

Examples of zonal efficacy evaluations

Clarification of efficacy data requirements for the authorization of herbicide for the control of weeds in maize (ZEAMX) in the European Central authorization zone

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This document is intended to assist applicants and evaluators to interpret EPPO Standard PP 1/278 *Principles of zonal data production and evaluation*. Expert judgment should be applied in all cases.

The focus of this paper is in particular on the number and location of trials for the justification of effectiveness, phytotoxicity and resistance issues. There is a need to provide clarification of these areas as part of the zonal authorization process for plant protection products (as defined in EC Regulation 1107/2009, (EC, 2009)).

All trials should be carried out under Good Experimental Practice (GEP) and using all relevant general EPPO Standards. Effectiveness and selectivity trials should be performed according to the EPPO Standard PP 1/50 *Weeds in maize* (available at <http://pp1.eppo.int/>).

All tests should be carried out with the formulation of the product intended for use. If other formulations were used such data may still be used to support the proposed formulation, however bridging data or a sound scientific justification should be supplied to demonstrate comparability of the formulations and allow bridging between formulations. See EPPO PP 1 (in preparation) *Efficacy considerations and data generation when making changes to the chemical composition of plant protection products*.

General information

The EU Zonal Rapporteur Member State (zRMS) and Concerned Member states (cMS) where a product authorization is sought should be named, together with the relevant EPPO climatic zones. Where the product/formulation is already authorized in countries, information should be provided about the herbicide (e.g. active substance, content, type of formulation), the current registration situation and the registration history in the zRMS and the cMS. Some information should be provided about the active substance(s) (e.g. approval status, mode of action, uptake and transport in the plant, behaviour in the soil, RAC classification).

Information on weed spectrum in the Central European zone

The applicant should provide relevant details of the biology of the weeds and the agronomic importance in all Zonal Rapporteur Member State (zRMS) and Concerned Member States (cMS) where authorization is intended. There are useful reference documents available that provide some of this background. Examples include:

- 1) Jensen PK, Bibard V, E. Czembor S Dumitru, Foucart G, Froud-Williams RJ, Jensen JE, Saavedra M, Sattin M, Soukup J, Palou AT, Thibord J-B, Voegler W & P Kudsk (2011) *Survey of weeds in maize crops in Europe* DJF Report Agricultural Science No. 149.¹
- 2) Meissle M *et al.* (2010) Pests, pesticide use and alternative options in European maize production: Current status and future prospects. *Journal of Applied Entomology* 134. 357-375.

Information on grain and forage maize production in the Central Zone

Grain and forage maize are the same species, *Zea mays* (ZEAMX). However, grain maize is harvested as the mature crop for the grain while forage maize is harvested at an earlier stage for ensiling. In certain countries in the Central zone such as the UK only forage maize is grown, while in others the grain crop predominates. In terms of area grown Romania, Hungary, Germany and Poland are the main producers of grain maize in the Central zone

In terms of area grown Germany, Poland, the Netherlands, the Czech Republic and Belgium are the main producers of forage maize in the Central zone. Further information on maize production is available from the [Eurostat](#) website.

Intended Use(s)

The applicant should clearly describe the details of the recommended use/uses for each country where registration is sought (See EPPO Standard PP 1/240, *Harmonized basic information for databases on plant protection products*, particularly points 15 - 34).

Both effectiveness and crop safety trials should be conducted at the growth stages proposed for the intended uses.

Number and distribution of trials required for an authorization

Effectiveness (6.2) Commission Regulation 284/2013), (OECD KIIIA1 6.1.3)

EPPO Standard PP 1/226 *Number of efficacy trials* indicates that for authorization in a single country/climatic zone, 6 to 15 fully supportive results are required over two years for each intended use. Clearly there is scope to reduce the number of trials for those targets considered minor within the requested region.

To support an authorization in the Central Zone, which may encompass different EPPO climatic regions, more than the EPPO recommended number of trials results (6-15) for a single EPPO zone may be needed.

The Central zone encompasses three different EPPO zones of comparable climate: the Maritime zone (Ireland, UK, The Netherlands, Belgium, Luxembourg, Germany, Czech Republic and Austria); the North-east zone (Poland); and the South-east zone (Slovenia, Slovakia, Hungary and Romania). A sufficient number of trials distributed across the 3 zones are necessary to encompass the likely range of conditions encountered for an authorization across the whole Central zone. A minimum of at least 22 fully supportive effectiveness trials results are expected to be required to support an authorization for each intended use.

