AUTHORISATION OF PLANT PROTECTION PRODUCTS

Assessment process of data belonging to biological efficacy studies of PPPs for authorization

R.Bugiani

Content

- Organization of Authorization procedure in Italy
- Expert Committee
- Authorization Procedure
- Kind of Authorizations
- Zonal Authorization
- Mutual Recognition
- dRR

PPP Authorisation – the Italian experience

Competent Authority
Ministry of Health

Technical evaluation carried out by:

Advising Scientific Institute(s)

Experts Commission

The Experts Commission

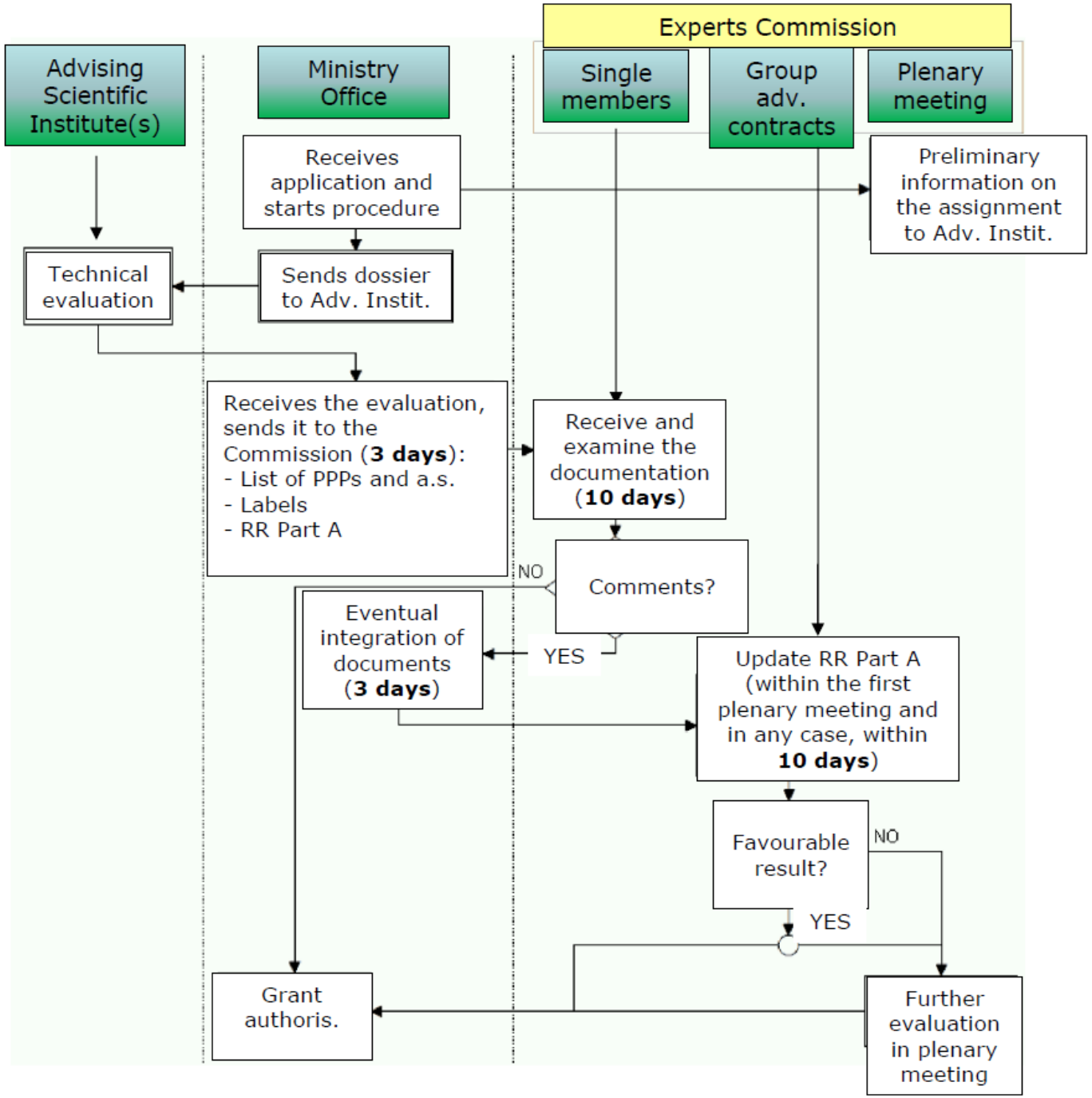
23 permanent members (and substitutes) + 32 additional members from different Scientific Institutions

Institutions:

- Ministry of Health
- Ministry of Agriculture
- Ministry of Environment
- Istituto Superiore di Sanità
- National Institute of prevention of accidents at work

Skills

- Plant pathology
- Entomology
- Weeds
- Microbiology
- Chemistry
- Soil chemistry
- Environment
- Food safety
- Toxicology
- Eco-toxicology
- Pharmacology
- Biology
- Cancer research
- Microbiology


Experts Commission
Advising Scientific Institute(s)
Ministry Office
Single members
Group adv. contracts
Plenary meeting
Receives application and starts procedure
Preliminary information on the assignment to Adv. Instit.
Technical evaluation
Sends dossier to Adv. Instit.
Receives the evaluation, sends it to the Commission (3 days):
- List of PPPs and a.s.
- Labels
- RR Part A
Receive and examine the documentation (10 days)
NO
Comments?
YES
Eventual integration of documents (3 days)
Update RR Part A (within the first plenary meeting and in any case, within 10 days)
Favourable result?
NO
YES
Grant authoris.
Further evaluation in plenary meeting

Kind of authorisations

- Authorisation of a new Plant Protection Product containing approved active substance(s) with complete Annex III of Dir. 1991/414 (Annex to Reg. 545/2011) or different source already evaluated as equivalent to the reference one(s)
- Exceptional authorisation of a Plant Protection Product
- Adaptation of the label(s) of Plant Protection Product(s) to more restrictive conditions specified in EU Regulations modifying the annexes of the Regulation (CE) n. 396/2005
- Mutual recognition of a Plant Protection Product
- Renewal of the authorisation of a Plant Protection Product
- Withdrawal or amendment of an authorisation of a Plant Protection Product

Kind of authorisations

- Authorization of a Plant Protection Product identical to an existing authorized product
- Technical modifications of authorized Plant Protection Product(s) or adjuvants - agronomic modifications
- Technical modifications of authorized Plant Protection Product(s) or adjuvants - major modifications of composition
- Technical modifications of authorized Plant Protection Product(s) or adjuvants - modifications of classification and labelling
- Technical modifications of authorized Plant Protection Product(s) or adjuvants - minor modifications
- Authorization of parallel trade of Plant Protection Product(s)
- Provisional authorization of Plant Protection Product(s)

Kind of authorizations

- Re-registration of a Plant Protection Product following the approval of an active substance at the end of its review process - Step 1: equivalent/compliance assessment based on reference source (source identical to the one evaluated during the assessment for the approval of the active substance)
- Re-registration of a Plant Protection Product following the approval of an active substance at the end of its review process - Step 1: equivalent/compliance assessment based on source(s) different from the reference one (source(s) different from the one evaluated during the assessment for the approval of the active substance)
- Re-registration of a Plant Protection Product following the approval of an active substance at the end of its review process - Step 2 (formulate dossier compliant to Annex III of Dir. 1991/414 or to the Annex to Reg. 545/2011)

SANCO guidelines

Technical guidance

- Phys-chem, analytics
- Toxicity
- Residues
- Fate and behaviour
- Ecotoxicology
- Crop specific

Procedural guidance

- Dossier and draft assessment report
- Post approval issues
- Procedures

http://ec.europa.eu/food/plant/pesticides/approval_active_substances/guideline_documents_en.htm

SANCO guidelines

Guideline	Topic
SANCO10796/2003 rev. 12.2	Procedures on the authorisation of PPP following inclusion of an existing active substance in annex I of Dir. 91/414
SANCO 13169/2010 rev. 7	Zonal evaluation and mutual recognition
SANCO/6896/2009 rev. 1	Intra & inter-zonal work-sharing
SANCO 2010/1370 rev. 7	Renewal, withdrawal and amendment of authorisations
SANCO 10087/2013 rev. 0	Emergency situations according to article 53 of Reg 1107/2009
SANCO 12638/2011 20 Nov. 2012 rev. 2	Significant and non-significant changes of the chemical composition
SANCO 10524/2012	Parallel trade
SANCO 11244/2011 rev. 5	Risk envelope approach
SANCO/6895/2009 rev. 1	Format of draft Registration Report

