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Federal Department of Economic Affairs,
Education and Research EAER
Federal Office for Agriculture FOAG

EPPO Workshop

Comparative Assessment

First Experiences from Switzerland

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General Aspects I

CA is performed:

- During re-evaluation of PPPs containing the same a.i. after renewal of a.i. in EU (but: independent time schedule in CH)
- For all follow-up applications for PPPs containing a CfS where the aforementioned procedure has already taken place
- For PPPs containing a new a.i. which is a CfS
- CA is performed by the authority – companies are not obliged to provide data

General Aspects II

Our first experiences are based on:

- One application for several uses of a fungicide
- Mixture product with one CfS
- CfS due to PBT (persistence, aquatic toxicity)
- All following examples are fictional and for illustration only

Overview of CA procedure

Step 1: Listing of all uses of the candidate product

- All major uses are subject to CA.
- Minor uses are excluded.

Step 2: Listing and pre-examination of alternative product uses

- Potential alternatives that pose risks in other areas not only related to the CFS criterion are excluded

Step 3: Resistance Risk Analysis

Step 4: Comparative Risk Assessment

Risk assessment scheme still under preparation.

Criterion 1: Human Health ADI, AOEL, ARfD

Criterion 2: Environment PBT

Criterion 3: Develop-mental, Neuro- and Immunotox

Criterion 4: Non-active isomers (no issue in CH)

Criteria 5,6,7: Cut-off **CR Cat1A/B ED**

Risk assessment scheme has been established.

Step 1 – Uses of Candidate Product

- Listing of all major and minor uses of the candidate product
- Only uses with full efficacy are considered
- Minor uses are excluded from CA process
- In case of mixture products: Efficacy of each single a.i. is assigned to the diseases

Use No.	Crop	Disease		Minor use
		1st a.i. CfS	2nd a.i.	
1	Wheat	A	A	no
		B	B	
		C	C	
			D	
2	Wheat	E	E	no
3	Barley	A	A	no
		B	B	
4	Rye	A	A	no
		F	F	
5	Spelt	A	A	yes

All major uses are subject to CA.

For alternative products: Only diseases A, B and C are relevant for use No. 1 !

Step 2: Listing and Pre-Examination of Alternative Products

- 2a) **Listing** of all alternative products with the same uses compared to candidate product
  - in case of mixture candidate product: only contribution of CfS to efficacy is considered
  - non-chemical alternatives are not considered

- 2b) **Exclusion** of alternative products with
  - CfS a.i.
  - non renewal a.i.
  - near-time expiry dates

- 2c) **Pre-examination** of human health and environmental properties

Step 2c: Pre-examination of Human Health and Environmental Properties

- Exclusion of alternative products with properties that are worse compared to candidate product

  a) human health properties related to CMR classification

  → Evaluation according to authorized classification/labelling

  b) environmental properties related to

  - groundwater
  - aquatic organisms
  - NTA and NTTP
  - Bees

  → Evaluation according to authorized risk mitigation measures (RMM) in the same use category

Steps 2a, b and c: Possible Outcome

		Candidate product	Alternative products							
			1	2	3	4	5	6	7	8
CfS		yes	no	no	no	no	no	no	no	yes
Non renewal a.i.		---	no	no	no	no	no	no	yes	no
Non renewal PPP		---	no	no	no	no	no	yes	no	no
Human health properties	**CMR**	H351	---	---	---	---	H361d	H351	---	---
RMM environment	**Groundwater**	---	---	---	---	---	---	---	---	---
	SPe 3 - aquatic drift	20 m	6 m	20 m	---	20 m	50 m	20 m	50 m	---
	SPe 3 - aquatic run-off	6 m	6 m	---	---	6 m	---	6 m	---	---
	SPe 3 - NTA/ NTTP	---	---	---	---	---	---	---	---	---
	SPe 8 - bees	---	---	---	---	---	---	---	---	---

→ Alternatives 1 to 4 are still appropriate for CA and can enter Step 3

→ Alternatives 5 to 8 are not considered further in CA due to higher risks

Step 3 – Resistance Risk Analysis

- Grouping of alternatives according to resistance groups (e.g. FRAC code)
- 3a) Search for alternatives in the same resistance group as CfS in candidate product

