PLANT PROTECTION

REQUIREMENTS APPLIED IN BELGIUM TO AN APPLICATION FOR THE AUTHORIZATION OF AN "ADJUVANT" FOR AGRICULTURAL USE

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1 Introduction

The present document aims at clarifying the Belgian requirements with regard to an application for authorization of an adjuvant for agricultural use.

Under 'requirements', we mean the contents of the authorization dossier including studies and waivers to be assessed with the evaluation of the product to be authorized in Belgium.

The overall assessment and submission procedure of a dossier for authorization in Belgium is the same as the one applied to plant protection products, including the application of the Uniform Principles, where appropriate, as laid down in Regulation 546/2011. More details on the submission procedure can be consulted on the site www.fytoweb.be using the following link: https://fytoweb.be/fr/produits-phytopharmaceutiques/procedure-dautorisation . That document provides information on the ways of presentation of the dossier and on the administrative packages (non-confidential dossier, indications for first aid, …) which must be also submitted and which are not part of the present guidelines.

The aim of the present document is to give instructions to companies for completing their authorization dossier. The diversity of products encountered may exceed the cases taken into consideration in the present document or some requirements may not apply to certain products. In case of any problem or question, please contact directly the Service Pesticides and Fertilizers (Jérémy Denis: jeremy.denis@health.fgov.be, 0032 (0)2 524 72 77).

Belgium will use the uniform principles to evaluate the application for authorization.

2 Definition and legal framework

Adjuvants for agricultural use are chemical or non-chemical products aiming at improving dispersion, spreading, adherence, etc. of plant protection products. An adjuvant will make it possible to obtain better results from active substances and plant protection products and in some cases to reduce the doses of product used.

The substance(s) present in the adjuvant and responsible for the claimed activity of the adjuvant are called ‘active ingredients’ in this document.

The Royal Decree of 28 February 1994 concerning the conservation, the placing on the market and the use of pesticides for agricultural use considers adjuvants as pesticides for agricultural use, classified under the category of "other pesticides likely to be used in agriculture".

Article 1er – 1°. Pesticides for agricultural use : plant protection products and other pesticides likely to be used in agriculture;

Article 1er – 2°. Plant protection products : active substances and preparations containing one or more active substances, put up in the form in which they are supplied to the user, intended to:

- protect plants or plant products against all harmful organisms or prevent the action of such organisms, in so far as such substances or preparations are not otherwise defined below;
- influence the life processes of plants, other than as a nutrient, (e.g. growth regulators);
- preserve plant products, in so far as such substances or products are not subject to special Council of Commission provisions on preservatives;
- destroy undesired plants; or
- destroy parts of plants, check or prevent undesired growth of plants.

Article 1er – 3°. Other pesticides likely to be used in agriculture:

b) humidifying agents, adhesive agents, synergists, safeners and other adjuvants aiming at enhancing the activity of substances and preparations meant under 2° provided they are placed on the market with this purpose.

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 Directives 79/117/EEC and 91/414/EEC lays down the legal framework with regard to the assessment and placing on the market of adjuvants. This legal basis is set out in Article 81(3) where it's indicated that Member States may apply national provisions for authorization of adjuvants until the adoption of detailed rules at EU level as foreseen in art. 58(2) of the Regulation.

Four categories of adjuvants can be distinguished:

- **Wetters :** these are products aiming at improving the efficacy (adherence to crops, spreading,…) of plant protection products.
- **Adjuvants of the 'other adjuvants' type :** these are products aiming at enabling the authorization of plant protection products needing those adjuvants for their efficacy (acidifiers, precursors,...).

- **Stickers :** these are products aiming at enabling better adherence of products for seed treatment and at preventing important dust formation during sowing.
- **Anti-foaming agents :** these are products aiming at preventing excessive foam formation when several formulations are used together.

However, the requirements applied to those different categories are all the same. In the registrations, all those categories of adjuvants are classified under the generic name of 'additives'.