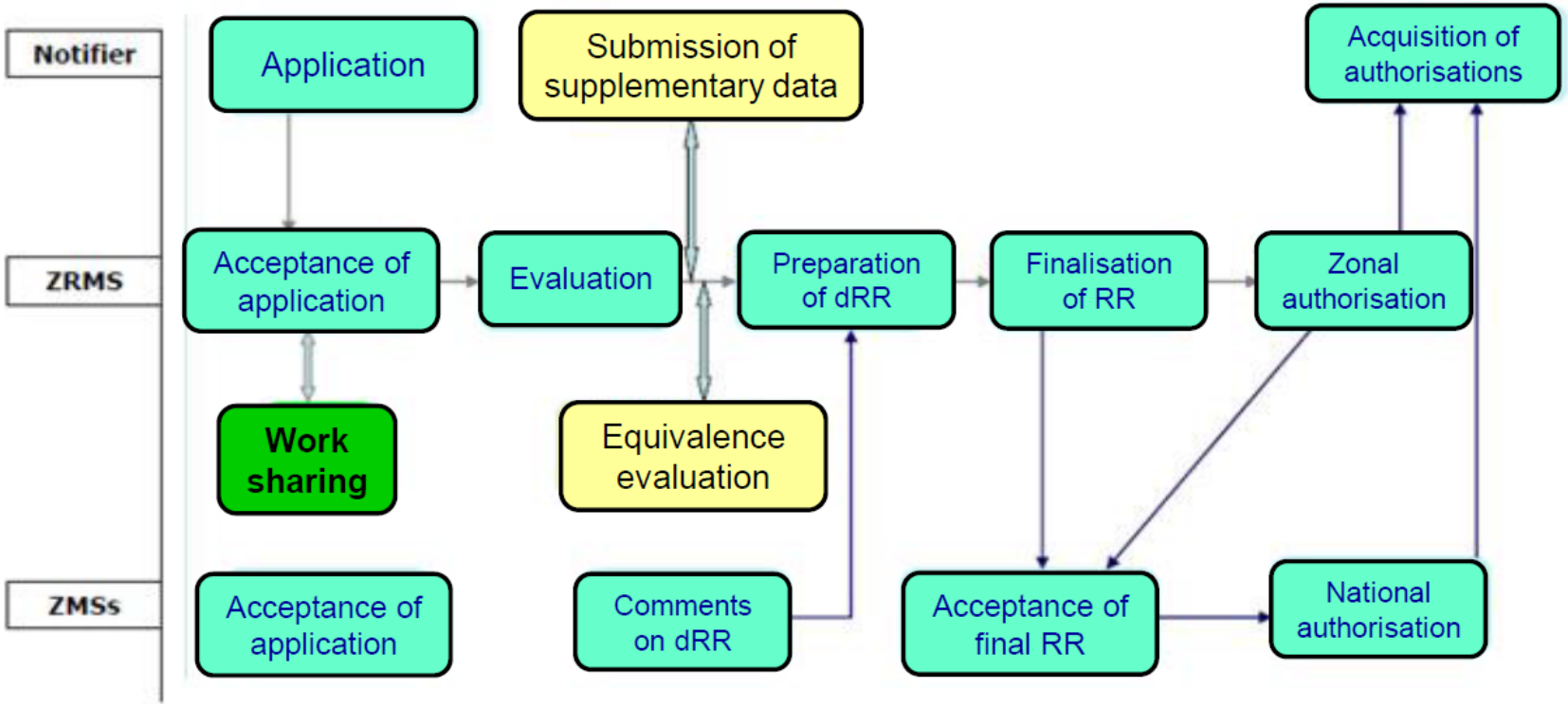
New process of authorisation

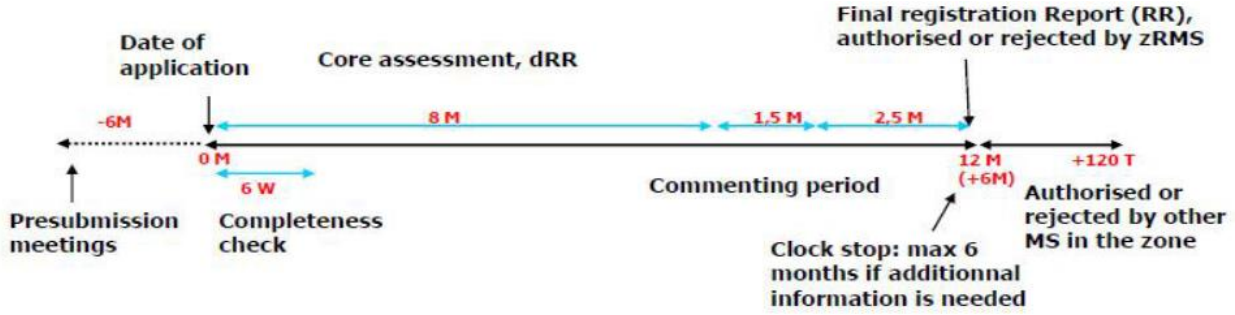
ZONAL AUTHORIZATION	MUTUAL RECOGNITION (MR)
The applicant submits the dossier to MS where the authorisation is requested	Application for authorization for the same use and comparable agricultural practices in: • MS in the same Zone • Other Zones for uses in greenhouse, post-harvest, treatment of empty rooms, containers for storing plant or plant products, seed treatment • MS in a different Zone, provided that the authorization is not used for the purpose of mutual recognition in another MS within the same zone
Evaluation carried out by the Zonal Rapporteur Member State (zRMS) (**8 months**)	
Comments by other MS (**1.5 months**) Registration Report (zRMS) (**2.5 months**) National Authorisation (**4 months**)	Authorisation granted or denied in **120 days**

BENEFITS

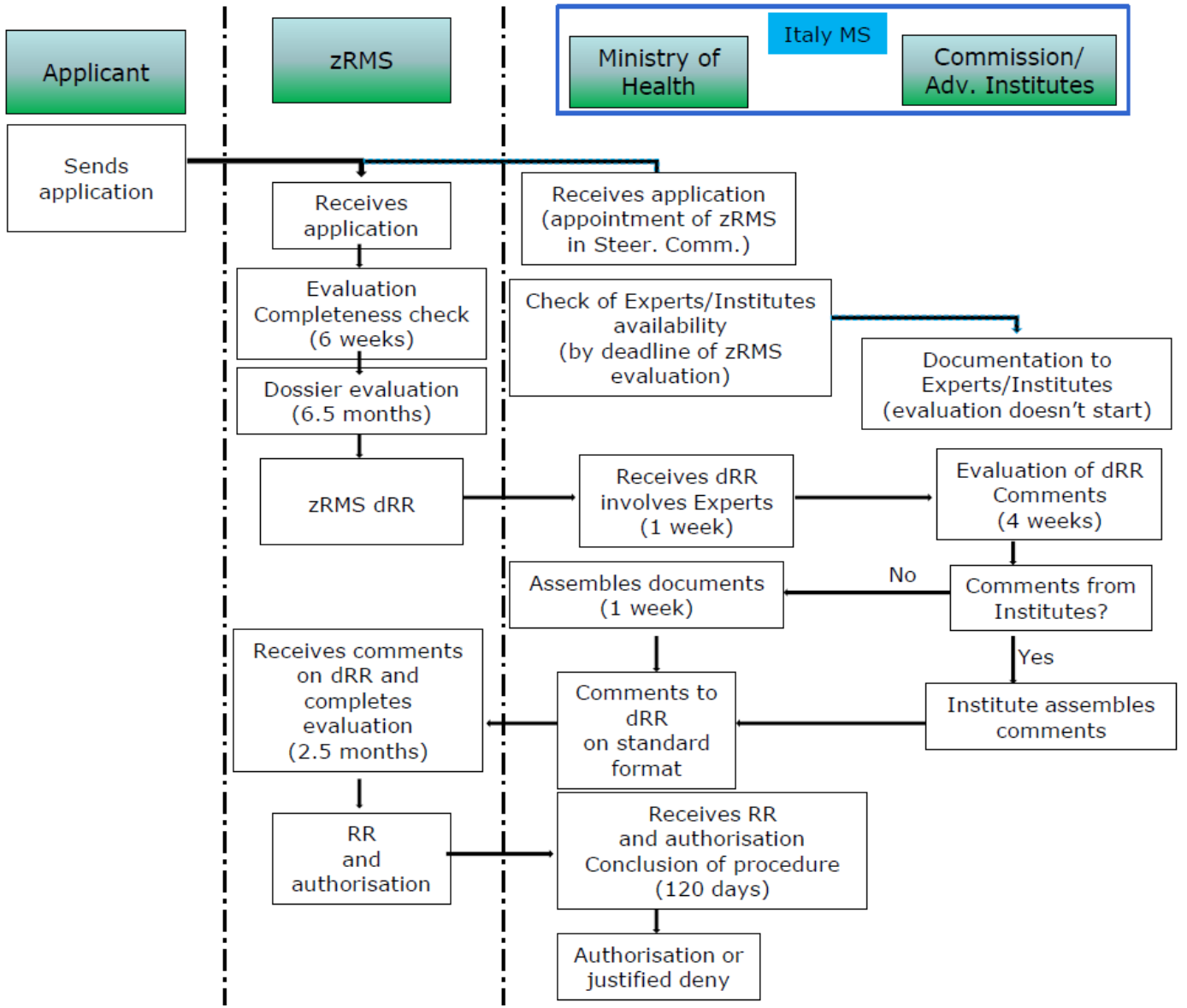
1. Reduced workload for MS and Industry (repetition of work)
2. Avoid numbers of different formulation on the market
3. Cheaper than standard route for assessment (re-registration)
4. Increased availability of harmonised PPPs to farmers

