CUSTOMIZATION AND ASSESSMENT OF BIOLOGICAL EFFICACY STUDIES UPON DIFFERENT CONDITIONS

Assessment of biological efficacy studies upon different conditions

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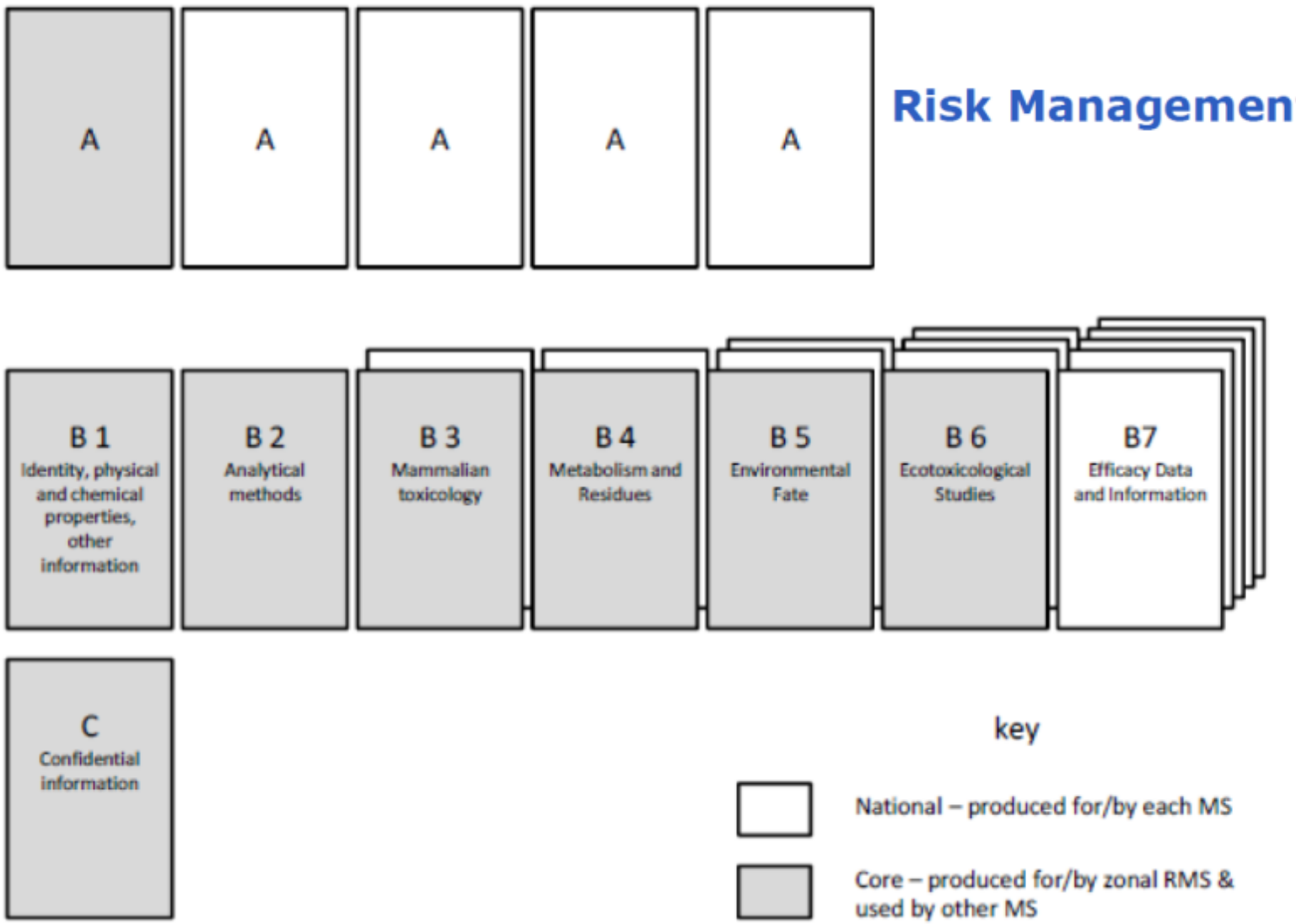
Content

- dRR
- EPPO Guidelines
- Efficacy evaluation of PPPs
- Good Experimental Practice (GEP)
- Conduct of trials
- Major and minor crops
- Extrapolation of data for minor crops

Plant Protection Product (PPP)

- Plant Protection Products are substances, or mixtures of substances, of a chemical or biological nature, or formulated preparation of microorganisms (fungi, viruses, bacteria, protozoa or other microscopic self-replicating biotic entities), intended for use in agriculture, horticulture, forestry, gardens and amenity areas, on stored plant products and on land not intended for cropping, for the purpose of :
  - protecting plants or plant products by destroying,
  - repelling or limiting the growth of pests
  - destroying or limiting the growth of weeds or undesired plants
  - controlling or modifying the growth of plants (other than as nutrients).

The dRR


A
A
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Risk Management
B 1
Identity, physical and chemical properties, other information
B 2
Analytical methods
B 3
Mammalian toxicology
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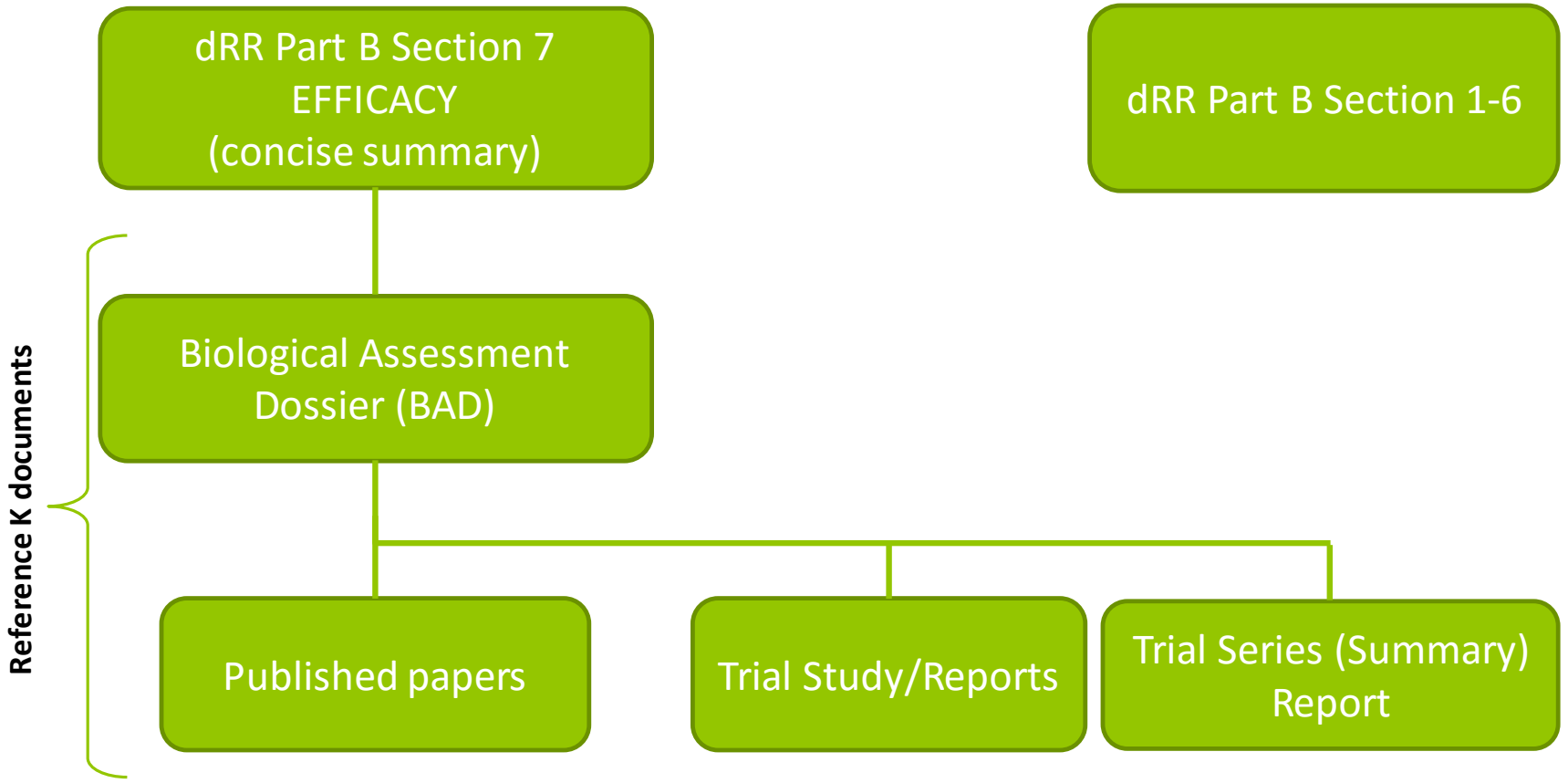
C
Confidential information
key
National – produced for/by each MS
Core – produced for/by zonal RMS & used by other MS