3 Requirements for a dossier of an adjuvant for agricultural use

The dossier must be presented in the dRR format (available on: https://ec.europa.eu/food/sites/food/files/plant/docs/pesticides_ppp_app-proc_guide_doss_reg-report-draft.zip)

3.1 Physical-chemical requirements

The same test methods are applicable as for plant protection products (Regulations 283/2013 and 284/2013). These include CIPAC, OECD and EU methods. A GLP compliant testing is required in the same way as for plant protection products.

Some of these tests may be unnecessary for adjuvants.

The distinction between the evaluation of adjuvants and plant protection products originates from the difference in use. Adjuvants are mixed with plant protection products to improve their action in some way. Therefore, those **mixtures** (and not the adjuvants by themselves) need to possess acceptable **technical characteristics** for proper use. Nevertheless, some **intrinsic properties of the adjuvants** also need to be evaluated to ensure the safety and the stability of the marketed adjuvant.

3.1.1 Intrinsic properties of adjuvant

These tests need to be conducted with the **adjuvant only** to determine its properties, stability and classification.

Properties of the adjuvant active ingredient(s):

The following data are required and can be used from the REACH evaluation if available.

- specifications (purity and if available, impurity profile)
- the following properties if necessary for the evaluation of other sections (mainly ecotoxicology and environmental fate):
    - melting/freezing point
    - boiling point
    - (relative) density
    - vapour pressure
    - surface tension
    - water solubility
    - partition coefficient (*n*-octanol/water)
    - …

Properties of the adjuvant formulation (for all formulations types):

- appearance (colour, odour and physical state)
- content of the adjuvant active ingredient in the formulation (including validated analytical method)
- Hazard parameters (explosive and oxidizing properties, auto-flammability and flammability (*if solid or gas*) or flash point (*if liquid*))
- Density
- Viscosity
- Surface tension
- pH

Stability: low temperature (1 week at 0°C; *for liquids only* according to CIPAC MT 39.3), accelerated storage (2 weeks at 54°C or another combination, CIPAC MT 46.3) and shelf life (2 years at ambient T, CropLife Technical Monograph n° 17)
After ambient and accelerated storage, the following is required:

- appearance (colour, odour, physical state including the stability of the packaging)
- the content of the active ingredient (+/- 5% deviation with regard to the initial value)
- pH

Tests for specific adjuvant formulation types

The required technical properties depend on the formulation type. The following intrinsic properties are needed for the adjuvant formulation:

- Pourability for suspensions and emulsions
- Wettability for solids to be dispersed in water*
- Spontaneity of dispersion for solids to be dispersed in water*
- Particle size distribution*
- Dust content and particle size of dust for granules*
- Attrition for granules and tablets*

Stability: all tests need to be determined after accelerated and ambient storage

It has to be noted that the properties indicated with * are required for solid formulation types. Adjuvants are generally liquids.

3.1.2 Properties of mixtures with relevant plant protection products

The **tank mixture test** is requested to support the applicability of the mixture of the adjuvant and the relevant plant protection product(s). The test ASTM E1518-99 should be used with a 75 µm (200 mesh) sieve and in addition, the **pH of the mixture** should be determined. The test is required only **before storage**.

Both the adjuvant and the plant protection product need to be diluted in the above test. The **concentration ratios** to be tested are determined by the recommended application concentration(s) of the adjuvant and the recommended **maximum application concentration** of the plant protection product.

Generally speaking, relevant mixtures should be tested. However, since it is sometimes difficult to determine which mixtures and which plant protection products are relevant, additional guidance is provided below.