General scheme and timelines of Zonal authorisation

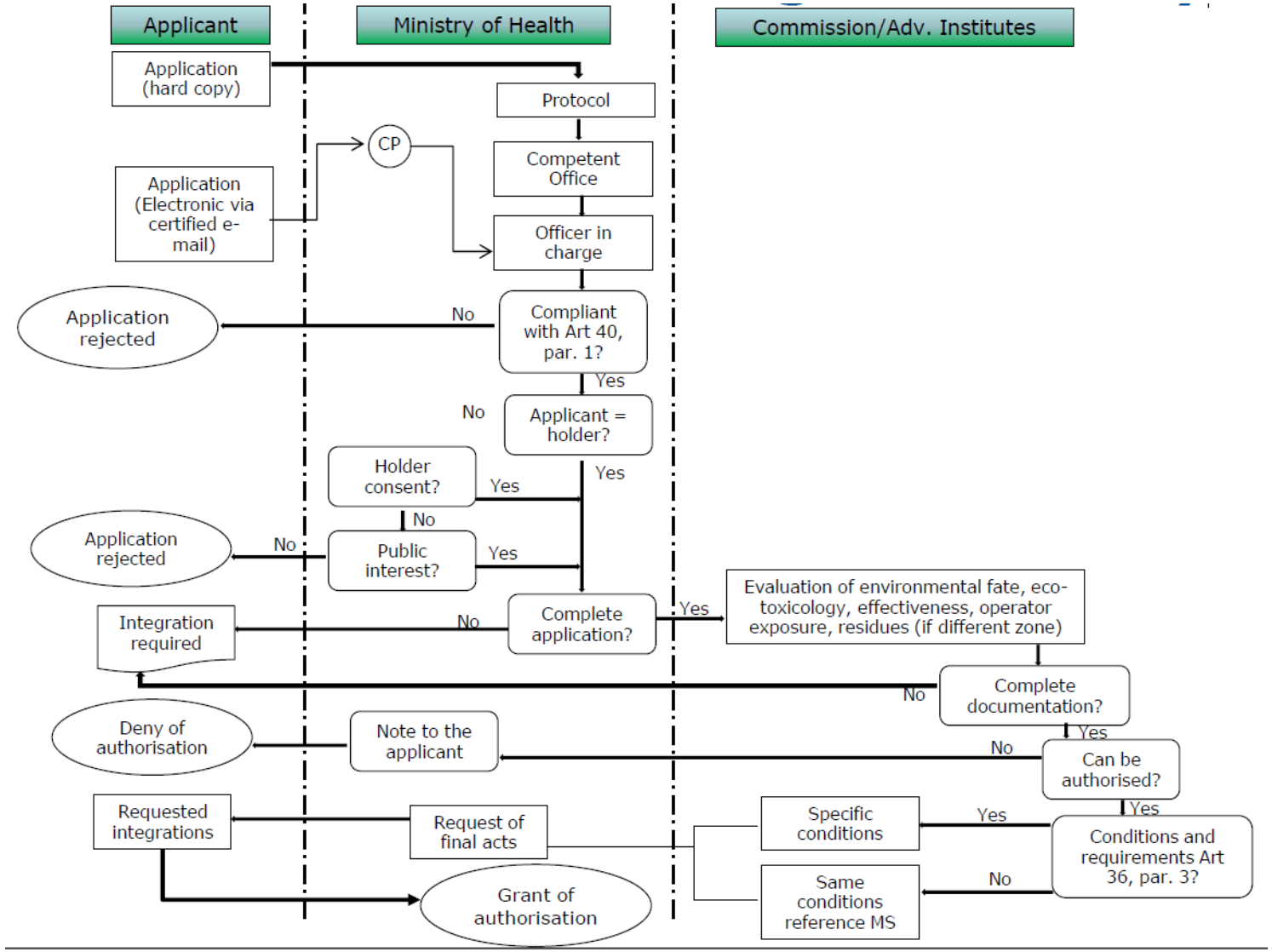




Scheme of Zonal authorisation - Italy



Scheme of mutual recognition - Italy



Zonal authorisation - Organisation

- A Zonal Steering Committee has been established in each zone, to which each MS in the zone takes part
- An Inter-Zonal Steering Committee has been established, to which 2 MS per zone (3 for the Central zone) plus the Commission, take part
- Within each MS, zonal Contact Point(s) have been identified

The Contact Point in Italy

- Acceptance of applications
- Classifies applications on the basis of the line of activity and the role of Italy in the evaluation procedure (i.e. zRMS or cMS)
- Sets up and updates a data-base of the applications highlighting timelines and deadlines of the different steps of the authorisation process; the data-base is arranged on the basis of the role of Italy and the type of application
- Assigns applications to officers in charge of the different lines of activity
- Identifies the needs in terms of resources for the planning of the evaluation activity

The Contact Point in Italy

- Attend the meetings of the zonal Steering Committee
- Identifies the topics to be discussed or clarified in the zSC
- Acts as Ministry interface with relevant competent Authorities of the other Countries of the zone
- Sends the update list of received application to the Chair of the zSC, when in the role of zRMS