The dRR part B



Description of PPP

Description of the plant protection product

PRODUCT 80 WG is a Water dispersible Granular (WG) formulation containing 800 grams per Kilogram (g/kg) XXX for use on pome fruits, tomato and peach.

Proposed trade name:	PRODUCT 80 WG
XXX content:	800 g/kg (XXX)
Formulation type:	Water Dispersible granules (WG)
Synonyms:	-
Active ingredient	**XXX**
IUPAC name:	
Chemical group:	
Mode of action:	
Plant translocation:	

For further physico-chemical properties, please refer to Registration Report Part B Section 1: Identity, physical and chemical properties, other information.

Supporting information from earlier formulations of the active substance or similar active substances

Due to the numerous products, in the following overview details are given only for an assortment of the most common products granted in the EU South zone.

Example of current approvals of XXX containing products in the EU South zone

Country	Product(s)	Approval Number
MS1		
MS2		
MS3		
MS4		
MS5		

The dRR Part B Sect. 7 Efficacy

- Part B, Section 7 of the dRR should provide concise summaries for each of the Annex points, cross-referencing to the relevant sections within the BAD
- The BAD (OECD) format should provide the assessment of the data and associated study reports + concise summaries
- The BAD and Study reports are submitted as a K-document
- The summaries are transferred to the dRR
- It is not always necessary or appropriate to provide an individual BAD for each regulatory zone. A single multiple-zonal BAD can be appropriate with summarisation of the relevant data for each zone only in the dRR
- If particular National Requirements are needed, these should be addressed in accompanying National addenda.

Efficacy

Trials in this dossier were carried out by contractor companies and Official Research institutes, all of which follow the EPPO guidelines and are officially recognized by the competent authorities to carry out field registration trials in accordance with the principles of Good Experimental Practice (GEP).

On the basis of the EPPO guideline 1/241(1) "Guidance on comparable climates", the trials included in this dossier have been grouped and summarized by EPPO zones. EPPO zones have been defined by taking into account differences between the agro-climatic sub-areas of the EPPO region.

In general the trials were conducted according to the respective EPPO guidelines.

Country	EPPO zone	regulatory zone
MS1, MS2, MS3	MEDITERRANEAN	SOUTH
MS4	SOUTH-EAST	SOUTH and CENTRAL
MS5, MS6, MS7	MARITIME	SOUTH and CENTRAL

The South European zone covers countries in EPPO climatic zones Mediterranean, Maritime and South-East as described in EPPO PP1 / 241(1). This submission includes data from the Mediterranean, the Maritime as well as the South-East EPPO zones which represents the proposed GAP.

The EPPO Standards

- The EPPO standards for the efficacy evaluation of plant protection products (more than 270 standards covering a wide range of crops and pests) describe the conduct of trials carried out to assess the efficacy of PPPs against specific targets
- They are addressed to all Institutions, official registration Authorities, public institutes or private firms carrying out such trials
- They are considered as reference documents in Reg. 545/2011 as regards the data requirements for PPPs
- All General Standards (e.g. design, conduct, reporting and analysis of trials, phytotoxicity, effects on succeeding crops, analysis of resistance risk, minor uses) can be accessed free of charge
- Access to Specific Standards (e.g. aphids on potato, weeds in cereals) is provided for an annual fee

Conduct and reporting of efficacy evaluation trials, including good experimental practice (GEP) PP 1/181(4)

- EPPO Standards are generally laid out in the following
- order:
  - 'Experimental conditions', covering the aspects on which the experimenter can take decisions in setting up the trial.
  - 'Application of treatments', covering the products and the application conditions, which again the experimenter decides.
  - 'Mode of assessment, recording and measurements', covering the data on pest populations, damage and loss which the experimenter records during the trial. Also included are observations on meteorological and soil conditions, which are not normally within the experimenter's control.
  - 'Results'.

Testing Facilities

- Authorized and certified by competent authority to carry out field registration trials in accordance with the principles of Good Experimental Practice (GEP).
- Trials in dossier were carried out by contractor companies and Official Research institutes, all of which follow the EPPO guidelines
- Inspected and check every second year
- List of Auditors certified by competent authority

Good experimental practice (GEP)

- The primary aim of Good Experimental Practice (GEP) is to ensure that high-quality trials are conducted. This ensures that results can be used by different registration authorities.
- GEP is concerned with the management of efficacy evaluation trials and with the conditions under which trials should be planned, conducted, assessed, recorded and interpreted so that their results should be comparable and reliable.
- GEP relates to various aspects: staff qualifications, use of suitable equipment and facilities, protocols, modes of operation, recording of results.
- GEP requires consideration of the following:
  - The criteria to be respected by the organizations responsible for the trials;
  - The modes of operation of these organizations;
  - The internal procedures for verification of the use of GEP.
  - A quality control unit is not required.

GEP:

Criteria for organizations responsible for the trials

- Identity of the organization: The organization should be official or officially recognized.
- The field of activity, location and structure of the organization should be known over the whole area in which a trial series is conducted. The organization should be able to ensure that GEP is applied over the whole period and geographical extent of its trials.
- Identity of the trial sites: The organization should establish the identity of the trial sites and of the data coming from each, so that this identity can be maintained throughout all successive documents from the first set-up of the trial to the final report.
- Management of trials: The organization should ensure structured management of its trials. It should have sufficient staff and resources to set up and manage trial series to the same standard.
- Staff: The organization should employ scientific and technical staff with the appropriate training, knowledge and experience to perform the tasks assigned to them. These qualifications may derive from formal education in agriculture or a related subject, from professional experience or from continued training. Temporary staff should be adequately directed by permanent staff to ensure high-quality work.

