Data requirements for biopesticides in EU – problems and needs

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The European Parliament has been critical for the past few years of the "data gaps in the case of low-risk biological pesticides primarily occur because the [existing] data requirements are designed for chemical plant protection products, and are thus unsuitable for low-risk biological ones".

The EU Parliament considers the current regulatory handling as one of the main reasons for the lack of availability of low-risk plant protection products and the implementation and development of integrated pest management – a view strongly echoed, for example, by the European Court of Auditors. In their special report on "Sustainable use of plant protection products: limited progress in measuring and reducing risks"[2] of February 2020, they criticise that the "progress towards measuring and reducing risks from pesticide use in the EU has been limited" and that several member states have been late in fully transposing the directive on sustainable use of pesticides, while incentives for farmers to adopt alternative methods remain weak. The report acknowledges that the Commission and member states are currently "taking actions to increase availability of low risk PPPs but [that] there is a need for further efforts to meet the timelines set for authorisation". This

is also in line with the multitude of scientific publications discussing biological characteristics, mainly of micro-organisms for use in biological control, and the EU data requirements for the registration of biological plant protection active substances and products, for example, Scheepmaker *et al* 2019[3], Köhl *et al* 2019[4].

For information to be generated and submitted within the scope of a registration dossier, EU Regulation 283/2013 on the data requirements for active substances clearly states that "such information shall not be required, where … it is not necessary owing to the nature of the product or its proposed uses, or it is not scientifically necessary or it is technically not possible to supply. In such a case a justification shall be provided". But, partially owing to the precautionary principle, justification, using basic, general scientific knowledge is seldom sufficient to fulfil the regulatory data requirements as interpreted by many authorities. However, as Köhl *et al* (2019) state, for environmental fate considerations for many micro-organisms "the precautionary principle of the risk assessment can be fulfilled by referring to the general microbiological principles of population dynamics in competitive environments", that is, field conditions.

Reflecting the opinion of many scientific experts, the authors further conclude that "precautionary principles and avoiding any theoretical risk predominates the procedures for MBCAs [microbial biological control agents] leading to unnecessary and costly data collection. Switching to 'principles of evidence-based acceptable risks' instead would allow more restricted data requirements, which may have to be adapted whenever new knowledge and technology becomes available or new safety questions are raised".

Following up on the development of the regulatory process and the data requirements for biopesticides in the EU, it very quickly becomes obvious that the data requirements according to the currently applicable Regulations 283/2013 and 284/2013 are not only "designed for chemical plant protection products" as the EU Parliament criticises. In addition, in case for example for micro-organisms, the current data requirements are also more than 20 years old. This raises the question: what happened to the scientific and technical progress for biopesticides made in these last decades? The answer is unfortunately: very little.

It was already evident at the beginning of the RENDER 4 (Review of EU-notifications under Directive 91/414/EEC and related Regulations) project in 2002 that plant protection product manufacturers (whether large industry or SMEs) would only subject these plant protection products to costly active substance testing – and later registration – if a profitable market for their products could be identified in Europe. Furthermore, there could be available or at least registered competing products which would lower the willingness for the company to try to register a biological product. Therefore, many active substances and products entered the market using the less expensive way of so-called emergency uses as "an EU member state may, under certain circumstances, authorise the placing of a plant protection product on the market for a limited and controlled use for a period not exceeding 120 days in accordance with Article 53 of EU Regulation 1107/2009".

However, using this procedure for active substances which had to be withdrawn from the market about twenty years ago due to their toxicity profile and their environmental incompatibility has resulted in a critical view to the mentioned emergency uses. There have been many attempts to limit emergency use registrations. One example is the introduction of the so-called harmonised risk indicators. According to Commission Directive 2019/782, the hazard weighting for the purpose of calculating Harmonised Risk Indicators is 64 for emergency uses whereat for approved low risk biopesticides it is only 1.

On the other hand, as a result of the emergency use procedure, numerous non-registered biological substances, for example, entomopathogenic fungal products of the genera Beauveria and Metarhizium or bacteria of the genus Bacillus, have been available on the European market for decades. Nevertheless, because of this, they never obtained the official regulatory status as low-risk substance. Long-term safe use in agricultural practise thus has already been shown for many of these biocontrol species. In addition, based on the procedures started with RENDER 4, among others, many research projects were conducted in regard to the requirements for bringing low risk biocontrol agents onto the EU market. For micro-organisms, for example, in the EU, numerous national and EU-funded re-search projects such as BIPESCO (Biological Pest Control), RAFBCA (Risk Assessment for Fungal Bio-logical Control Agents), REBECA (Registration of Biological Control Agents) or INBIOSOIL (Innovative Biological Products For Soil Pest Control) were conducted, to name only some. Work conducted in these research projects already provided some essential risk assessment studies. Most recent examples are a genotoxicity study of *Beauveria* spp and *Metarhizium* spp metabolites, which was carried out in co-operation between project partners of the Eco-Innovation INBIOSOIL and Agriculture and Agri-Food Canada or a long-term field study to assess the persistence of the fungal active agent *Beauveria brongniartii*, which was carried out over a period of twenty years in the EU-region of Tyrol. These and more studies, which were conducted by independent, renowned experts, ensure data security and help companies to place their promising low risk active substances on the market in good time.