Examples of issues discussed at the zSC

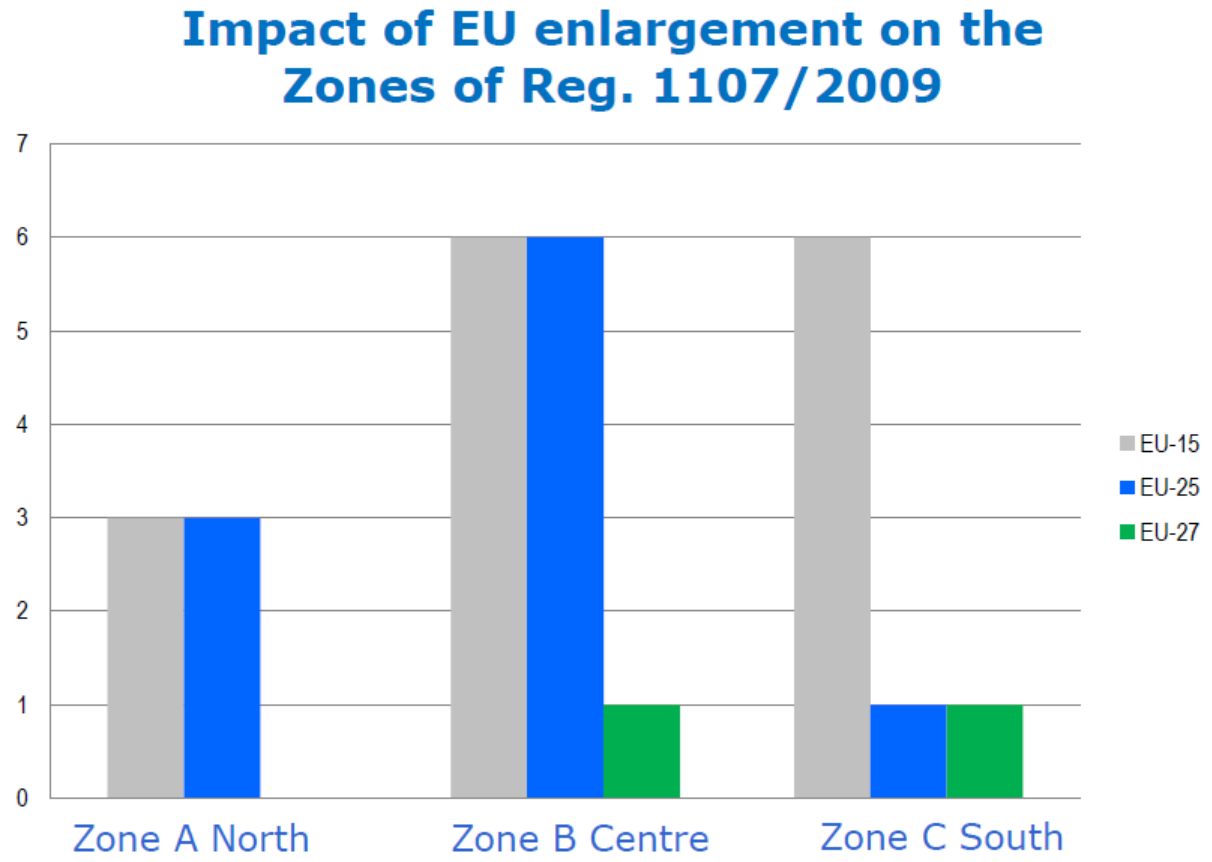
- **Q** National addenda and requirements must be evaluated by the zRMS?
- **A** They pertain to MS. The zRMS must evaluate the core dossier
- **Q** National addenda have been required in the zonal registration process without justifications
- **A** It’s necessary to identify a set of possible requests at zonal level
- **Q** A simplified RR has been accepted and proposed by Germany for minor uses
- **A** It’s necessary to notify the authorisation to the other MS, even if it has been granted only at national level

The Contact Point in Italy

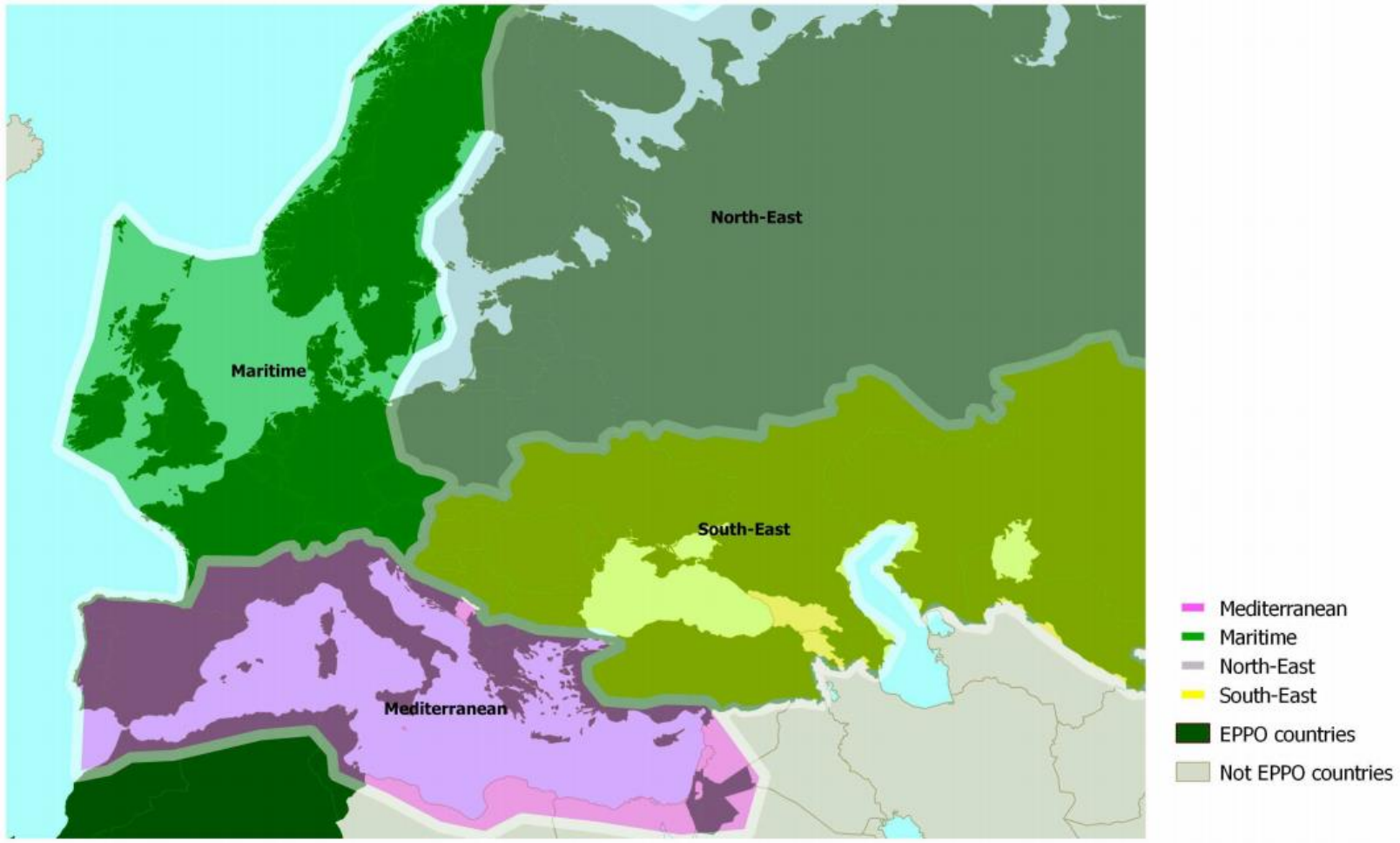
- Gathers the update list of application from zRMS
- Consequently updates the zonal data-base
- Organises the meetings of the zSC and proposes relevant agenda
- Attends the meetings of the zSC
- Attends the meetings of the izSC
- Updates the zMS regarding the outputs of the izSC and provides for related documents
- Acts as spoke person of the whole zone in the izSC regarding problems arisen in the application of Reg 1107/2009

The creation of the Zones in EU

- The creation of the zones resulted in a concentration of many of the MS who joined EU only in 2004 in the Central zone, thus having a limited experience with relevant EU legislation