GEP:

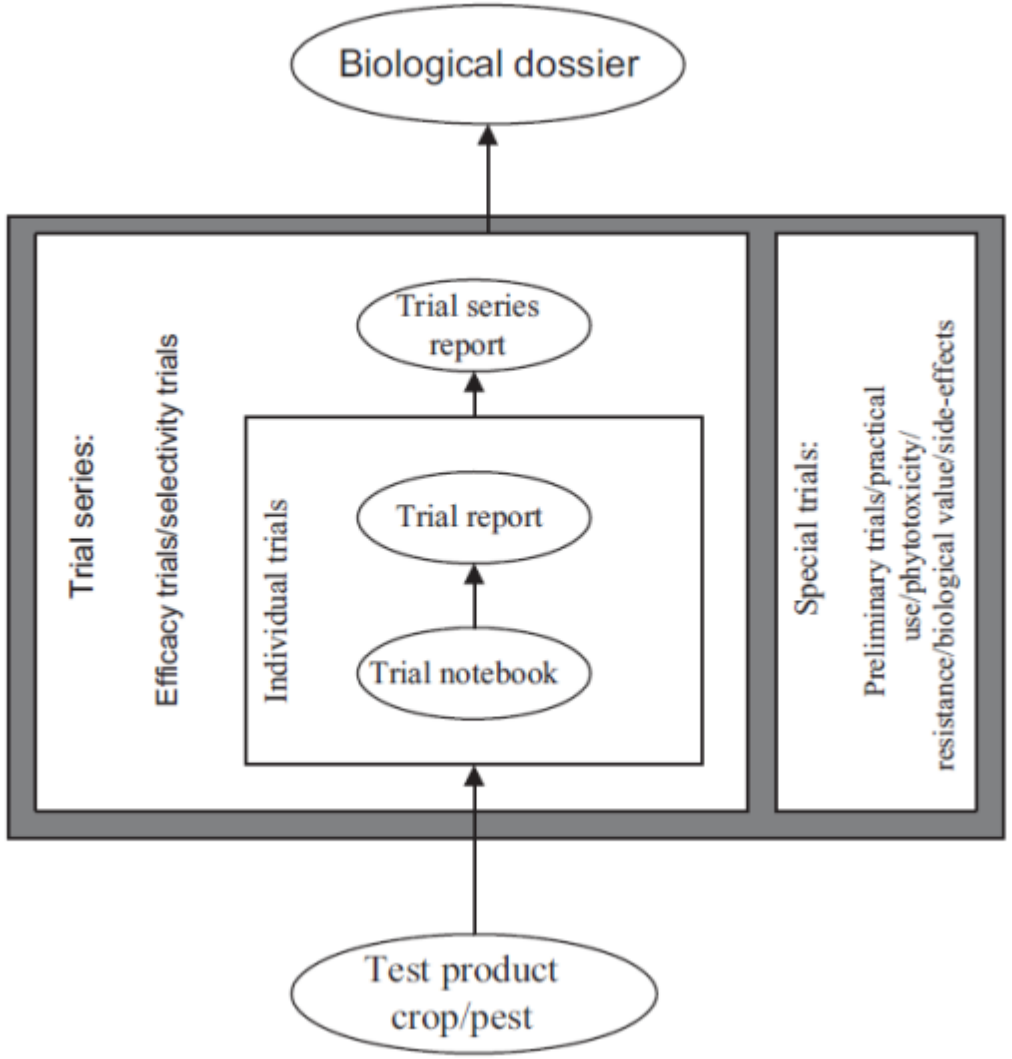
Criteria for organizations responsible for the trials

- Assignment of responsibilities: The organization should clearly assign the tasks of the staff responsible for drawing up protocols, planning trials within a series, performing trials, writing reports. The organization should ascertain that staff have the resources required for the tasks assigned and that their responsibilities are clearly defined.
- Equipment: The organization should have available equipment of suitable design, in suitable quantities. The different types of equipment should be inventoried; modes of operation for their use, maintenance, adjustment and calibration should be established.
- Facilities: The facilities used by the organization (buildings for storing and preparing products, buildings for storing and maintaining equipment, field plots, glasshouses and shelters, dataprocessing facilities, as appropriate) should be located and designed so that they can be used for high-quality trials.

Conduct and reporting of efficacy evaluation trials, including good experimental practice (GEP)

- Trial series
- Product performance should be based on the interpretation of the results of a trial series as a whole, and not only on those of single trials. A trial series is a set of trials on the same subject (e.g. efficacy, or crop safety, of a given product) set up following a general experimental protocol as applicable, at different locations and/or in different years or growing seasons.
- In practice, a general experimental protocol describes the core treatments to be tested on all selected environments, allowing the experimenter to add specific practices only used locally. The analysis of a trial series is primarily based on analysing the core protocol.

Origins of biological dossier.



Conclusions to draw from the biological dossier

- The duration of the effects of the treatment and, if relevant, the number of applications required and the suitable intervals between applications;
- Evidence that the proposed dose, timing and mode of application provide adequate results for control or protection and that they produce the required effect for all the proposed uses;
- If relevant, influence of environmental factors such as temperature or rainfall on the action of the plant protection product;
- Evidence that the plant protection product does not have unacceptable effects (such as phytotoxicity, yield reduction, quality decrease of treated crop, impact on succeeding or adjacent crops, appearance of resistance);
- If the proposed use includes recommendations on the use of the plant protection product in a mixture with other plant protection products and/or adjuvants, information on the expected results of the mixture;
- If the proposed use is to cover a broader area such as demonstrating performance and seeking authorization across a substantive area or 'authorization zone', information on the different conditions encountered across that region and performance under those conditions. Further information on such zonal submissions and evaluations is available in PP 1/278 Principles of zonal data production and evaluation.

Example of a site details summary for a single application.

Trial series Trial no. Country, Region	Testing Facility GEP Y/N EPPO GL	Test crop Variety Sowing or planting date Artificial inoculation Previous crop	Soil type Soil pH/ OM% Sand/Silt/Clay (%) Soil CEC	Application details: Type of equip./Type of nozzles/ Temp/Pressure/Volume Application Date	Experim. design No. of replicates Plot Size Test method
1 DEV-F-1999-ZX-012-A-01,0 DE-D01-018 GERMANY BADEN-WUERTTEMBERG —	BASF yes 26, 135, 152, 181	WHEAT, WINTER KANZLER 30/09/1998 no	LOAM 6.6 / 1.8 13 / 65 / 21 —	SPT / XR8003 / 22 C / 2.8 BAR / 400 L/HA / 22Mar99	RCB 4 10 M2 ---
2 DEV-F-1999-ZX-012-A-01,0 DE-D02-012 GERMANY SAXONY-ANHALT —	BASF yes 26, 135, 152, 181	WHEAT, WINTER KANZLER — no	— — — —	SPT / XR8002VS / 25 C / 2 BAR / 400 L/HA 01Apr99	RCB 4 10 M2 —
3 DEV-F-1999-ZX-012-A-01,0 DE-D03-012 GERMANY SCHLESWIG-HOLSTEIN —	BASF yes 26, 135, 152, 181	WHEAT, WINTER RITMO 19/10/1998 no	LOAM 6.8 / 1.0 — —	SPT / XR 8002VS / 29 C / 2 BAR / 300 L/HA / 29Mar99	RCB 4 10 M2 —
4 DEV-F-1999-ZX-012-A-01,0 DE-D04-027 AUSTRIA STYRIA —	BASF yes 26, 135, 152, 181	WHEAT, WINTER RITMO 16/10/1998 no	LOAM 6.9 / 4.4 10 / 76 / 14 —	SPT / XR 8004VS / 20 C / 1.8 BAR / 300 L/HA / 18Apr99	RCB 4 12.5 M2 —
5 DEV-F-1999-ZX-012-A-01,0 DE-D05-319 GERMANY SAXONY-ANHALT —	BASF yes 26, 135, 152, 181	WHEAT, WINTER RITMO 24/09/1998 no	SANDY LOAM 6.9 /2.0 — —	FPT / XR8002 / 16 C / 2.6 BAR / 300 L/HA / 15Apr99	RCB 4 14.75 M2 —

Example of a site details summary for a multiple application.

