes several respective measures such as rules for a more uniform approach to reduce the risk of accidental contamination from pesticides, steps to simplify organic farming certification for small farmers via a new system of group certification, or a strict control system and precautionary measures along the entire supply chain to safeguard organic products. The new regulation also requires producers in third countries to comply with the same requirements as farmers producing in the EU. Further examples for actions already initiated are several public consultations of the EU Commission ongoing at the moment, e.g. on a new EU soil strategy or in regard to the revision of the SUD and stricter rules for the sustainable use of pesticides. Several ongoing or upcoming actions of the Commission are in turn complemented by EU Parliament initiatives. The Commissions' public consultation on an EU soil protection strategy, for example, is mirrored by an EU Parliament draft motion for a resolution on Soil protection, published in February 2021. As with many topics referred to in the Green Deal, the EU Parliament not only highlights the importance of certain actions (in this case soil protection) in regard to environmental or human and animal health problems and needs which are no longer disputed by the majority of stakeholders, but rather stresses the economic relevance of such measures, emphasising costs caused by 'inaction on soil degradation, with estimates in the Union exceeding €50 billion per year'.

The European Green Deal also underlines the need to raise public awareness and include the general public in these reforms. A major aim is to build up the trust of EU citizens in the agricultural sector, the food supply chain and in the availability of safe, residue-free food. Based on the synergistic principle of EU legislation, part of the Green Deal

measures are already anchored and reflected in the new General food law which entered into force in March 2021. General Food Law provisions have a main focus on the transparency of the food chain and thus also the registration procedures and use of plant protection products. With Regulation 2019/1381 – on the transparency and sustainability of the EU risk assessment in the food chain – various new regulatory procedures were introduced. Some examples are the requirement for mandatory notification of all studies used for an active substance approval procedure before the start of the studies, the so-called Pre-Submission and Renewal Pre-Submission Advise as well as the mandatory use of the electronic data submission platform IUCLID (International Uniform Chemical Information Database) for evaluations carried out on EU level such as plant protection product active substances, MRL evaluations or basic substance approvals. This shall also guarantee an early publication of submitted data and evaluation results and easy access on the results for all stakeholders as well as the public. Access is guaranteed by the EFSA webpage. As the first months under the new Regulation already have shown, the new requirements are changing the daily work in the plant protection product registration procedure significantly.

Besides plant protection, the Green Deal and the General Food law also influence the registration of biostimulants from a regulatory point of view. The importance of biostimulants to fight, for example, the consequences of climate change, i.e. heat, drought and salinity stress or the need to reduce mineral fertiliser inputs, was the basis for inclusion of biostimulants in a harmonised EU-wide regulation. This, at least in theory, could achieve the desired effect, namely to make biostimulants more easily available on the market and thus complement farmers' toolbox to support sustainability and Green Deal goals. However, the new fertiliser/biostimulant regulation explicitly allows for ongoing national registration/notification procedures, provided they do not infringe EU standards. And thus, the new fertiliser regulation is accompanied by another new regulation (Regulation 2019/515) simplifying the mutual recognition procedure for nationally registered products and the free movement of fertiliser/biostimulant products in all EU Member States.

In addition to the few examples described above, there are many more influencing plant protection product and fertiliser/biostimulant registration, and there are more to come. Overall, it seems that the process of Greening and Sustainability, long neglected in the EU, significantly gains momentum.

BIOPESTICIDE REGISTRATION PROCESS IN US

The U.S. EPA defines biochemical pesticides as pesticidal substances that:
- are naturally occurring chemicals or are synthetically derived equivalents;
- have a history of exposure to humans and the environment demonstrating minimal toxicity, or in the case of synthetically derived biochemical pesticides, are equivalent to a naturally occurring chemical that has such a history; and
- have a nontoxic mode of action to the target pest(s).

Biochemical pesticide registrations are generally significantly less expensive and usually take less time to register than conventional or antimicrobial pesticide product registrations. There is a reduced data set for these naturally occurring chemicals compared to other registrations. Therefore, companies can have considerable cost savings in studies. In addition, the fees to register a biochemical pesticide with the U.S. EPA in PRIA (Pesticide Registration Improvement Extension Act) are typically lower as compared to registration costs for conventional pesticides. The review of a biochemical pesticide registration submission by the EPA also takes less time. Thus, a company can save a lot of money and time upon submission.

