The complex world of efficacy trial programs and meeting national requirements

In terms of numbers of studies, there is nearly no other section within registration dossiers for plant protection products (PPP) in Europe that contain as many trials as the dRR Part B Section 3 (Efficacy) under the European Regulation (EC) No 1107/2009.

Depending on the product, the uses and the countries for which registration is sought, dossiers containing more than 100 trials evaluating the efficacy, crop safety and other Section 3 data points are very common. Therefore, it is really important to thoroughly analyze which trials are needed under which conditions to fully support the GAP table intended to be registered.

Since European Regulation (EC) No 1107/2009 came into force in 2011, evaluation of the registration reports has been done on a zonal level (interzonal, Northern, Central and Southern authorization zones of Europe) aiming to reduce the required dataset relative to what might be needed for a country by country approach. However, these are purely administrative zones. The efficacy and crop safety of a PPP is affected by numerous factors, such as agronomic practices, edaphic aspects, pest biology, and climatic conditions. Those factors can differ significantly between countries within an authorization zone. It is fairly difficult to justify that overall conditions for a trial conducted in Hungary are similar to one conducted in Ireland although they both belong to the Central authorization zone! According to EPPO PP 1/278(1), "the key objective of a zonal trials programme is to ensure that the range of conditions likely to be encountered across the authorization zone is adequately addressed by the data"[1].

To address the climatic differences, open field trial programs are normally arranged per EPPO climatic zone as defined by EPPO Standard PP 1/241 (2) "Guidance on comparable climates"[2]. Countries within one zone are considered to have comparable conditions in relation to climate and therefore data generated in one of the countries of an EPPO climatic zone are considered supportive towards demonstrating the efficacy of a PPP in other countries within the same EPPO climatic zone.

Climatic, agronomic, edaphic and/or target-related conditions that only apply for a single country or a small area are sometimes not as well considered with this EPPO climatic zone approach. Therefore, some countries have also published specific requirements to assure that the performance of the product under their national conditions is sufficiently addressed.

Ireland, for example, is a country with a very humid climate within the Maritime EPPO climatic zone, resulting in exceptionally high pressure for so-called "wet weather diseases". To assure that the registered product will be sufficiently effective on diseases such as Septoria leaf blotch and Net blotch in cereals or blight in potato, placing of a PPP on the market in Ireland against these diseases and the like requires a certain number of trials conducted in moderate to high disease pressure situations (>20% infection in the untreated control) within this country and/or countries with similar climatic conditions[3]. Requirements vary between the different fungal diseases and crops.

Although Northern zone countries belong to either the Maritime (Denmark, Sweden, Norway) or the North-east EPPO climatic zone (Finland, Baltics), growing conditions such as the day length, the duration of the growing season, the temperature, etc. are different for those Northern countries when compared to countries within the Maritime and North-east EPPO climatic zones but belonging to another registration zone. Therefore, the Northern zone guidance document for efficacy[4] asks for a minimum of trials to be conducted in some of the previously mentioned countries belonging to the Northern zone. The amount of trials required from Denmark, Sweden, Norway, Finland and the Baltics depend on the

[1] Principles of zonal data production and evaluation. Bulletin OEPP/EPPO Bulletin (2012) 42 (3), 358-366
[2] Guidance on comparable climates. Bulletin OEPP/EPPO Bulletin (2014) 44 (3), 281-283
[3] https://www.pcs.agriculture.gov.ie
[4] Guidance on requirement for efficacy data for zonal evaluation of a plant protection product in the Northern zone. Version 7.0, April 2018

product type, whether the formulation contains new active ingredients and/or the importance of the target in the Northern zone.

Greece identified Greek agricultural practices and soil climatic conditions to be different from other countries within Europe. In their guidance document on national requirements for PPPs[5], they list several uses of national importance such as olive fruit flies in olives or root-knot nematodes in vegetables that require some efficacy trials to be specifically carried out in Greece to evaluate possible differences in the effectiveness of the PPP under Greek conditions. Furthermore, for crops that include cultivars of national importance, namely some varieties of olives, pears and grapevine, specific Greek selectivity trials, processing trials and/or taint tests are necessary in those cultivars to demonstrate that the PPP is safe to use and has no negative impact on the quality and sensory characteristics of fresh and processed plant produce.

Those are examples of national requirements that tend to increase the number of efficacy and selectivity trials, but there are some countries that decided to lower the burden of trials needed to demonstrate the efficacy and crop safety of a PPP in reasonable cases. They see the efficacy sufficiently supported with a smaller data set when fully valid trials conducted in other crops or from other regions are available.

Poland[6], for example, accepts some trials conducted in neighbouring countries as supportive. As Poland is the only country within the Central authorization zone that is located in the North-east EPPO climatic zone, data from the Maritime countries Germany and Czech Republic or the South-east country Slovakia could help reducing the number of trials that is necessary for registration in Poland. Italy[7] allows reduction in the number of efficacy trials per use if the same or a similar pest is targeted in different crops. As long as pest biology and cultivation methods are similar, the full data package can be split between 2 crops for example. The Netherlands[8] give significantly more possibilities for the extrapolation of efficacy and crop safety data of PPPs than the extrapolation tables for minor uses provided by EPPO and in contrast to the extrapolation possibilities accepted by EPPO, which is restricted to minor uses, the Dutch extrapolation table allows extrapolation to minor as well as to major uses.

Compilation of an efficacy trial program that supports all uses in all countries intended for registration while keeping costs at an acceptable level is therefore highly complex. The first step, before a trial series for registration of a PPP is initiated, should therefore be an in-depth analysis of the total number of trials required and a smart distribution of the trials to make them acceptable to as many countries as possible. If this step of the registration process of a PPP is not done properly, a lot of money could be wasted by either conducting unnecessary trials or by the non-approval of the PPP by the authorities, because (national) requirements are not met.

If you have any questions on this article, please reach out to Nadja Liebig

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