Testing Facility GEP Y/N EPPO GL	Test crop Variety Sowing or planting date Artificial inoculation Previous Crop	Soil type Soil pH/ OM% Sand/Silt/Clay (%) Soil CEC	Application details: Type of equip./Type of nozzles/ Temp/Pressure/Volume Application Date	Experim. design No. of replicates Plot Size Test method
BASF yes 31, 152,181	GRAPE, EUROPEAN MULLER-THURGEAU 1992 no ---	SANDY LOAM 6.7 / 1.8 23 / 55 / 21 ---	TSP / 110015 / 17C / 10BAR / 600 L/HA / 01Apr99 TSP / 110015 / 26C / 10BAR / 600 L/HA / 15Apr99 TSP / 110015 / 20C / 10BAR / 800 L/HA / 02May99 TSP / 110015 / 14C / 10BAR / 1000 L/HA / 18May99 TSP / 110015 / – / 10BAR / 1200 L/HA / 29May99 SPT / XR8002VS / 25 C / 2 BAR / 1200 L/HA / 16Jun99	RCB 4 30 M2 ---
BASF yes 31, 152,181	GRAPE, EUROPEAN --- --- no ---	LOAM 6.6 / 1.8 13 / 65 / 21 ---	TSP / ALBUSGELB / 18C / 8BAR / 600 L/HA / 18Apr99 TSP / ALBUSGELB / 22C / 8BAR / 600 L/HA / 02May99 TSP / ALBUSGELB / 18C / 8BAR / 800 L/HA / 18May99 TSP / ALBUSGELB / 19C / 8BAR / 1000 L/HA / 30May99 TSP / ALBUSGELB / 21C / 8BAR / 1200 L/HA / 19Jun99 TSP / ALBUSGELB / 22C / 8BAR / 1400 L/HA / 30Jun99	RCB 4 24 M2 ---
BASF yes 31, 152,181	GRAPE, EUROPEAN --- --- no ---	LOAMY SAND	SDG / XR8002VS / 19C / 3BAR / 800 L/HA / 02May99 SDG / XR8002VS / 21C / 3BAR / 800 L/HA / 22May99 SDG / XR8002VS / 20C / 3BAR / 1200 L/HA / 04Jun99 SDG / XR8002VS / 23C / 3BAR / 1200 L/HA / 14Jun99 SDG / XR8002VS / 26C / 3BAR / 1400 L/HA / 01Jul99	RCB 4 20 M2 ---
BASF yes 31, 152,181	GRAPE, EUROPEAN --- 1986 no ---	SAND	SDG / XR8002VS / 24C / 3BAR / 800 L/HA / 03May99 SDG / XR8002VS / 19C / 3BAR / 1000 L/HA / 13May99 SDG / XR8002VS / 24C / 3BAR / 1000 L/HA / 30May99 SDG / XR8002VS / 21C / 3BAR / 1200 L/HA / 15Jun99 SDG / XR8002VS / 26C / 3BAR / 1400 L/HA / 01Jul99 SDG / XR8002VS / 22C / 3BAR / 1400 L/HA / 18Jul99 SDG / XR8002VS / 27C / 3BAR / 1800 L/HA / 04Aug99	RCB 4 20 M2 ---

Example of a single-trial summary.

		Evaluation date			24May02	03June02		16July02	
		Trt-Eval interval			0DAA1	10DAA1		13DAA3	
		Target			PIERBR	PIERBR		PIERBR	
		Crop growth stage			37-39	39		45	
		Target stage			L 1-2	L2		L4 P	
		Evaluation type			Control	Control		Control	
		Part evaluated			Plant	Plant		Plant	
Treatment Name	**Conc.**	**Application rate**	**Application Date**	**GS crop Application**	**Count**	**Count**	**% control (log transformation)**	**Count**	**% control (log transformation)**
Product A	100 g a.s./L	0.1 L/ha	24May02	37-39	1	4.3	28.3 b	8.6	49.4 c
Product A	100 g a.s./L	0.15 L/ha	24May02	37-39	1	3.5	41.7 b	5.2	69.4 ab
Product A	100 g a.s./L	0.2 L/ha	24May02	37-39	1	1.2	80 a	0.3	98.2 a
Standard B	500 g a.s./kg	0.5 kg/ha	24May02	37-39	1	1.6	73.3 a	0.34	98 a
Standard C	150 g a.s./L	1.0 L/ha	24May02	37-39	1	4.2	30 b	8.9	47.6 c
Untreated	-	-	24May02	37-39	1	6	0 c	17	0 d
			CV%				12.6		18.9
			SE_mean				0.24		0.34
			Replicate Prob (F)				0.56		0.98
			Treatment Prob (F)				0.001		0.001
			MRT				SNK (0.05)		Tukeys (0.05)

Example of a multi-trial summary for a single application.

Trial series Trial no. GEP Y/N	Country Region Crop Cultivar	Date of treatment/ Growth stage crop (BBCH)/ Growth stage target (BBCH)/ Water volume	Timing of Assessment DAFT	Assessed Variable (calculated)	Untreated	BAS 48107F 1.5 L/ha	BAS 49303F 1.0 L/ha	Standard		
								1	2	Code
1 DEV-F-1999-ZX-012-A-01,0 DE-D01-018 no	GERMANY --- WHEAT, WINTER KANZLER	26.05.1999 / - 39 - / --- / 400 L/HA	115	Yield (dt/ha) SNK	57,91 a	68,83 b	69,44 b	68,26 b	70,03 b	1=A 2=B
2 DEV-F-1999-ZX-012-A-01,0 DE-D02-012 no	GERMANY --- WHEAT, WINTER KANZLER	31.05.1999 / 47 - 49 - / --- / 400 L/HA	104	Yield (dt/ha) SNK	74,96 a	84,84 b	86,78 b	82,16 b		1=A
3 DEV-F-1999-ZX-012-A-01,0 DE-D03-012 no	GERMANY --- WHEAT, WINTER RITMO	29.05.1999 / - 49 - / --- / 300 L/HA	96	Yield (dt/ha) SNK	80,53 a	97,83 b	100,62 b	95,6 b		1=B
4 DEV-F-1999-ZX-012-A-01,0 DE-D04-027 no	GERMANY --- WHEAT, WINTER RITMO	31.05.1999 / 39 - 49 - / --- / 300 L/HA	112	Yield (dt/ha) SNK	100,65 a	111,65 b	114,14 c	113,21 b		1=B
10 DEV-F-1999-ZX-012-A-01,0 DE-D12-120 no	GERMANY --- WHEAT, WINTER MONOPOL	19.05.1999 / - - 45 - / --- / 300 L/HA	114	Yield (dt/ha) SNK	67,13 a	75,53 b	77,21 b	78,1 b		1=A
11 DEV-F-1999-ZX-012-A-01,0 DE-D13-912 no	GERMANY --- WHEAT, WINTER RITMO	28.05.1999 / 49 - 49 - / --- / 300 L/HA	97	Yield (dt/ha) SNK	74,01 a	87,06 b	91,48 c	87		1=A
12 DEV-F-1999-ZX-012-A-01,0 DE-D14-016 no	GERMANY --- WHEAT, WINTER MONOPOL	31.05.1999 / 39 - 45 - / --- / 400 L/HA	103	Yield (dt/ha) SNK	72,18 a	82,74 b	85,48 b	---		---
13 DEV-F-1999-ZX-012-A-01,0 DE-D15-016 no	GERMANY --- WHEAT, WINTER BATIS	30.05.1999 / 39 - 49 - / --- / 300 L/HA	99	Yield (dt/ha) SNK	62,7 a	74,34 b	74,96 b	74,11		1=A
				Yield (dt/ha) SNK	75,65	91,39	94,11			

Standard A Product X 1. L pr/ha
Standard B Product X 2.0 L pr/ha
Standard C Product Y 2.5 L pr/ha

Example of a multi-trial summary for multiple applications.