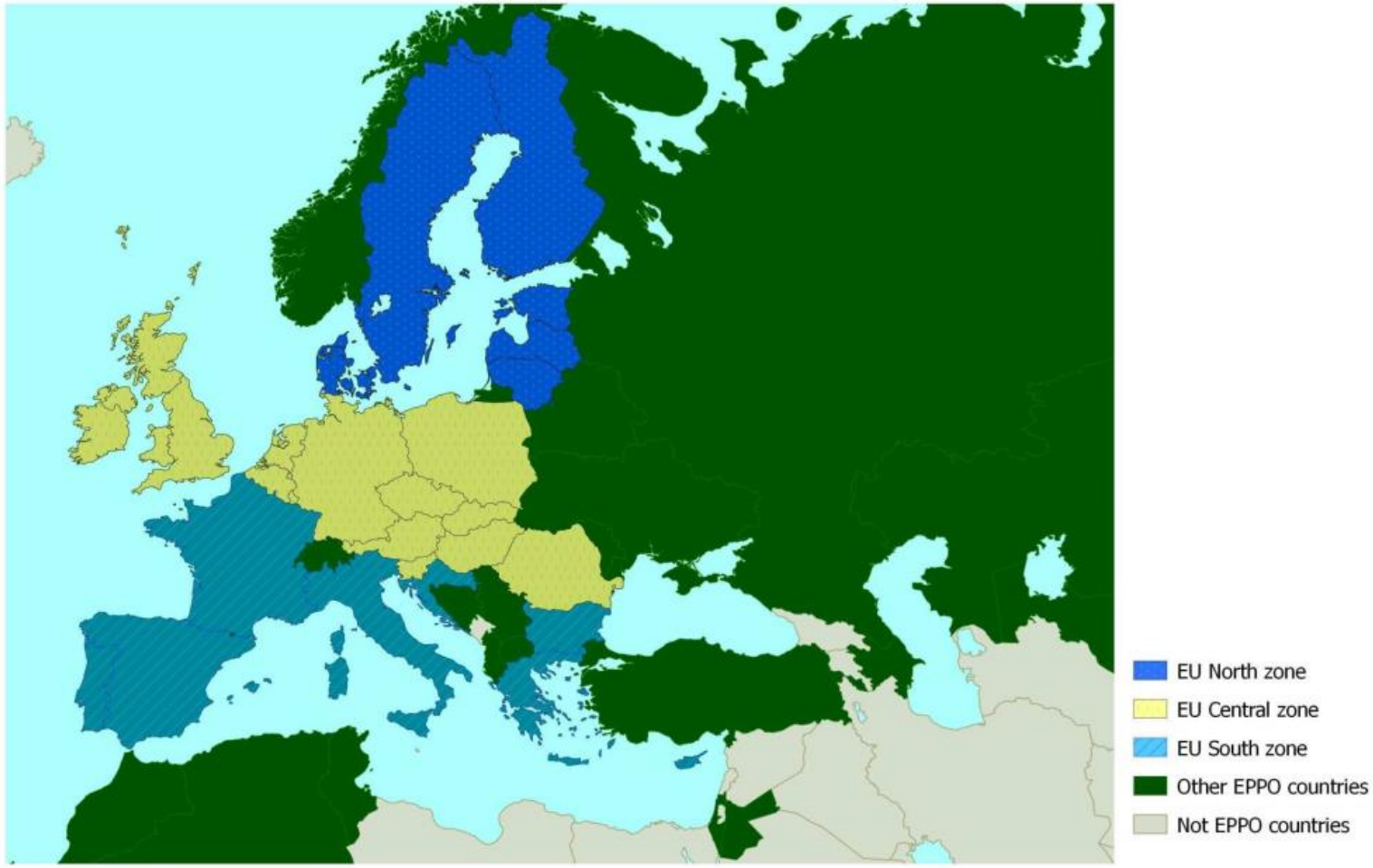


EPPO Climatic Zones



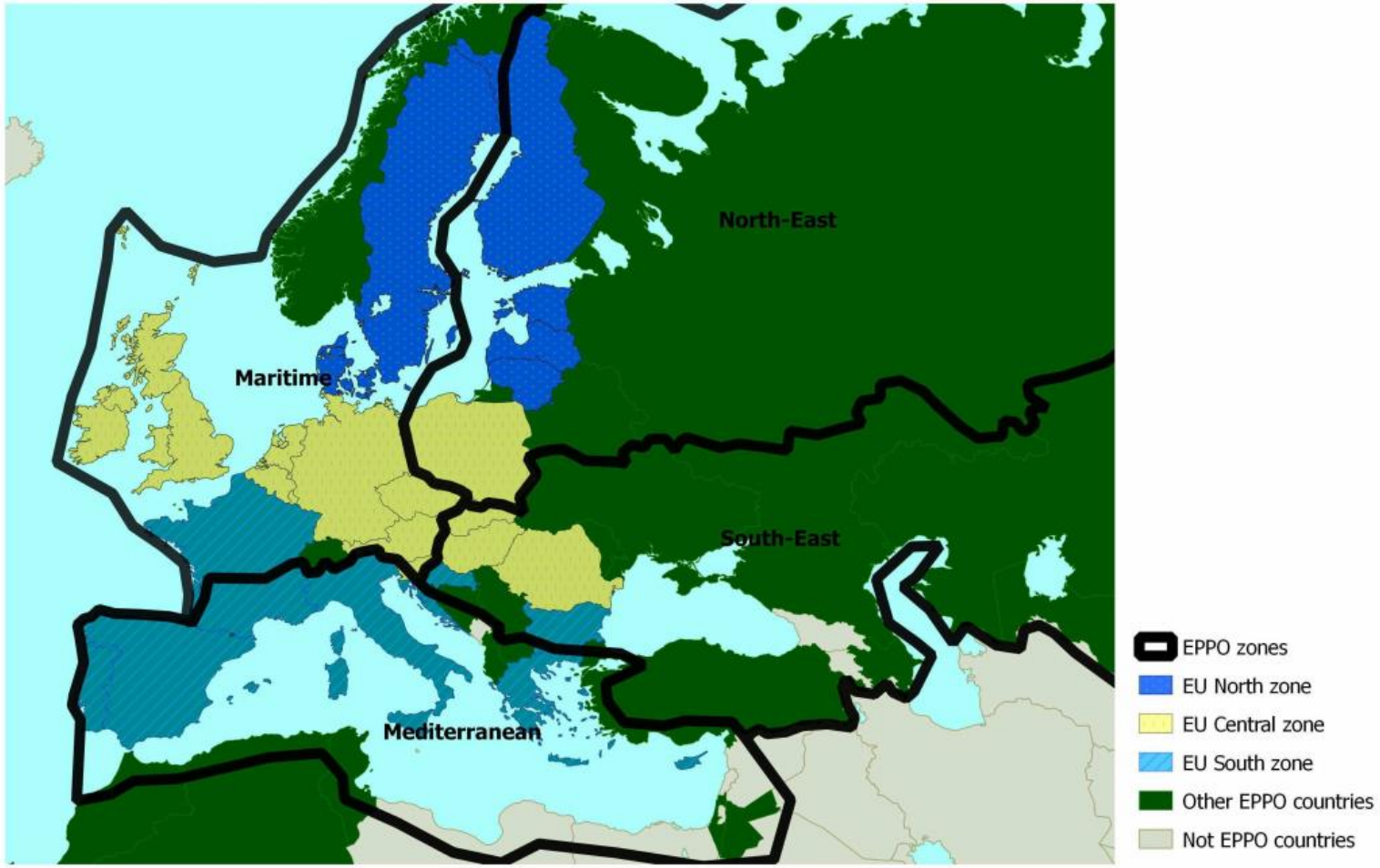
Zones of comparable climate in the EPPO region as defined in EPPO Standard PP 1/241 Guidance on comparable climates for the purposes of efficacy evaluation trials on plant protection products. The borders are intentionally broad indicating that there is an area of gradual change in climate between the zones proposed

The creation of the Zones in EU



* according to Regulation (EC) No 1107/2009

EPPO Climatic Zones and EU Authorisation Zones



Zones of comparable climate in the EPPO region as defined in EPPO Standard PP 1/241 Guidance on comparable climates for the purposes of efficacy evaluation trials on plant protection products. The borders are intentionally broad indicating that there is an area of gradual change in climate between the zones proposed

The creation of the Zones in EU

- The three zones have a complex and not homogeneous situation from the agricultural point of view. A certain variability exists even within the same area, as well. It is necessary that the simplification of administrative procedures takes into account the agronomic and structural properties of the agricultural sector of each Zone.
- The Zones settled by Reg. 1107/2009 do not correspond with those used in the assessment and authorization processes of pesticides, such as those settled by EPPO for the extrapolation of efficacy studies between MS, or those indicated in the EU guidelines for the comparability, extrapolation and data requirements for setting MRLs (Doc. SANCO 7525/VI/95 - rev.9, March 2011)

In the framework of the new procedures the agronomic characterisation of the zone(s) is crucial for relevant competent Authorities

Examples of zonal efficacy evaluations

- Important note: These documents are intended to assist applicants and evaluators to interpret EPPO Standard PP1/278 Principles of zonal data production and evaluation. They provide specific examples of the data required to support intended uses. It should be noted that the number and distribution of trials will vary depending on the zone and the intended use. Expert judgement should be applied in all cases.
- These case studies are 'working documents' meaning that they may be modified over time. The approval body for these documents is the Working Party on Plant Protection Products.

Product	Pest	Crop	Zone
Herbicide	*Apera spica-venti* - Loose silky bent (APESV)	Winter wheat	European Central Zone
Herbicide	Weeds	Maize	European Central Zone
Fungicide	*Mycosphaerella graminicola* - Septoria leaf blotch (SEPTTR)	Winter wheat	European Central Zone
Fungicide	*Puccinia striiformis* f. sp. *tritici* - Yellow rust (PUCCST)	Wheat	European Central Zone
Insecticide	Aphids, thrips and whiteflies	Ornamental plants in greenhouses	European Union

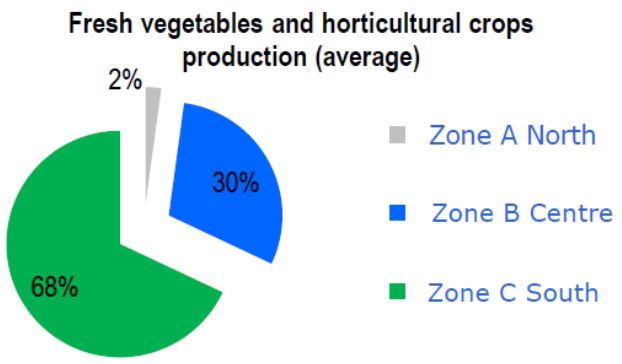
NB. Further examples of zonal efficacy evaluations will be added here when they are completed.