¹ The Survey can be obtained by using one of the following links http://www.researchgate.net/publication/232775702_SURVEY_OF_WEEDS_IN_MAIZE_CROPS_IN_EUROPE or <http://web.agrsci.dk/djfpublikation/index.asp?action=show&id=1113>

The distribution of trials should consider the major maize growing areas and relative importance of the target weeds. *Chenopodium album* (CHEAL), for example, is a major target in grain and forage maize crops across the zone. Effectiveness trials should be conducted in those countries where CHEAL is a key target and also where grain and/or forage maize is a major crop. Effectiveness trials conducted in grain maize should also be relevant to forage maize (or *vice versa*) since these crops are the same species and the date of sowing and crop phenology are comparable. An effectiveness programme to represent the Central zone might, therefore, include trials conducted in Germany, the Czech Republic, the Netherlands and Belgium to represent the Maritime zone (at least 10 trials results), Poland to represent the North East zone (at least 6 trials results), with the remainder conducted in the South-East zone (at least 6 trials results). Data from other countries that are climatically and agronomically comparable to those in the Central Zone and where CHEAL is a major weed may also be used to provide evidence of effectiveness and could potentially replace some of the trials conducted in the Maritime countries of the Central zone. For example forage and grain maize are grown extensively in Northern France. The precise distribution of trials, however, should consider the major maize growing areas and relative importance of the target weeds. Thus expert judgment should be applied in all cases.

Data may need to be presented separately for different EPPO climatic zones (or any other pest relevant geographic areas) to enable a consideration of whether there is any impact of climatic conditions on performance. If data from all three zones are considered to show no detectable differences in performances, it may be possible to combine all relevant data together. But some initial analysis to demonstrate this is an acceptable approach may be required. When the data are supporting e.g. a new formulation/product, where it has been established that the whole zone can be considered comparable, then summarizing data for the whole zone may be more justified.

Results should be presented in accordance with EPPO Standards PP 1/181 *Conduct and reporting of efficacy evaluation trials including good experimental practice* and PP1/152 *Design and analysis of efficacy evaluation trials*. The key information to provide in summary tables should include:

For all product types: crop growth stage (BBCH) at time of application; population levels at time of application and at each assessment; number of trials; mean percentage control/effect and the range of minimum and maximum levels, for both the test product and also for the reference products, at each assessment timing.

For weeds: weed species; weed growth stage (BBCH) at time of application and time of assessment; weed numbers at application (percentage ground cover or number/m²).

Results should only be included from trials conducted in accordance with EPPO Standards and where there are agronomically relevant pest populations present.

Minimum Effective Dose (6.2) (OECD KIIIA1 6.1.2)

Minimum effective dose trials should be conducted across the relevant different EPPO climatic zones (or any other pest relevant geographic areas) in the Zone to demonstrate that the proposed dose is justified for representative uses. The majority of data should be generated where pest pressure is highest, but a proportion of trials should still include areas of more variable pest pressure. Trials should be conducted in accordance with EPPO PP 1/225 *Minimum effective dose*. A justification for the number of applications applied may also be

required if applications are proposed in different seasons (e.g. autumn, spring) or timings (e.g. pre- or post-emergence).

Resistance (6.3) (OECD KIIIA1 6.2.8)

Reference should be made to EPPO Standard PP 1/213 *Resistance Risk Analysis*.

For high risk pests: Certain weed species are considered a high risk target very likely to develop resistance, based on resistance history. Therefore sensitivity data should be generated, which allow a measure of sensitivity shift and resistance development in future. Populations need to be tested with standardized methods (e.g. HRAC recommended methods). Samples should be taken from different areas in the relevant Zone (similar to efficacy data distribution), with the majority being sampled in regions with high maize production and high need for weed control. But some samples should also be collected in areas with low need for weed control. If there are areas known in which resistance to other active substances has been noticed, such regions should also be sampled. Data from other Zones should also be presented if available. Samples from regions with known resistance to other actives should be tested for cross resistance as well as some samples from regions where no such resistance is expected. In some cases standard populations of known resistance status may be available.

For a new active substance, a sufficient number of populations from the relevant EU Zone should be presented, plus those data for other EU Zones if present².

A resistance management option has to be presented which may vary between regions depending on local practice e.g. availability of alternatives, use of cultural control measures. General proposals for good management practice and modifiers, e.g. rotation, diversification of actives, soil management may form a ‘toolbox of modifiers’. Detailed resistance management strategies will often need to be country specific and individual countries could consider the ‘toolbox of modifiers’ when elaborating country specific strategies. Reference may be made to relevant ‘Resistance Action Committee’ (RAC) recommendations, but should be tailored to individual Member States and reflect e.g. number of applications required, availability of other control options etc. In particular any advice from local ‘Resistance Action Groups’ should be followed, along with any individual National statutory restrictions.

For example, there have been cases of resistance to herbicides reported in CHEAL (The International Survey of Herbicide Resistant Weeds - <http://www.weedscience.org/in.asp>). Thus CHEAL presents a high inherent risk of resistance development. Therefore, sensitivity data might be expected across a range of populations within the zone. Sensitivity testing data from outside the zone but in climatically and agronomically comparable situations may also be useful in this context. It is possible that even for low resistance risk active substances that a resistance management strategy should be developed, tailored according to regional conditions and any Member State statutory restrictions.