Trial series Trial no. GEP Y/N	Country Region Crop Cultivar	Date of treatment/ Growth stage crop (BBCH)/ Growth stage target (BBCH)/ Water volume	Plant part	Timing of assessment DAFT	Assessed Variable (calculated)	Eval. Unit	Untreated	ABCD 0,16 % W/V	ABCD 0,20 % W/V	Standard 1,00	Standard 2,00	Standard Code
1 DEV-F-1999-ZX-311-A-01,0 DE-D06-006 no	GERMANY, FED.REP. --- GRAPE, EUROPEAN ORTEGA	14.05.1999 / 13 - 14 - / — / 600 L/HA 26.05.1999 / 53 - 54 - / — / 600 L/HA 08.06.1999 / 61 - 62 - / — / 800 L/HA 22.06.1999 / 68 - 69 - / — / 1000 L/HA 08.07.1999 / 72 - 73 - / — / 1200 L/HA 26.07.1999 / 78 - 79 - / — / 1400 L/HA 09.08.1999 / 81 - 82 - / — / 1600 L/HA	RACEME RACEME RACEME RACEME	82 82 95 95	Frequency Intensity Frequency Intensity	% % % %	16,75 2,69 19,54 2,10	0,00 0,00 0,00 0,00	0,00 0,00 0,00 0,00	0,00 0,00 0,00 0,00	0,00 0,00 0,00 0,00	1=A 2=B
2 DEV-F-1999-ZX-311-A-01,0 DE-D09-951 no	GERMANY, FED.REP. --- GRAPE, EUROPEAN KERNER	18.05.1999 / 11 - 13 - / — / 600 L/HA 31.05.1999 / 30 - - / — / 600 L/HA 14.06.1999 / 57 - - / — / 800 L/HA 28.06.1999 / 68 - - / — / 1000 L/HA 12.07.1999 / 71 - - / — / 1200 L/HA 27.07.1999 / 75 - - / — / 1400 L/HA 10.08.1999 / 81 - - / — / 1600 L/HA	RACEME RACEME	76 76	Frequency Intensity	% %	42,75 13,42	2,00 1,25	0,50 0,00	0,75 0,00	0,75 0,00	1=A 2=C
3 DEV-F-1999-ZX-501-A-01,0 DE-VTV-001 no	GERMANY, FED.REP. --- GRAPE, EUROPEAN KERNER	19.05.1999 / 53 - 53 - / — / 800 L/HA 01.06.1999 / 55 - 55 - / — / 800 L/HA 15.06.1999 / 57 - 61 - / — / 800 L/HA 29.06.1999 / 69 - 71 - / — / 1200 L/HA 13.07.1999 / 75 - 77 - / — / 1200 L/HA 27.07.1999 / 78 - 79 - / — / 1600 L/HA 09.08.1999 / 81 - 81 - / — / 1600 L/HA	RACEME RACEME	86 86	Frequency Intensity	% %	32,00 1,87	0,00 0,00	0,00 0,00	0,00 0,00	0,00 0,00	1=D 2=B
4 DEV-F-1999-ZX-503-A-01,0 DE-VTV-005 no	GERMANY, FED.REP. --- GRAPE, EUROPEAN MUELLER THURGAU	02.06.1999 / 55 - 55 - / — / 800 L/HA 16.06.1999 / 57 - 61 - / — / 800 L/HA 30.06.1999 / 69 - 71 - / — / 1200 L/HA 16.07.1999 / 75 - 77 - / — / 1200 L/HA 28.07.1999 / 78 - 79 - / — / 1600 L/HA 11.08.1999 / 81 - 81 - / — / 1600 L/HA	RACEME RACEME RACEME RACEME RACEME RACEME	67 67 76 76 89 89	Frequency Intensity Frequency Intensity Frequency Intensity	% % % % % %	98,00 40,98 100,00 47,84 100,00 67,07	2,67 0,13 6,67 0,33 5,33 0,27	4,67 0,23 7,33 0,37 8,00 0,40	11,33 0,67 30,00 1,83 38,67 3,23		1=A
Meanvalues				67 67	Frequency Intensity	% %	98,00 40,98	2,67 0,13	4,67 0,23	11,33 0,67		
				n			1	1	1	1		
				76 76	Frequency Intensity	% %	71,37 30,63	4,33 0,79	3,91 0,18	15,38 0,91		
				n			2	2	2	2		
				82 - 86 82 - 86	Frequency Intensity	% %	24,37 2,28	0,00 0,00	0,00 0,00	0,00 0,00		
				n			2	2	2	2		
				89 - 95 89 - 95	Frequency Intensity	% %	59,77 34,58	2,67 0,13	4,00 0,20	19,34 1,61		
				n			2	2	2	2		

Standard A Product X 1.0 L pr/hL
Standard B Product X 1.2 L pr/hL
Standard C Product Y 0.35 L pr/hL
Standard D Product Z 0.75 kg pr/hL

The efficacy parameters

- Conduct of efficacy evaluation trials
- Testing organizations
- Test conditions and guidelines
- Location
- Efficacy
- Effectiveness (direct efficacy)
- Resistance
- Absence of unacceptable effects
  - Phytotoxicity
  - Yield
  - Quality (including transformation processes)
  - Plants or plant parts used for propagation
  - Succeeding crops
  - Adjacent crops
  - Pollinators and natural enemies
  - Subsequently treated crops (effect of tank cleaning)

The evaluation

- Testing organisations
  - All trials should be conducted according to the principles of good experimental practice (GEP) by officially recognized, testing organisations
- Test conditions
  - Trials should have been carried out in accordance with specific EPPO Standards, where available. In cases where no test guideline was available and other experimental methods have been used, or where deviations had been made from accepted test guidelines, the applicant should explain, and the Authority should evaluate, the suitability of the experimental methods used
- Locations
  - Trials should have been conducted in locations that represent the range of agricultural, plant health and environmental conditions (including climatic conditions) likely to be encountered in practice in the area of proposed use

Efficacy evaluation

- The efficacy evaluation should establish that there is an overall benefit from the use of a product, and should confirm the proposed recommendations for use of the product, as envisaged by the draft label
- Sound experimental data should support the claims made on the draft label
- Trials have to be conducted in areas where the level of infection/infestation of the host by the harmful organism is usually satisfactorily high, so that valid evaluation of the outcome is feasible
- The first criterion of acceptable performance is that the product shows results that are significantly superior to those recorded in the untreated control
- Satisfactory levels of performance are generally met when the performance of the test product is comparable with that of a reference product

Efficacy evaluation

- The number of trials to be conducted and reported is not standardised and is primarily determined by:
- a)the importance of the crop and pest (major or minor), and the possibility of extrapolation between crops and pests
- b)prior knowledge of the active substance or product
- c)the range of conditions that arise during its use, (i.e., variability in plant health conditions, climatic differences, range of agricultural practices, uniformity of the crops, mode of application, type of harmful organism and the type of ppp). As a general guide, a total of 6-10 trials against a major pest on a major crop are fully supportive of direct efficacy Trials should be designed to investigate specified issues, minimize the effects of random variation between different parts of each site and enable appropriate statistical analysis to be applied to the obtained results