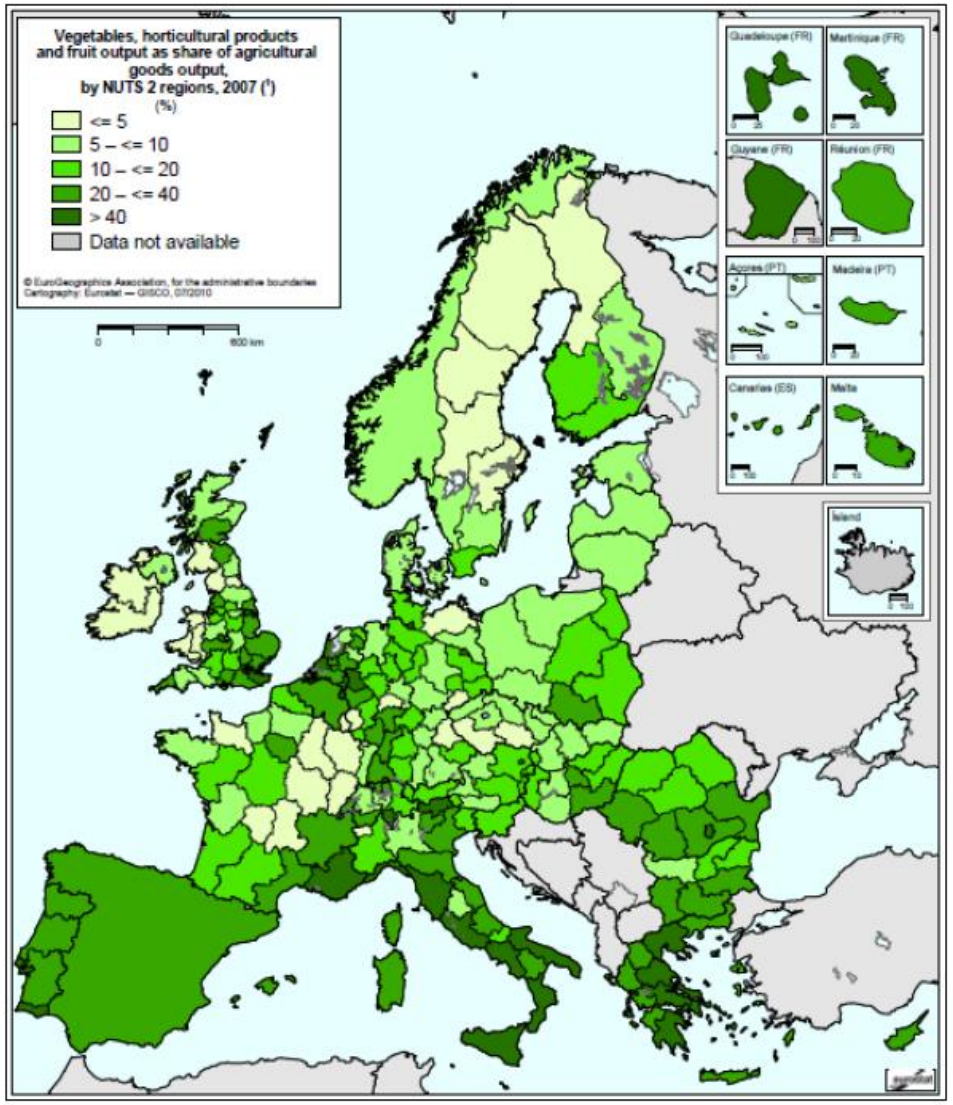
Regulation (EC) No 1107/2009

- the applicants have to conceive and to prepare dossiers that will be used for granting authorizations at the level of a zone comprising several EU Member States.
- the regulatory authorities (Rapporteur Member State) have to evaluate the dossier taking into account the agronomic conditions of a large geographical zone and not only their own local conditions and peculiarities.
  - • What is the optimal location of the trials in order to cover the conditions of several countries?
  - • What is the meaning of major/minor crop or use at zonal level?
  - • What are the different agricultural techniques for a crop within a zone (e.g. winter/spring varieties, outdoor/indoor, fresh market/industrial processing, human/animal consumption, etc.?

Crop distribution (Eurostat, 2011)

- The most important crops in Europe are cereals
- The Regions producing >25% of cereals fall into Central and North Zones
- Fresh vegetables and horticultural crops are mainly concentrated in the Southern Zone



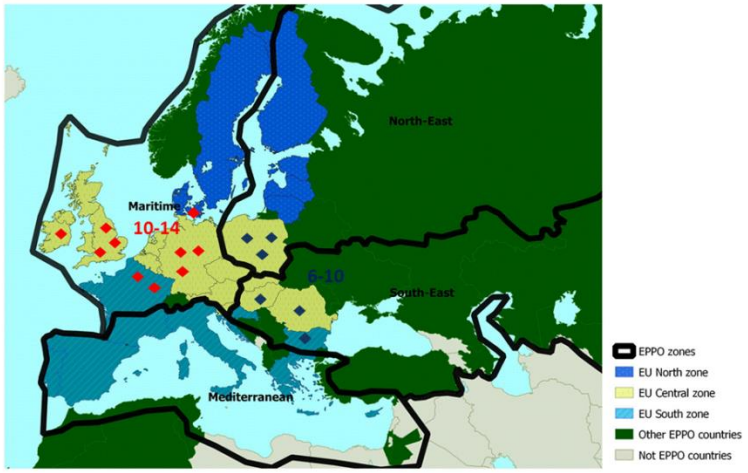


Number and distribution of trials required for an authorization

Reasons

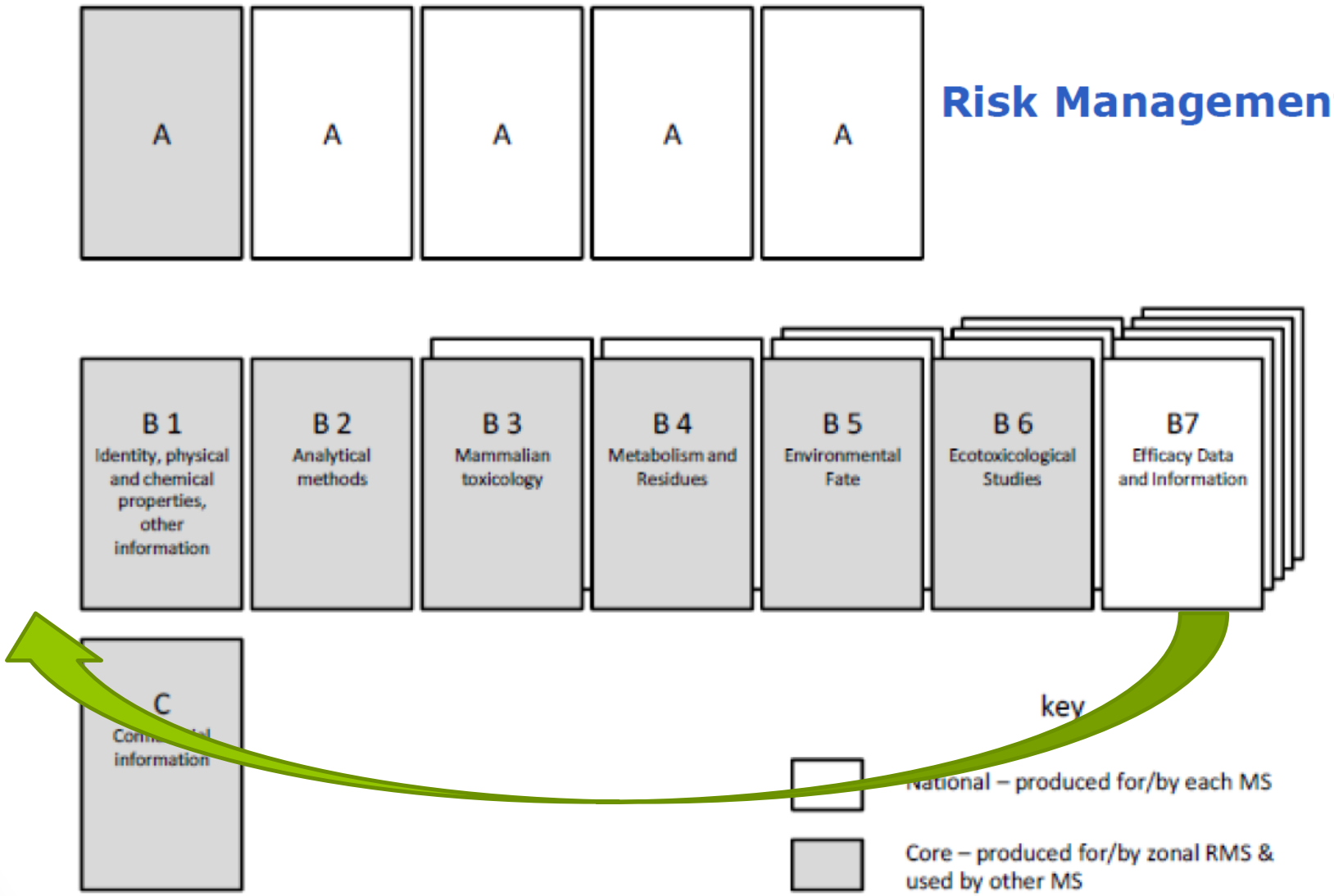
- Regions with drier spring/early summer climates (e.g. South Eastern EPPO countries) typically have less severe and shorter epidemics. In these countries the GAP (in terms of the dose and the number of applications) may differ from that required in the more disease prone wetter Maritime countries. Trials should cover the typical variation in climatic conditions.