² The methodology for sensitivity testing including the number of populations to be tested is currently under discussion as an outcome of the EPPO Workshop on Herbicide Resistance Analysis in the framework of Zonal Evaluation. (http://archives.eppo.int/MEETINGS/2012_conferences/herbicide_resistance.htm)

Phytotoxicity to target plants (including different cultivars), or to target plant products (6.4.1) (OECD KIIIA1 6.2.1, 6.2.5, KIIIA-6.1.4.1-3)

Observations on phytotoxicity should be made in both effectiveness and specific crop safety trials (including 2N doses) in the absence of weeds. Phytotoxicity can depend on BBCH growth stage at application, climatic conditions and the varieties grown. Therefore it is necessary to have phytotoxicity data from all the different climatic zones concerned. Trials should also include a range of commercially grown varieties. Varietal sensitivity testing may also be conducted (see EPPO Standard PP 1/135 *Phytotoxicity assessment*).

Effects on the yield of treated plants or plant products (6.4.2) (OECD KIIIA1 6.1.4.3)

Specific crop safety trials should be located across the Zone in areas representative of maize cultivation. EPPO Standard PP 1/226 *Number of efficacy trials* indicates that for authorization in a single country/climatic zone, typically, at least 8 trials per major crop are required in an area of similar conditions, to cover the range of conditions of use, including soil types, weather conditions that are likely to be encountered. To support an authorization in the Central Zone which may encompass different EPPO climatic zones, more than the EPPO recommended number of trials (8) may be needed. The Central Zone encompasses 3 different EPPO zones of comparable climate and in order to encompass the range of conditions it is expected that for a major crop such as grain or forage maize at least 20 specific crop safety trials will be required. *The total number of specific crop safety trials may be reduced where trials are conducted in both grain and forage maize, and particularly where the plant protection product only has activity against broad-leaved weeds.* These should be located in areas where forage/grain maize is predominantly grown. It is essential that symptoms of phytotoxicity are clearly linked to any subsequent yield effects. Specific crop safety trials must include applications at N and 2N doses and trials should cover the range of proposed growth stages and treatment times for each use.

In grain maize: Total grain yield in kg⁻¹ ha adjusted to a fixed moisture level (specified national or international standard) should be recorded.

In forage maize: Fresh and dry weight of forage (for forage maize) should be recorded.

Effects on the quality of plants or plant product (6.4.3.) (OECD KIIIA1 6.1.4.1)

Appropriate quality assessments relevant to that crop should be made. In some instances additional observations in the effectiveness trials may be sufficient to address the relevant point. See EPPO PP 1/135 *Phytotoxicity assessment* for further details.

Effects on transformation processes (6.4.4) (OECD KIIIA1 6.1.4.2)

If relevant, reference may be made to EPPO Standard PP 1/243 *Effects of plant protection products on transformation processes* which provides an indication of the circumstances under which data on transformation processes are required.

Taint

Reference may be made to EPPO Standard PP 1/242 *Taint tests*.

Impact on treated plants or plant products to be used for propagation (6.4.5) (OECD KIIIA1 6.2.5)

Reference may be made to EPPO Standard PP 1/135 *Phytotoxicity assessment* which provides an indication of the circumstances under which data on plant parts for propagation are required.

Impact on succeeding crops (6.5.1) (OECD KIIIA1 6.2.6)

A step-wise approach should be taken following EPPO Standard PP 1/207 *Effects on succeeding crops*, starting with the herbicidal activity of the active substance, through glasshouse screening, laboratory bio-assays of treated field soils, field screening, monitoring of effectiveness/crop safety field trials and if necessary, specific following crop ‘replanting’ trials using risk mitigation measures such as different cultivation techniques. It is important to consider crops which are likely to be present in rotation with maize across the zone. For testing the biological activity of the test product, the product should be incorporated into the soil and the activity given as an EC (effective concentration).

Impact on other plants, including adjacent crops (6.5.2) (OECD KIIIA1 6.2.7)

A step-wise approach should be taken following EPPO Standard PP 1/256 *Effects on adjacent crops* and should be fully presented. It is important to consider crops which are likely to be present as adjacent crops (either already emerged or yet to emerge) across the zone. Data from other parts of the submission (e.g. ecotoxicology, non-target plant pre- and post-emergence data) can be included in this section. In addition to drift, other routes of exposure should be considered for the formulated product as this may affect adjacent crops.

Effects on beneficial and other non-target organisms (6.5.3) (OECD KIIIA1 6.2.4)

No special trials are required for herbicides if there are no claims for use as part of an Integrated Pest Management Strategy. Reference to individual Member States for any specific national requirements may be required.

References

Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directive 79/117/EEC and 91/414/EEC. Official Journal of the European Union L 309, 1-50.

Commission Regulation (EU) No 284/2013 of 1 March 2013 setting out the data requirements for plant protection products, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market

<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:093:0085:0152:EN:PDF>

OECD Guidance Documents for Pesticide Registration

<http://www.oecd.org/env/ehs/pesticides-biocides/oecdguidancedocumentsforpesticideregistration.htm>