Efficacy evaluation

- In general, the effects on harmful organisms, the spectrum of activity and method of application of the reference product should be close to those of the tested one
- Dose rates lower than the recommended one must be included in some trials to enable a valid assessment of whether the recommended dose is the minimum necessary to achieve the desired effect (dose response)
- Evidence should be sufficient to confirm that performance, and absence of any unacceptable effects, are consistent over the range of conditions (including agricultural, climatic, plant health and environmental) likely to be encountered in practical use
- In addition to experimental data, the evidence submitted can includes supporting information, such as published papers and reports relating to the product

Minimum effective dose

- the ‘minimum effective dose’ of a plant protection product is the dose that is the minimum necessary to achieve sufficient efficacy against a target pest across the broad range of situations in which the product will be applied.
- trials where the recommended dose provide one or more of the following:
  - A higher level of effectiveness compared to the lower dose;
  - A longer persistence of action compared to the lower dose.
- At least 3 dosages should be tested
- Where the recommended dose can be identified as the minimum effective dose from preliminary tests and efficacy trials, with lower doses meeting the criteria, no additional trials are necessary to establish that the dose recommended is the minimum necessary for efficacy.

Efficacy evaluation

- The submitted experimental data is evaluated in a uniform way among all MS according to harmonised approaches and criteria established in the Uniform Principles of Reg 546/2011
- Comparison with untreated controls and with reference products should also form the basis of decision-making on the acceptability of any adverse effects

Principles of acceptable efficacy

- Efficacy can be considered to be a balance between:
  - the positive effects of treatment in performing the desired plant protection activity, that is controlling the target pest or modifying crop growth in order to achieve improvement in the quantity and/or quality of crop yield, premature or delayed ripening;
  - the negative effects (such as reduction of quality or quantity of yield/phytotoxicity, damage to beneficial organisms, damage to succeeding or adjacent crops, development of resistance);
  - other aspects of efficacy which, depending on the product, can be either positive or negative; these include effects on other non-target pests, length of time in which the plant protection product continues to be active, ease of its use, and compatibility with other cultural practices and crop protection measures.
  - The untreated control can also be a point of reference for deciding on the acceptability of a certain level of efficacy
  - In nearly every efficacy evaluation trial, an evaluation of a reference product is included. (product registered for the intended use in the country in which the trial is performed)

Number of efficacy trials

- As a general guide, a total of 10 trials (Table 1) with results that are fully supportive of the direct efficacy (effectiveness) of the product should be sufficient to demonstrate efficacy against a major target pest species.
- These trials should be done across the range of climatic and environmental conditions likely to be encountered, and over at least 2 years
- Fully supportive results are those where the pest has occurred in sufficient numbers to be considered a challenging attack, and where the results show the product gave effective control or reduction of damage compared with the untreated plots and comparable with a reference treatment.

Table 1 Basic number of direct efficacy trials in an area of similar conditions required (for further explanation, see four bullet points in section on Reduced number of trials)

	Fully supportive results required
Major pest on major crop	10 (range 6–15)
Minor uses	3 (range 2–6)
Major pest; protected conditions	6 (range 4–8)

Principles of efficacy evaluation for microbial plant protection products

- Micro-organisms are defined by EC Regulation 1107/2009 (EC, 2009) as 'any microbiological entity, including lower fungi and viruses, cellular or non-cellular, capable of replication or of transferring genetic material'.
- EPPO Standard 1/214 Principles of acceptable efficacy states that because of the 'risk attached to the use of plant protection products, it is thus necessary to decide if the benefits from the use of the plant protection product outweigh any disadvantages.

Principles of efficacy evaluation for microbial plant protection products

- efficacy can be considered to be a balance between the following points:
  - The positive effects of treatment in performing the desired plant protection activity to fulfil the claims made on the proposed label, in order to achieve improvement in the quantity and/or quality of the crop;
  - Any negative effects, such as reduction of quality or quantity of yield/phytotoxicity, damage to beneficial organisms, damage to succeeding or adjacent crops, development of resistance;
  - Other aspects of efficacy which, depending on the product, can be either positive or negative; these include effects on non-target pests, length of time in which the plant protection product continues to be active, ease of its use, and compatibility with cultural practices and other crop protection measures.

Principles of efficacy evaluation for microbial plant protection products

- Efficacy data are mainly obtained in trials correctly set up according to the principles of good experimental practice (GEP) and performed by official or officially recognized
- organizations.
- Data from other sources e.g. published papers, laboratory studies may be used to supplement these data.
- To support the registration of a pesticide product the following efficacy issues should be considered:
  - Evidence of pest/weed/disease control to support the label claims;
  - Evidence of safety to the treated crops;
  - Evidence of safety to subsequent crops;
  - A justification of the label recommended dose(s);
  - Evidence that yield and quality of yield will not be adversely affected;
  - Consideration of the likelihood of pest resistance to the active substance developing;
  - Evidence of biological compatibility (lack of antagonism) if tank mix is recommended;
  - Compatibility with IPM

Principles of efficacy evaluation for microbial plant protection products

- Effect of environmental and agronomic factors on product performance
- Dose justification
- Assessment of direct efficacy
- Phytotoxicity
- Yield (quantity and quality)
  - A reasoned case may be made based on phytotoxicity assessments made in the effectiveness trials and again, in the absence of adverse symptoms, no specific yield data may be required.
- Effects on natural enemies
- Effects on plant parts for propagation
  - For fungicidal and insecticidal products data are generally not required unless the product has systemic activity, is applied close to harvest, and phytotoxic effects have been observed on some of the tested crops. For microbial products therefore generally a reasoned case may suffice in lieu of data, which should include reference to the phytoxicity assessments.
- Damage to succeeding or adjacent crops
  - Such information will generally only be required if the micro-organism survives in the soil in the long term, and there is evidence to suggest that they may have an adverse effect on seed germination or plant growth.
  - Small scale screening tests against a range of appropriate plant species may be sufficient to demonstrate safety of formulated products to adjacent crops.
- Impact of other crop protection measures, especially fungicides
- Development of resistance

Reducing the number of trials

- Where there is a large amount of supporting evidence from use of the product, or of similar products with the same active substance, on closely related pests or against the same pests on different crops, the number of trials necessary will be determined by the amount of supporting evidence and the similarity of the pests and crops sought.
- Where the target pest or crop is of minor importance, once direct efficacy (effectiveness) against a major pest has been demonstrated, and where the additional pest is of minor importance or use on a minor crop is to be recommended on the label, a reduced number of trials may be accepted.
- Where there is little variation in climatic conditions in the use of the product, for example, in some protected situations or in storage premises (grain stores), a reduced number of trials may be sufficient to demonstrate effectiveness.
- In exceptional circumstances, the number of trials required may be reduced when there are extreme difficulties associated with their conduct. Such difficulties may include use against pests of sporadic occurrence, or special conditions (e.g. trials on quarantine pests); or testing of pheromones (where very large plots are necessary); or use in large structures requiring whole-site fumigation.
- The number of bridging trials where there is a significant change in formulation, and as included in previous versions of this Standard, should be 5.