Different cases can be distinguished with regard to the adjuvant's scope of plant protection products:

1. *The adjuvant is marketed with a specific plant protection product*
   The mixture with the product should be tested.
2. *The adjuvant is to be applied with certain plant protection products (specified by name)*
   The mixture with each specified product should be tested.
3. *The adjuvant is to be applied with a certain group of plant protection products (for example herbicides, a specific active substance, …) or for a certain use*
   This is the least evident case. Relevant mixtures should be determined on the basis of the type (herbicide, fungicide, …) and the formulation type (SC, EC, WG, …) of the plant

protection products. When a specific active substance is mentioned, plant protection products containing that active substance should be tested, obviously.
Tests should be conducted preferably with common formulation types, such as the solid SG (soluble granules), WG (water dispersible granule) and WP (wettable powder) formulations and the liquid SL (soluble concentrate), SC (suspension concentrate), EC (emulsion concentrate) and EW (oil in water emulsion) formulations.

Examples

(1) For an adjuvant that is to be used with herbicide formulations, 7 tests could be submitted including mixtures of the adjuvant with SG, WG, WP, SL, SC, EC and EW formulations if all of these are relevant.
(2) For an adjuvant that is to be used with WP formulations to improve their wettability, a herbicide, fungicide and insecticide should be tested if all relevant. If plant protection products of another formulation type are recommended, those should also be tested.
(3) For an adjuvant recommended for herbicides containing a particular active substance, relevant formulation types containing that (those) active substance(s) should be tested.

Where the number of theoretically required tests becomes large (for the 7 mixtures as for (1) or with a representative set), a selection of representative combinations should be tested and supported by argumentation.

In some cases, an argumentation may be acceptable for not supplying all tests.

It is assumed that the applicability of the adjuvant with relevant plant protection products is supported by the efficacy trials.

3.1.3 Additional specific tests

Some adjuvants improve a specific property of a plant protection product in the mixture. This is the case for an antifoaming agent, for example. In such cases, the relevant test (here, the persistent foam test) should be conducted with the mixture. The mixtures should be selected as explained above (section 2). Of course, the test should also be conducted with the plant protection product without the adjuvant as a control for comparison.

Examples

- Anti-foaming agent → reduce foaming: persistent foaming
- Adhesive for seed treatment products → to increase adherence to seeds: adherence to and distribution on seeds (CIPAC MT 175 and 194)

- Wetting agent → to decrease surface tension to better interact with plant surfaces: surface tension and wettability
- Buffer → to control the pH of the spraying solution (pH, see also tank mixture tests (section 2)), …

Other examples are possible on the basis of the function of the adjuvant.

3.1.4 Analytical methods

An analytical method is required to determine the content of the adjuvant active ingredient in the adjuvant formulation. This method should be validated in accordance with the latest revision of SANCO/3030/99.

If a residue definition would exist for the adjuvant active ingredient or its metabolites (or any co-formulant), then validated methods should be submitted for relevant matrices and compartments (latest revision of SANCO/825/00).

3.2 Toxicology

Active ingredient identification : CAS No (or EINECS/ELINCS).

Reference to the ECHA notification under REACH + amount of tons produced in Europe + toxicology dossier submitted if data are required in accordance with the amount of tons produced.

Apart from the toxicology dossier referred to in the previous paragraph, a dossier for the active ingredient needs to be submitted in line with the same principles as for dossiers submitted for active substances of list IV of the review programme under the Directive 91/414/EEC.

- In principle, a dossier according to the data requirements as laid down in Regulation 283/2013 needs to be submitted, but, depending on the substance, an argumentation for not submitting the data required under Regulation 283/2013 is possible.
- Several sources of information/data are possible : studies, rough summary of studies assessed under REACH or by other international organisations (JECFA, EPA, ECB, EFSA, …), data from the literature (primary sources).
- Chemical grouping and read-across : comparison with similar chemicals.
- Use of QSAR : identification of toxicological alerts.
- Definition of reference values (AOEL, TTC…): if relevant.
- Proposal for classification of the substance.

- Safety data file of the substance.
- Possibility to submit waivers and bibliography.