For example, to register a new active ingredient for food use a company may expect the following PRIA costs upon submission:
- Biochemical: $33,506 and 18 months for U.S. EPA to review
- Conventional: $790,737 and 24 months for U.S. EPA to review (or $658,947 and 18 months if the active ingredient is considered reduced risk). Costs may be lower depending upon the proposed use.

Because less data is required to support biochemical pesticide products, generally those proposals can be reviewed by U.S. EPA in less time and get to market faster than conventional chemical products. Due to the U.S. public concern with conventional pesticides, the EPA is interested in registering more biochemicals. If companies are interested in marketing their products with organic labelling, most products for organic cultivation are biochemical products. However, there are conventional products that have organic labelling.

BIOPESTICIDE REGISTRATION PROCESS AND TRENDS IN INDIA

The registration of biopesticides in India is governed under the Insecticides Act 1968 and handled by the Central Insecticides Board (CIB). Realising the importance of biopesticides in agriculture, CIB has approved several categories of products such as:
1. Entomotoxic bacteria (*Bacillus thuringiensis, B. sphaericus*, etc.)
2. Antagonistic bacteria (Paenibacillus polymyxa, *Pseudomonas* sp.)
3. Entomopathogenic fungi (*Beauveria bassiana*, *Metarrhizium anisopliae*, *Nomuraea rileyi*, etc.)
4. Antagonistic fungi (*Trichoderma* sp., *Verticillium* sp., etc.)
5. Baculoviruses (Nucleopolyhedroviruses (NPV) and Granuloviruses (GV))
6. Botanical pesticides (Pyrethrum, Karanjin, Neem, *Cymbopogan*, etc.).

CIB has developed guidelines and data requirements covering physical-chemical properties including methods of analysis, toxicity (e.g. acute studies), ecotoxicity, packaging, and labelling information. Biological characteristics include DNA fingerprints reported by the National Bureau of Agriculturally Important Microorganisms (NBAIM), certifying the strains submitted by applicants. Efficacy data need to be generated by controlled research centres according to the Indian Council of Agriculture Research (ICAR/state agricultural universities (SAUs). In addition, CIB has developed standards (minimal infrastructure facilities) to produce biopesticides in regard to general requirements for production, mixing, formulation, laboratory equipment, etc.

In 2019, CIB reclassified the registration categories for biopesticides: Tier-I category (Insecticides Act 9(3b)) with temporary registration based on limited data and Tier-II-category (Insecticides Act 9(3)) with permanent registration based on a complete data package. The committee also decided that handle registrations (me-too) for the same strain/compound of biopesticides (including also botanical products and pheromones) under the Tier-II category, because these have already been introduced in the country according to the relevant provisions of the Law.

Beside the above mentioned regulations, the Indian government has introduced several other policy areas and regulations fostering the organic farming sector. This includes for example the National Programme for Organic Production (NPOP) launched in the year 2001 by the Agricultural and Pro-cessed Food Products Export Development Authority (APEDA) under the Ministry of Commerce and Industry. The institutional framework for accreditation and certification of organic agriculture was the major goal of NPOP, which gained recognition agreements with the European Union and United States Department of Agriculture (USDA).

Further, The National Mission for Sustainable Agriculture (NMSA) under the National Action Plan on Climate Change (NAPCC), was launched in the year 2010, aiming at sustainable pest management and intensifying research, commercial production, and marketing of biopesticides. The major focus was to develop new biopesticides and technologies such as sterile insect techniques, transgenic insects, novel botanicals, semio-chemicals and microbial metabolites for pest control and the use of disease forecasting systems (NMSA 2010). Zero-Budget Farming, introduced by the government of India in 2015, was a huge success in southern states encouraging the use of biopesticides.

For the Indian biopesticides market a Compound Annual Growth Rate (CAGR) of 7.3% during the forecast period (2020-2025) is assumed. The Indian biopesticides market was dominated by bioinsecticides in 2019, assumed to stay stable during the forecast period. Wheat, cotton and rice are the major crops cultivated in the country. Bioinsecticides related to these crops are expected to have a higher increase in sales as compared to products used in other crops.

Increasing awareness regarding food safety, organic farming, government policies and subsidies are currently the major factors driving India's biopesticides market. According to Fibl (Research Institute for Organic Agriculture) statistics, the area under organic cultivation in India increased from 1.5 million hectares in 2016 to 1.9 million hectares in 2018.