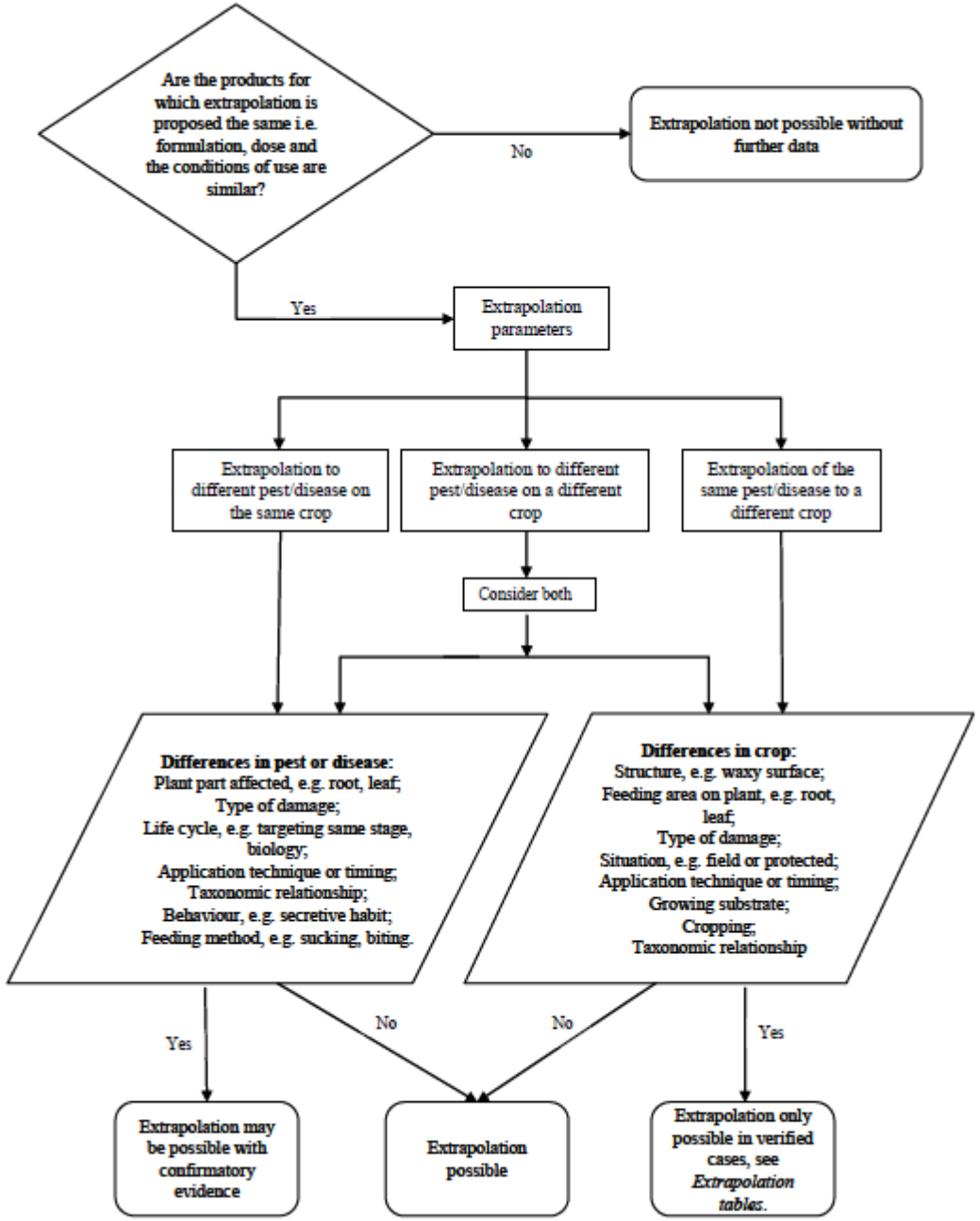
Efficacy and crop safety extrapolations for minor uses

- Minor uses are those uses of plant protection products (defined in relation to crops and pests) in which either the crop is considered to be of low economic importance at a national level (minor crop), or the pest is of limited importance on a major crop (minor pest).
- to simplify and speed up the process the following information may be used, as far as possible:
  - comparison and extrapolation from the original registered uses
  - use of data from a limited number of efficacy trials
  - use of data from other sources.
- extrapolation as one of the possibilities for demonstrating efficacy.
- Many extrapolations will be applicable across Europe. However, differences may exist between different regions, e.g. the northern and the southern part of Europe. This has been considered for the extrapolations which are included in the extrapolation tables for effectiveness/crop safety of plant protection products.