Dossier for the adjuvant formulation:

- Acute toxicity studies (oral, percutaneous, by inhalation).
- Tests on skin and eye irritation
- Test on skin sensitization (Local Lymph Node Assay or preferably Magnusson & Kligman).
- Proposal for classification of the formulation.
- Data relating to percutaneous absorption:
    - individually, if relevant, standard value : 100% (or standard 10% when justified), in vitro test on human skin, or « triple pack » : in vivo test on rat + in vitro tests on human skin/rat ;
    - estimation of the operators' exposure: individually (same models as for active substances).

3.3 Efficacy

The same test methods are applicable as for plant protection products (Regulation 284/2013).

The initial examination of the properties of the adjuvant should be in accordance with EPPO standard PP1/291 in particular its Part 2.

Efficacy trials should be performed in accordance with EPPO standard PP1/291, in particular its Part 3. The specific case of trials testing the anti-drift function of the adjuvant is out of the scope of Part 3. Efficacy trials of EPPO standard PP1/291. For supporting this kind of function, the trials should be in accordance with the French method CEB 245:

- P.Y. Yeme. Commission des essais biologiques, méthode N°245 : méthode d'étude pour l'évaluation de la faculté d'un adjuvant à réduire le potentiel de dérive des préparations phytopharmaceutiques sur les cultures basses.
  Association française de protection des plantes

In any case, the trials should be conducted by official or officially recognised testing facilities or organisations and report should be in accordance with EPPO standard PP1/181 and include a detailed and critical assessment of the data.

3.4 Residues

No residue data are required if at least one of the following criteria is fulfilled:

(1) The proposed adjuvant use is restricted to combination with plant protection products used on crops not destined for human or animal consumption.

(2) The adjuvant is recommended for use with 'half the approved rate of plant protection product' (or less than half).

Examples:

Approved rate of plant protection product (N: max individual dose recommended on the label)	**Half approved rate of plant protection product (when combined with adjuvant)**
1 x N or 2 x 0.5 N	1x 0.5 N or 2 x 0.25 N
4 x N	3 x 0.5 N

(3) The proposed adjuvant use is restricted to combination with plant protection products applied before a significant part of the consumable part of the crop (refers to both animal and human consumption) has developed

(4) The proposed adjuvant use is restricted to combination with plant protection products applied at the latest 7 days before harvest. A recommendation for respecting a PHI of at least 7 days should be mentioned on the label of the adjuvant as condition of the authorized use.

(5) The proposed adjuvant use is restricted to combination with plant protection product uses that do not imply a direct treatment of the crop (e.g. local herbicide treatment in orchards).

Note:
There may be other situations where the generation of residue data is not deemed required, but the applicant must in those cases provide a reasoned scientific case to justify the non-submission of residue data. Such reasoned cases shall be based on sound scientific arguments, shall be sufficiently detailed and well documented. The focus should lie on the physical/chemical properties and mode of action of the adjuvant, rather than on its claimed function. Other considerations related to the specific recommended use of the adjuvant (proposed crops, plant protection products and/or application method) are possible.

However, the arguments provided should always provide a clear rationale on why the adjuvant is unlikely to have an impact on processes determining the fate, behavior and magnitude of the plant protection product residue during and after application.

Residue data are required in other cases:

Basic requirements:

- The trials should be conducted using plant protection products (PPPs) according to their authorized GAP (specified number of applications and latest timings), by using PPP with adjuvant versus PPP alone using the same conditions of use for the PPP within a trial site.
- All comparative trials should preferably be conducted at the same trial site, under conditions representative for the country and/or zone (Northern EU residue zone relevant for outdoor uses in Belgium).
- Specific instructions for use of the adjuvant, as recommended on the proposed label should be taken into account (e.g. adjuvant at maximum spray concentration).
- Residue decline trials and residue data generated over more than one season are not specifically required, although they could provide useful information.
- Other aspects should be considered as for normal residue trials in accordance with current EU guidelines: stability of residues during sample/extract storage, use of fully validated analytical methods, analysis of compounds in line with the correct residue definition, GLP-compliance, etc.
- Residues of the adjuvant itself do not need to be determined.
- Where there is a choice of plant protection products to be used in the trials, active substances that would lead to positive residues (> LOQ) at harvest should be included (in view of a more reliable comparison of data). The choice should be well explained in the applicant's dossier with clear references.
- For the selection of representative crops to be tested in the trials, preference should be given to crops that are expected to show high levels of residue (in view of a more reliable comparison of data).