Despite these many successful projects, very little of the scientific and technical knowledge entered the regulatory system until now in the form of improved data requirements, guidance or guidelines.

One of the many recent examples from the daily practice may demonstrate the regulatory approach for handling of data requirements, which still exists. In the scope of the renewal of the active substance *Metarhizium brunneum* BIPESCO 5/F52 (formerly *Metarhizium anisopliae* var anisopliae strain BIPESCO 5/F52), a widespread, indigenous soil fungus with several decades of safe use, the applicant was asked the following question on the subject of "genetic stability" of the entomopathogenic fungus: "Could you please provide information on the genetic stability under field conditions? Is there evidence for horizontal gene transfer?" Is any applicant, whether a company or a research institution, able to address such questions fully?

This raises other questions such as: Are such data necessary? How can such data be generated? For one, as already stated, a great wealth of data is already available from research of the last decades. These data are ready to be implemented in the regulatory practise in agreed standardised procedures. Together with a suitable, non-regulatory but scientific approach to dossier and evaluation, this would already close a lot of the present data gaps for low risk biopesticides and their registration. An example is that of baculoviruses, which on family level are classified as low risk today according to Commission Regulation 2017/1432, provided that they show no adverse effects on non-target insects on strain level. Handling of baculoviruses is in addition a very good example for the original idea behind the use of the strain concept in the regulatory practise – for identification and data sets to answer specific questions necessary for risk assessment and not as proof of general microbiological concepts for each individual microbial strain again and again. Moreover, appropriate data requirements and scientific approaches would also increase the success to identify possible risks that might not be identified by the current procedure.

Besides, new data requirements for biological substances, new general concepts and data have to be generated. The "general public" is called upon to generate missing but necessary knowledge and thus also to support bioeconomy and manufacturers (including SMEs) in their registration projects. Sufficient research funds have to be available in order to be able to develop environmentally friendly and effective active substances and make these products marketable. This will only be possible if the necessary valid methods are developed with generous and large-scale research projects, if representative data are compiled and, finally, if the registration of promising active substances is financed publicly and thus realised. It is not enough to wait for the activities of the plant protection industry alone. This especially applies also for non-microbial biopesticides such as botanicals and other natural substances since previous research activities mainly focussed on microbials. Some of them do even qualify for being registered as basic substances, but often, registration is not worthwhile from an economic point of view, especially as it might be time

and cost intensive as well. Such a forward-looking strategy would finally bring to life, the general principles of Integrated Pest Management, which have long been discussed and published in Annex III of the Sustainable Use Directive 128/2009. The need for this approach and view is also urged on by EU Parliament's 2020 resolution on EUs Green Deal5 focussing on "an integrated and science-based approach and bring all sectors together in order to put them on the same track towards the same goal" considering "that the integration of different policies towards a holistic vision is the real added value of the European Green Deal". To this end, the Commission will present the EUs 2020 Farm to Fork Strategy to deliver a more sustainable food policy by bringing together efforts to tackle climate change, protect the environment and preserve and restore biodiversity.

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[1] *P8_TA(2019)0023: European Parliament resolution of 16 January 2019 on the Union's authorisa-tion procedure for pesticides (2018/2153(INI))*

[2] *European Court of Auditors (2020) Special Report 05/2020: Sustainable use of plant protection products: limited progress in measuring and reducing risks. Publication of the European Union.*

[3] *Scheepmaker, J.W.A.,Busschers, M.,Sundh, I., Eilenberg, J. & T.M. Butt (2019): Sense and non-sense of the secondary metabolites data requirements in the EU for beneficial microbial control agents.- Biological Control 136: 1-10.*

[4] *Köhl, J. Booij, K., Kolnaar, R. & W.J. Ravensberg (2019): Ecological arguments to reconsider data requirements regarding the environmental fate of microbial biocontrol agents in the registration procedure in the European Union.- BioControl 64: 469–487*

[5] *P9_TA(2020)0005: European Parliament resolution of 15 January 2020 on the European Green Deal (2019/2956(RSP))*