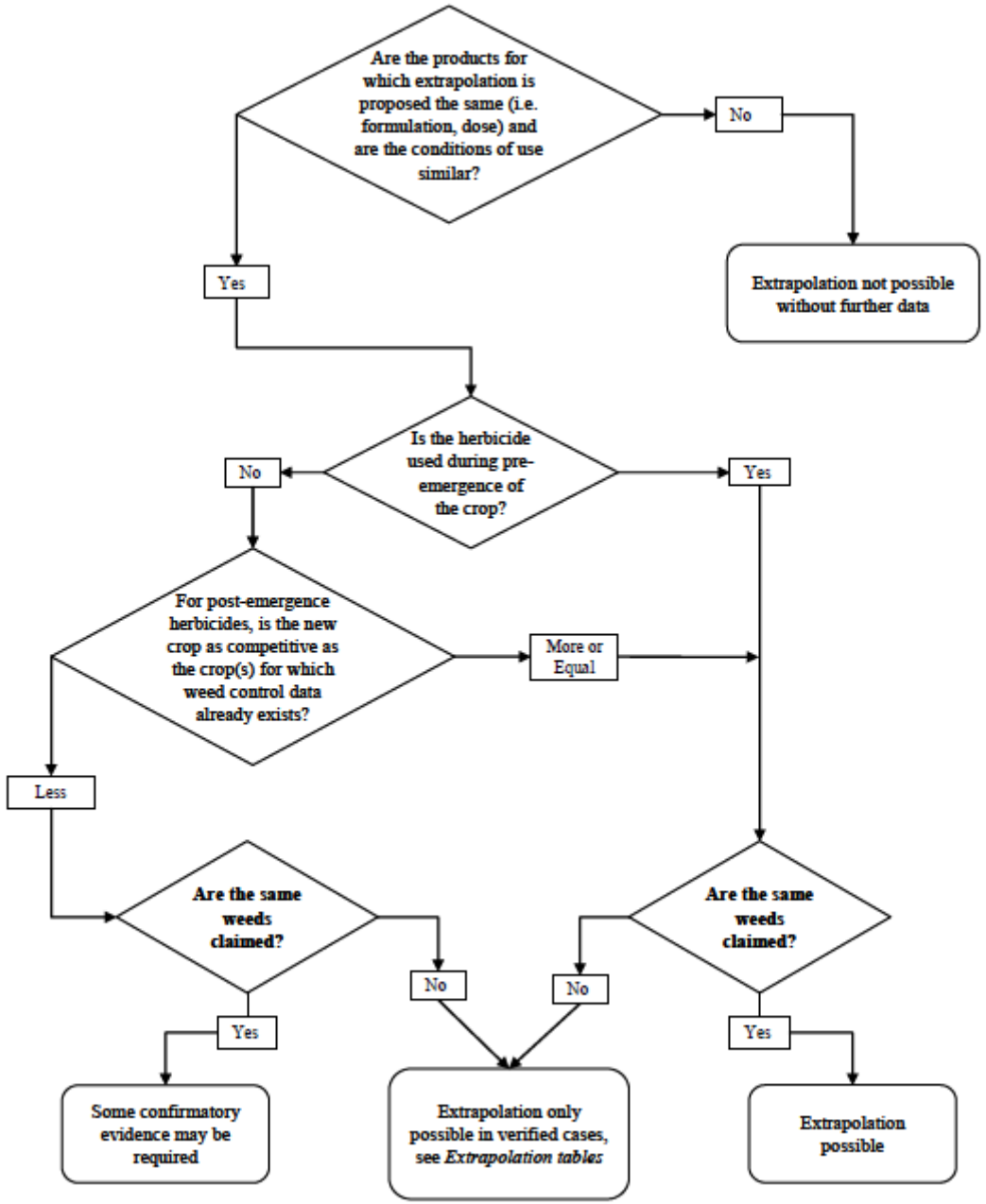
Key factors relevant for extrapolation

- Crop: morphology, botanical family, cropping system, growth pattern. It should be noted that closely related species may still differ significantly in growth pattern, leaf surface or the parts of plant that are harvested.
- Pest/disease: Taxonomic relationship, biology, life cycle, behaviour, plant parts attacked, damage caused. Closely-related species may have significant differences. A given pest species may behave differently between crops.
- Product: Mode of action, timing, frequency, method of application, preventative or curative treatment, systemic or non-systemic, formulation, dose, extent of existing database, existence of regional differences in susceptibility to plant protection products.
- Agronomic: Growing conditions (field or protected) and cultivation techniques, growing systems, soil type (particularly for soil treatments). Generally, protected situations are considered less challenging than field situations, particularly for foliar applications.
- Seed treatment: Extrapolation between seed treatments of different crops is normally more acceptable when the seeding density and thousand grain weight is similar.
- Other factors of importance, for which similarity is necessary, are: sowing period, time of appearance of pest, application technique, seed skin (rough surface or smooth surface).

Decision-support scheme for extrapolations for fungicides and insecticides



Decision-support scheme for extrapolations for herbicides



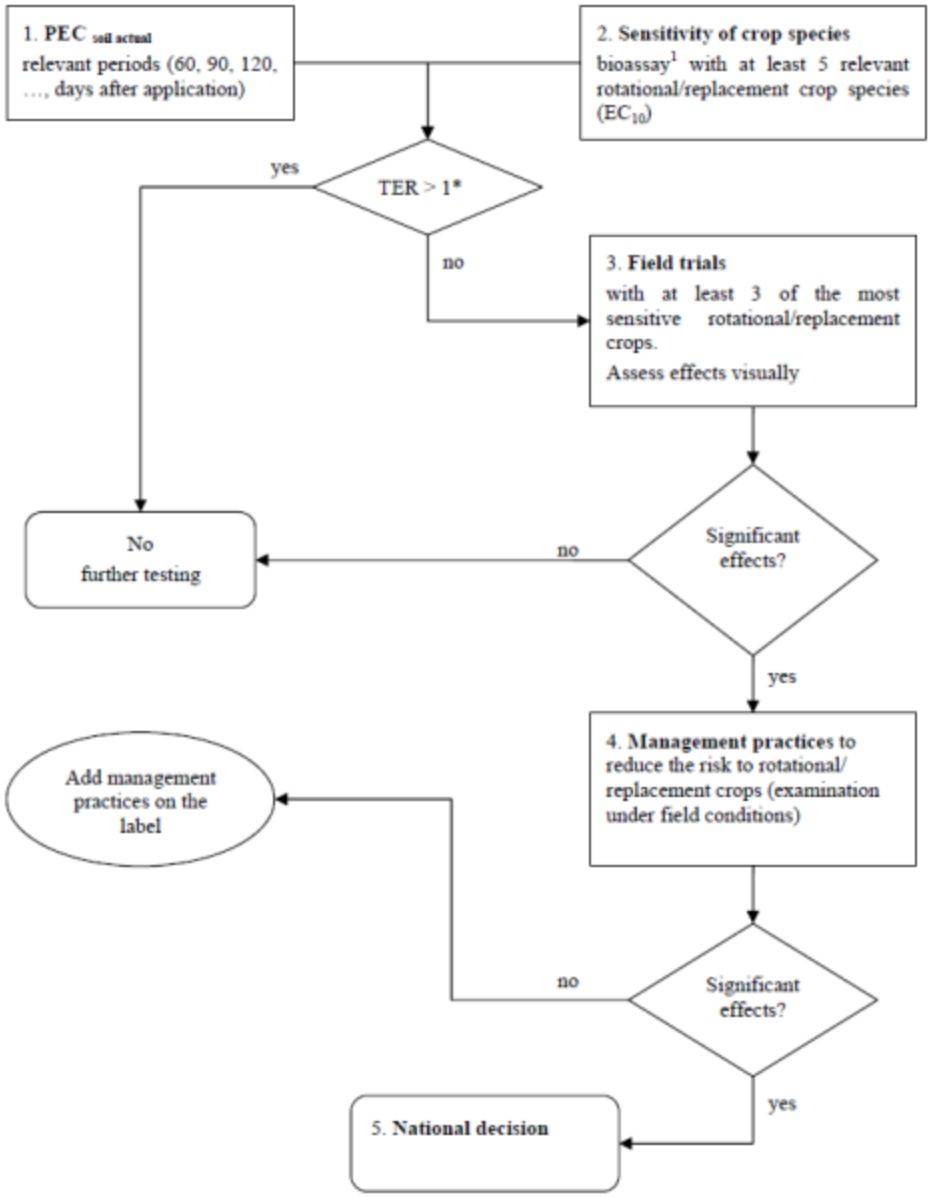
Adverse effects

- There should be no unacceptable adverse effects of
  - Phytotoxicity
  - Yield
  - Quality (including transformation processes)
  - Plants or plant parts used for propagation
  - Succeeding crops (including substitute crops)
  - Adjacent crops
  - Non-target organisms unless it is possible to impose appropriate limitations of use that avoid or ameliorate the effect to acceptable levels

Effect on succeding crops (PP 1/207 (2)

- *Studies on fate and behaviour in soil:* The calculation of the Predicted Environmental Concentrations (PEC) for the active substance and their relevant metabolites in the compartment soil can be performed with equations (1) and (2) (Kloskowski *et al.* 1999).
- *Biological activity of the active substance:* A bioassay on a range of representative rotational or replacement crop types should be made to examine whether the active substance affects germination in or growth through soil in which it is present. A simple study for non-herbicides considering biological data may be all that is required. These data may come from environmental risk assessments or other pot tests.
- If the active substance has no activity against plants in soil at the highest doses tested in the bioassays, then field trials are unnecessary.
  - If the TER (Toxicity-Exposure Ratio) values are >1 (or the specific national level,
  - if higher), then no further testing is necessary.
  - If the TER values are ≤1 (or the specific national level, if higher), damage to the relevant succeeding crops is possible and further field-testing is necessary as described under point 3.

Effect on succeding crops



Resistance risk

- The applicant should provide a summary of the information on which the assessment of resistance risk has been based. This is likely to include information, either from the laboratory or the field, on the target pest and on the active substance
- The evaluator takes into account the perceived resistance risk and the use pattern(s) of similar products already on the market, with known resistance status.
- When a risk for resistance development is recognised, appropriate risk management strategies are proposed to minimise the likelihood of resistance or cross resistance development
- In this kind of evaluation process, useful information and guidance can be gathered from the relevant EPPO Standard PP 1/213 Resistance risk analysis and from the three European Resistance Action Committees FRAC, IRAC and HRAC, responsible for resistance issues in fungicides, insecticides and herbicides, respectively

- Although the major criteria for evaluating efficacy are well defined in the Uniform Principles, expert judgement is an essential element in the final decision

OECD Guidance Documents for Pesticide Registration
http://www.oecd.org/env/ehs/pesticides-biocides/oecdguidancedocumentsforpesticideregistration.htm

Thanks for your attention !