Map

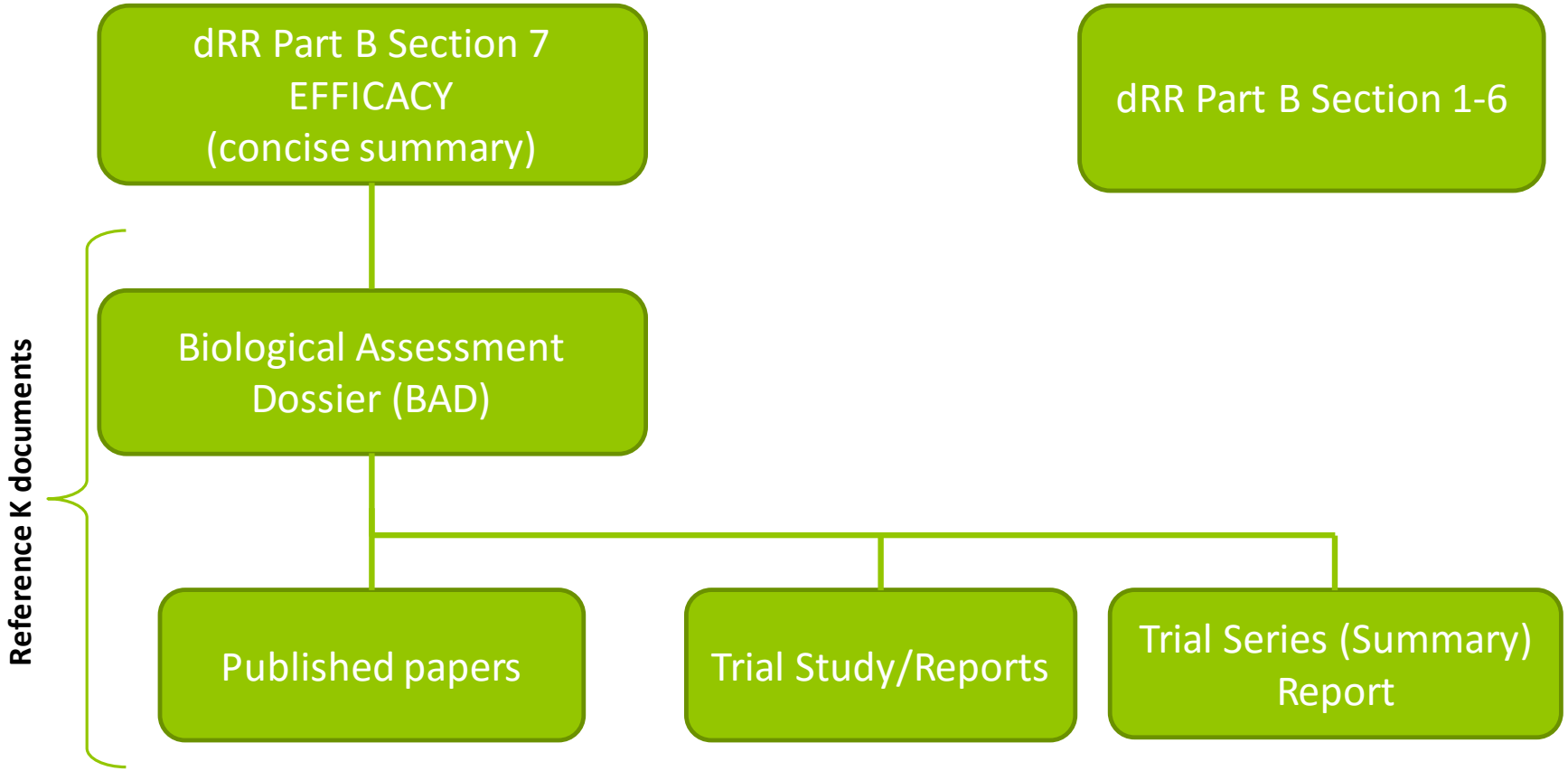


Effectiveness (6.2) Commission Regulation 284/2013), (OECD KIIIA1 6.1.3)

The dRR


A
A
A
A
A
Risk Management
B 1
Identity, physical and chemical properties, other information
B 2
Analytical methods
B 3
Mammalian toxicology
B 4
Metabolism and Residues
B 5
Environmental Fate
B 6
Ecotoxicological Studies
B7
Efficacy Data and Information
C
information
key
National – produced for/by each MS
Core – produced for/by zonal RMS & used by other MS

The dRR part B



GAP

SUMMARY OF GOOD AGRICULTURAL PRACTICE FOR PESTICIDE USES
(Application on agricultural and horticultural crops)

Responsible body for reporting (name, address): Submission date:
Pesticide(s) (common name) :
CCPR No(s) :
Trade name(s) :
Main uses (e.g. insecticide, fungicide) :

1	2	3	4	5	6				7			8	9
Crop and/or situation with code number(a)	F or G (b)	Pest or group of pest controlled (c)	Formulation rate Type (d-f)	Conc. of a.i. (i)	Application method, kind (f-h)	growth stage (j)	number (range)	spray interval (days)	Application rate per treatment g as/hl	water (l/ha)	g as/ha	PHI (days) (k)	Remarks (l)

a) code number according to Commission Regulation (EU) No 600/2010*
b) outdoor or field use (F), or glasshouse application (G)
c) e.g. biting and sucking insects, soil born insects, foliar fungi
d) e.g. wettable powder (WP), emulsifiable concentration (EC), granulate (GR)
e) use CIPAC/FAO Codes where appropriate
f) all abbreviations must be explained
g) method e.g. high volume spraying, low volume spraying, spreading, dusting, drench
h) kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants
i) g/kg or g/l
j) growth stage at last treatment
k) PHI = Pre-harvest interval
l) remarks may include: Extent of use / economic importance / restrictions (e.g. feeding, grazing) / minimal intervals between applications

* Commission Regulation (EU) No 600/2010 of 8 July 2010 amending Annex I to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards additions and modification of the examples of related varieties or other products to which the same MRL applies. Official Journal of the European Union L 174/18 9.7.2010.