Extent of data required:

[Ref.: Residue data requirements for the inclusion of an adjuvant on the official list (PSD – The Applicant Guide, 14/06/2004 – Annex 7 (and associated UK Regulatory Updates))]

The minimum number of comparative trials required is dependent on the requested use of the adjuvant (i.e. on the specificity of the recommended combination(s) with authorized

PPP's) and ranges from 4 to 27. Any omissions or deviations from these requirements must be fully addressed by a scientifically justified argument.

(1) Comparative data

Residues data for adjuvants are generated by conducting comparative trials. In this context, a comparative trial is taken to be one trial for a plant protection product plus adjuvant treatment and one trial for the plant protection product alone. The number of trials must be sufficient to identify any significant effect of the adjuvant on plant protection product residue levels.

(2) For uses of adjuvants with pre-harvest uses of plant protection products, not including desiccants:

1. *A proposal for use of the adjuvant with a specific plant protection product on a single crop*
   Four comparative trials are required.
2. *A proposal for use of the adjuvant on all edible crops with all fungicides; or all herbicides; or all insecticides*
   The table below shows the number of plant protection products which must be represented across edible crops for each group of plant protection products. A range of crops covering representatives of a root crop and/or leafy crop, fruit crop, and cereal must be included. Four comparative trials must be carried out for each plant protection product and crop combination chosen.

   Sugar beet can be used to represent both leafy and root crops, provided both the root and leaves are analyzed for residues.

Table 1. The number of plant protection products which need to be included to support a recommendation for all herbicides, all fungicides, or all insecticides on all edible crops

Adjuvant recommended for use with:	Number of different plant protection products which need to be included	Individual types which must be included [ref 1 ref 2]	Number of comparative trials for each plant protection product /crop combination chosen	Number of comparative trials required
all herbicides	3	Phenoxypropionate + two others	4	12
all fungicides	4	i. benzimidazole ii. triazole or morpholine + two others	4	16
all insecticides	3	i. organophosphorus + two others	4	12

Examples of how this works in practice are:

to support a proposal for use of an adjuvant with **all** fungicides on edible crops **16** trials are needed:

(*4 x fungicide A/root crop*) + (*4 x fungicide B/fruit crop*) + (*4 x fungicide C/leafy crop*) + (*4 x fungicide D/cereal crop*) = *16 comparative trials.*

to support a proposal for use of an adjuvant with **all** insecticides **12** trials are needed:

(4 x insecticide A/root crop or leafy crop) + (4 x insecticide B/fruit crop) + (4 x insecticide C/cereal crop) = 12 comparative trials

ref 1 Agrochemicals: Preparation and mode of action. Cremlyn R.J. Ed. Wiley. (1991); *A source of information on the major chemical groups of plant protection products.*
ref 2 The chemistry of plant protection products. Hassall K.A. MacMillan Press. (1982): *Text which gives an overview of the chemistry and mode of action of plant protection products covering a range of chemical groups.*

3. A proposal for use of the adjuvant with all fungicides; or all herbicides; or all insecticides on a single crop
   The table below shows the number of plant protection products which must be represented on a single crop for each group of plant protection products. Four comparative trials must be carried out for each plant protection product and crop combination chosen.

Table 2. The number of plant protection products which need to be included to support a recommendation for all herbicides, for all fungicides, or all insecticides for use on a single crop.