BIOSTIMULANT REGULATIONS AND TRENDS IN INDIA

Recently, a regulatory body as well as compliance requirements for the biostimulant market in India have been established in line with the Fertiliser Control Order (FCO), issued in 1985. The Indian biostimulant market is largely dominated by micro, small and medium sized enterprises (MSME) and currently estimated to be worth about US$ 201mn becoming one of the fastest-growing sub-sectors of the economy. The new regulations require manufacturers to register products at authority providing a set of information on chemistry (composition, analytical methods, shelf-life), bio-efficacy trials conducted by the Indian Council of Agricultural Research (ICAR), state agricultural

universities (SAUs) preferably in agro-ecological zones, as well as toxicity data and heavy metal analysis. The regulations also allow for the establishment of a regulatory body to monitor the end-to-end movements within the industry. The committee is to control the quality and specifications of all biostimulants and ensure the use of safe substances and organic compounds in manufacturing of products. The agrochemical landscape in India is dominated by farming-related services and specialty products. The Federation of Indian Chambers of Commerce & Industry (FICCI) categorises biostimulants under the latter category alongside micronutrients, biopesticides, and biofertilisers that have recently begun to permeate the markets. Guiding the policymaking process toward levelling the playing field for both small and large players will help the sector contribute close to 20-25% of annual growth.

BIOPESTICIDE REGISTRATION PROCESS IN JAPAN

Biopesticides are widely used in Japan since the 1950s, with insecticides based on *Bacillus thuringiensis* (Bt) being introduced in the 1980s. Biopesticides are basically regulated under the Agricultural Chemical Regulation Law. However, from 1990 onwards, discussions on safety assessment of biopesticides ensued as a result of the development of novel products such as microbial pesticides. In 1997, the Ministry of Agriculture, Forestry and Fisheries (MAFF) established a guidance for biopesticide registration listing data requirements and numbers of studies. The guidance defines viruses, bacteria, fungi, protista and nematodes (with symbiotic bacteria producing active ingredients) as biopesticides. Natural enemies such as parasitoid wasps and predaceous insects as well as active substances derived from microbes have been excluded from the scope of the guideline.

While for the registration of chemical pesticides, a full data package as set out under the Agricultural Chemical Regulation Law is required, for the safety assessment of biopesticides a tiered approach is accepted, since most biopesticides are widely occurring in the natural environment and considered not to be harmful to humans and animals. In particular, the tiered approach is applied for the toxicological safety assessment of biopesticides under the guidance, i.e. 1. single dose studies, 2. repeated dose studies and 3. reproductive studies. If evidence indicates potential hazards, higher tier studies are required. In 2003, the Food Sanitation Law was amended to implement a positive list system setting maximum residue limits (MRLs) for all pesticides. Biopesticides are not subject to the positive list. This is an important incentive for biopesticides which have gained attention as key technology to achieve lower agrochemical inputs.

TRENDS AND DEVELOPMENTS IN THE JAPANESE BIOPESTICIDE MARKET

MAFF amended the Agricultural Chemical Regulation Law in 2018 and introduced a re-evaluation program for all plant protection products registered in Japan in line with the latest scientific information. The re-evaluation program will start in 2021 requiring a review of all registered plant protection products every 15 years. Though several biopesticides already have been registered as plant protection products, MAFF plans to establish a new guideline for biopesticides launching a re-evaluation process also for biopesticides.

Furthermore, on 12 May 2021, MAFF released the so-called "Green Food System Strategy – Achieving both productivity improvement and sustainability of food, agriculture, forestry and fisheries through innovation". Similar to the European Farm to Folk strategy, the "Green Food System Strategy" aims to achieve several goals such as CO_2 zero emission, 50% reduction of agrochemical risk or 30% reduction of chemical fertilizer use by 2050. To archive the strategic goals, MAFF is encouraging to develop and introduce biopesticides and related nature-based technologies. With the implementation of the “Green Food System Strategy”, the role of biopesticides in Japan’s agricultural market is expected to gain in importance.

BIOSTIMULANT REGISTRATION AND TRENDS IN JAPAN

Biostimulants are not legally defined in Japan. However, several products considered as biostimulants are broadly used with registration under the Fertiliser Control Law or Soil Fertility Enhancement Act. In response to the amendment of the Fertiliser Regulation in the EU, an industry group in Japan has been established to actively promote the communication with the competent authorities in order to facilitate the standardisation of biostimulants. With the newly adopted "Green Food System Strategy", MAFF is targeting the reduction of chemical fertilizer use, by recognizing biostimulants as a valuable tool to lower fertiliser inputs and to reduce environmental impacts. The Japanese Crop Protection Association has announced that industry will proceed with developing biostimulants to support this strategic goal. This can accelerate standardisation of the biostimulant regulatory background in Japan.

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