Supervised trials

SUMMARY OF SUPERVISED TRIALS
(Application on agricultural and horticultural crops)

Active ingredient (common name)..... :
Crop/crop group..... :
Responsible body for reporting (name, address):
Country..... :
Content of active substance (g/kg or g/l)..... :
Formulation (e.g. WP)..... :
Commercial Product (name)..... :

Producer of commercial product..... :
Submission date..... :

Indoor/outdoor..... :
Other active substance in the formulation..... :
(common name and content):
Residues calculated as..... :

Report No. Location including Postal Code	Commod-ity/ Varie-ty (a)	Date of (b) 1. Sowing or Planting 2. Flowering 3. Harvest	Application rate per treat-ment			Dates of treatment(s) or no of treatment(s) and last date (c)	Spray interval (days)	Growth stage at last treat-ment or date	Portion analyzed (a)	Residues (mg/kg)	PHI (days) (d)	Remarks: (e)
			g as/hl	Water l/ha	g as/ha							

a) code number according to Commission Regulation (EU) No 600/2010*
b) only if relevant
c) year must be indicated

d) days after last application (Label pre-harvest interval, PHI, underline)

e) remarks may include: Climatic conditions; Reference to analytical method; information concerning the metabolites included

* Commission Regulation (EU) No 600/2010 of 8 July 2010 amending Annex I to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards additions and modification of the examples of related varieties or other products to which the same MRL applies. Official Journal of the European Union L 174/18 9.7.2010.

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.

The dRR Part B Sect. 7 Efficacy

- IIIA 6.1 Efficacy data: summarise the type of organisations carrying out the trial work and the general location of the trials
  - IIIA 6.1.1. Preliminary range-finding tests
    - Early greenhouse/laboratory screening studies, to include details on pest spectrum
  - IIIA 6.1.2. Minimum effective dose tests (EPPO guideline 1/225 Minimum Effective Dose)
    - Summary describing a range of doses tested and justification of chosen dose based on (N and 60-80% N considered sufficient)
    - Broad spectrum product – justify dose on main targets
  - IIIA 6.1.3. Efficacy tests:
    - Summary of the appropriate section of BAD
    - Discussion of the product activity and level of control claimed
    - EPPO standard PP 1/226 'Number of efficacy trials' provides useful guidance on the number and type of trials in target crops needed

The dRR Part B Sect. 7 Efficacy

- IIIA 6. Efficacy Data and Information on the PPP
  - Reference to Inclusion Directive, including any specific provisions to be addressed as listed in Annex I of Inclusion Directive
  - General information such as active substances, chemical group(s), mode of action, other biological properties (e.g. mobility, persistence...). It is expected to be approx. 1-2 pages
  - For existing substances/products a table listing current registrations in Member States in the regulatory zone(s) may be useful

Country	Product	Formulation		Authorisation No.	Registered rate(s)	Uses
		Type	Conc.			

Active substance	AS1	<2>	<n>
g/kg or g/L	200		
Chemical group:	auxin		
Mode of action:	IAA regulator		
Biological action:	e.g. post-emergence herbicide		

General information regarding the active substance(s)/product should be included

The dRR Part B Sect. 7 Efficacy

- IIIA 6.1.3. Efficacy tests

Year / Country	2000	2001	2002	2003	2004	2009	2010	Total
France	8	-	6	7	13	9	4	**47**
Italy	2	-	-	-	-	-	-	**2**
Portugal	-	5	-	-	-	-	-	**5**
Spain	-	4	-	-	-	-	-	**4**
Total	**10**	**9**	**6**	**7**	**13**	**9**	**6**	**60**

Target	Grouping	# trials	% control			
			< Product > at <rate>		< Standard> at <rate>	
			Mean	Min & Max or S.D.*	Mean	Min & Max or S.D.
<Target 1>	All					
	A					
	B					
<Target 2>	All					
	A					
	B					
<Target 3>	All					
	A					
	B					

*standard deviation

The dRR Part B Sect. 7 Efficacy

- IIIA 6.1.4. Effects on yield and quality
  - IIIA 6.1.4.1. Impact on the quality of plants and plant products. Summary from EPPO guideline PP 1/242(1)
    - Ideally 6 to 7 trials per major crop per data region should be presented
    - Quality parameters, like Hl weight, Protein content, Oil content
  - IIIA 6.1.4.2. Effects on the processing procedure. (EPPO. Guidelines PP 1/268 and PP 1/243(1)
    - Summary of transformation processes including wine making, brewing or bread making and evidence of no effect of the PPP on these processes is required
  - IIIA 6.1.4.3. Effects on the yield of treated plants and plant products
    - Summary of assessment. If damage to the crop is observed during the efficacy trials or if there is a reasonable suspicion of phytotoxic effects, trials are required that examine this risk. For Herbicides, Growth Regulators and Seed Treatments, tolerance trials including 2 N are always required (including yield measurements).

The dRR Part B Sect. 7 Efficacy

- IIIA 6.2. Adverse effects
  - IIIA 6.2.1. Phytotoxicity to host crop
    - Summary of the Phytotoxicity assessments generated from crop safety trials and/or efficacy trials
  - IIIA 6.2.2. Adverse effects on health of host animals
    - Data not required
  - IIIA 6.2.3. Adverse effects on site of application
    - Data not required
  - IIIA 6.2.4. Adverse effects on beneficial organisms (other than
  - bees)
    - where beneficial species are not an important factor in providing control of targets, a cross reference to other sections of the dRR (e.g. ecotoxicology) should be included
  - IIIA 6.2.5. Adverse effects on parts of plant used for propagating purposes Refer also to EPPO PP1/135 'Phytotoxicity assessment'
    - Summary of Germination of seed (% viability) tests.
    - Summary of Rooting establishment and growth rate of cuttings tests

The dRR Part B Sect. 7 Efficacy

- IIIA 6.2.6. Impact on succeeding crops – EPPO PP 1\207
  - A summary of the observations conducted to assess impact on succeeding crops should be submitted. Data from other parts of the submission (e.g. Ecotoxicology – non-target plant pre-emergence data, Residues – soil) can be included in this section or cross referenced to where such data are located
- IIIA 6.2.7. Impact on other plants including adjacent crops. EPPO guideline PP 1/256
  - If observations on adverse effects on other plants, including the normal range adjacent crops have been done, a summary of these observations should be included. Data from other parts of the submission (e.g. Ecotoxicology – non-target plant pre-emergence data, Residues – soil) can be included in this section or cross referenced to where such data are located
- IIIA 6.2.8. Possible development of resistance or cross-resistance.
  - EPPO guideline PP 1/213 Resistance Risk Analysis
  - A summary of the analysis following the guideline.

The dRR Part B Sect. 7 Efficacy

- IIIA 6.3. Economics
  - Data not required
- IIIA 6.4. Benefits
  - IIIA1 6.4.1. Survey of alternative pest control measures
    - Data not required
  - IIIA 6.4.2. Compatibility with current management practices
    - including IPM.
    - The benefits of the product in integrated pest management systems may be described in this Annex Point. Add a positive label statement if this is the case.
  - IIIA 6.4.3. Contribution to risk reduction
    - Data not required
  - IIIA 6.5. Other/special studies
    - Suitable studies to include as core data are: rainfastness, cleaning application equipment, justification for recommended water volumes, compatibility (biological and/or physical) – if part of the label claims

The dRR Part B Sect. 7 Efficacy

- IIIA 6.6. Summary and assessment of data according to points 6.1 to 6.5
  - Short conclusion of the dossier with sentence like “The data/information provided fully support the proposed label recommendations for the use of product XXX.
  - Provide table of recommended uses for registration, uses conditions and restrictions
- IIIA 6.7 List of test facilities including the corresponding certificates

Efficacy evaluation – reference documents

- REGULATION 546/2011 Uniform principles for evaluation and authorisation of PPPs
- EPPO Guideline PP 1/181 Conduct and reporting of efficacy evaluation trials
- EPPO Guideline PP 1/152 Design and analysis of efficacy evaluation trials
- EPPO Guideline PP 1/226 Number of efficacy trials
- EPPO Guideline PP 1/135 Phytotoxicity assessment
- EPPO Guideline PP 1/223 Introduction to the efficacy evaluation of plant protection products
- EPPO Guideline PP 1/214 Principles of acceptable efficacy
- EPPO Guideline PP 1/213 Resistance risk analysis

http://archives.eppo.int/EPPOStandards/efficacy.htm

Efficacy evaluation – reference documents

- The following SANCO guidelines are being developed:
- SANCO/10054/2013
  - Draft guidance document on Data requirements on efficacy for the dossier to be submitted for the approval of new active substances contained in plant protection products
- SANCO/10055/2013
  - Draft guidance document on the Efficacy composition of Core Dossier and National Addenda submitted to support the authorization of plant protection products under Regulation (EC) No 1107/2009 of the EU Parliament and Council on placing of plant protection products on the market


Thanks for the attention !