Adjuvant recommended for use with:	Number of different plant protection products which need to be included	Individual types which must be included ref 14 ref 15	Number of comparative trials for each plant protection product /crop combination chosen	Number of comparative trials required
all herbicides	2	i. phenoxypropionate + one other	4	8
all fungicides	3	i. benzimidazole ii. triazole or morpholine + one other	4	12
all insecticides	2	i. organophosphorus + one other	4	8

Examples of how this works in practice are:

to support a proposal for use of an adjuvant with all **fungicides** on a **single** edible crop **12** trials will be needed:

(4 x fungicide A) + (4 x fungicide B) + (4 x fungicide C) = 12

comparative trials.

to support a proposal for use of an adjuvant with all **insecticides** on a **single** edible crop **8** trials will be needed:

(4 x insecticide A) + (4 x insecticide B) = 8 comparative trials.

4. A proposal for use of the adjuvant with a single plant protection product on all edible crops.
   Three comparative trials for each of three different 'crop groups' using the proposed plant protection product and adjuvant. The range of crops must include representatives of the following 'crop groups': root crop and/or leafy crop, fruit crop, and a cereal.
   An example of how this works in practice is:

to support a proposal for use of an adjuvant with **plant protection product X** on all edible crops **9** trials will be needed :

(3 x plant protection product X/root crop or leafy crop) + (3 x plant protection product X/fruit crop) + (3 x plant protection product X/cereal crop) = 9 comparative trials.

5. A proposal for use of the adjuvant with all plant protection products on all crops

   Three comparative trials must be carried out for each plant protection product and crop combination in accordance with the requirements shown in the table below.

Table 3. The number and combination of residues data required to support a recommendation for the use of an adjuvant with all plant protection products on all crops.

Crop group	plant protection product (refer to the table above for details of the types of plant protection products which must be included)	Number of comparative trials
cereal	a herbicide	3
cereal	an insecticide	3
cereal	a fungicide	3
leafy crop	a herbicide	3
leafy crop	an insecticide	3
leafy crop	a fungicide	3
fruit crop	an insecticide	3
fruit crop	a fungicide	3
root crop	an insecticide	3
		TOTAL 27 comparative trials.

Note: ideally a different herbicide, fungicide, or insecticide should be used for the different crop groups

(3) For uses of adjuvants with desiccant uses of plant protection products:

Where plant protection products can be used as herbicides and desiccants, trials generated to reflect herbicide use would not support use as desiccant. This distinction is made due to differences in timing and/or dose. Therefore, an early use in the crop as a herbicide would not support a much later, pre-harvest application as a desiccant with adjuvant. Data must be generated to enable use of adjuvants with desiccants on edible crops to be supported. Four comparative trials are required. The application regime used in the trials must be relevant to the proposed use.

(4) For uses of adjuvants with post-harvest uses of plant protection products:

A minimum of four comparative adjuvant residues trials should be conducted for a recommendation for a use of an adjuvant with a particular plant protection product. For a proposal to use an adjuvant with all post-harvest uses of plant protection products, a minimum of eight comparative adjuvant residues trials are required (four for each of two representative plant protection products). The application regime used in the trials must be relevant to the proposed use. Since residues data for adjuvants are comparative and because plant protection product residues from post-harvest use may be variable, it is recommended that bulk samples are analysed.

3.5 Fate in the environment

- To provide a REACH dossier.
- To provide data on mobility and persistence in soil, demonstrating the adjuvant is not likely to be persistent in the environment neither to move to underground or surface waters, in order to comply with the requirements of the uniform principles (these aspects can be assessed on the basis of the REACH dossier, of evaluations made by other authorities such as another EU Member State, US EPA, ECHA, … of appropriate studies or also on the basis of relevant literature).

3.6 Ecotoxicology

- To provide a REACH dossier
- To provide a proposal for classification
- To provide assessments made by other authorities (such as another EU Member State, EPA, ECHA…).
- To provide a review of the literature dealing with possible synergistic effects of the adjuvant and of the plant protection products towards non-target organisms (fish, daphnia, algae, aquatic plants (if mixed with a herbicide), bees and earthworms). In case of synergistic effect, specific tests left to the judgment of the Federal Public Service may be requested.
- If available, to provide tests on non-target organisms performed with a mixture adjuvant – plant protection product.