  → Substitution possible with **one «safer» alternative**
- 3b) Search for alternatives in other resistance groups

  → Substitution only possible if at least **three different resistence groups** remain for the use (exceptions possible)

Step 3: Possible Scenario I

Crop	Candidate product	Alternatives			
		1	2	3	4
	FRAC 4	FRAC 4	FRAC 3	FRAC 7	FRAC 11
Wheat	A	A	A	A	A
	B	B	B	B	B
	C	C	C	C	C
Barley	A	A			A
	B		B	B	B
		D	D		D

A, B, C and D are diseases

Wheat:

- Alternative in same resistance group
- Substitution possible if this alternative is significantly better in comparative RA (step 4)
- If no substitution in same resistance group possible

  → sufficient other resistance groups available (at least 3)
- Comparative RA (step 4) for alternatives in other resistance groups

Barley:

- No alternative in same resistance group
- Number of other resistance groups not sufficient (less than 3)

  → CA is stopped, no step 4

Step 3: Possible Scenario II

Special case of mixture products as alternatives

	Candidate product			Alternatives				
				1		2		3
Crop	CFS	A.I. 2		A.I.1	A.I.2	A.I.1	A.I.2	A.I.1
	FRAC 4	FRAC 5		FRAC 6	FRAC 5	FRAC 7	FRAC 5	FRAC 5
Wheat	A	A		A	A	A	A	A
	B	B		B	B	B	B	B
	C	C		C	C		C	C
		D		D	D		D	D

A, B, C and D are specific diseases

3 alternative products with 3 different resistance groups FRAC 5, 6 and 7

→ substitution possible ?

But: full efficacy in alternative 2 against diseases A, B and C due to FRAC 5; FRAC 7 does not contribute to C

→ 2 different resistance groups only, substitution **not** possible !

Step 4: Comparative Risk Assessment → Environment

- Search for safer alternatives in a comparative RA
- Selection of a set of non target organisms based on PBT criteria that are fulfilled by CfS,

  e.g. persistence in soil and aquatic toxicity:

  soil organisms, algae/aquatic plants, daphnia,

  sediment organisms, fishes
- Comparison of risk quotients (toxicity exposure ratios = TER values) based on chronic endpoints (lower tier data) for each use

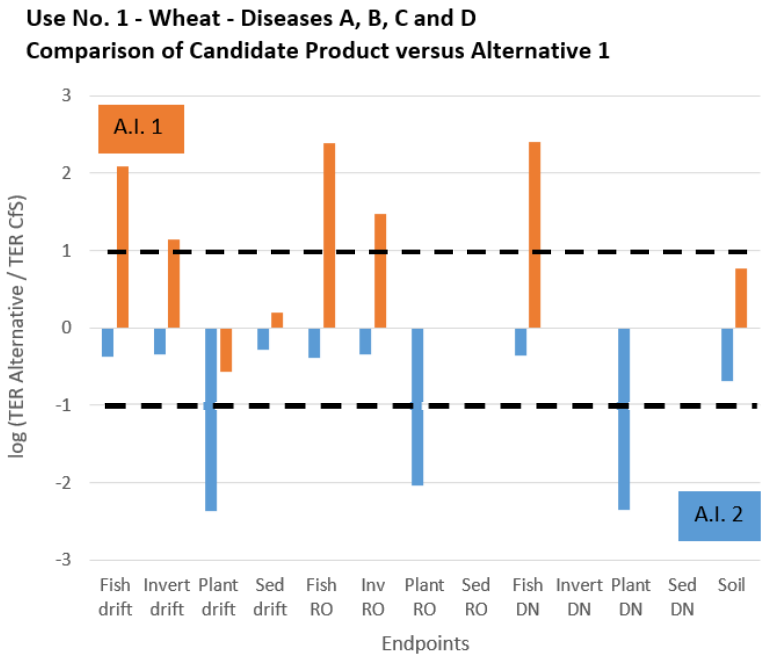
$$\log (TER_{alternative} / TER_{candidate\ product})$$

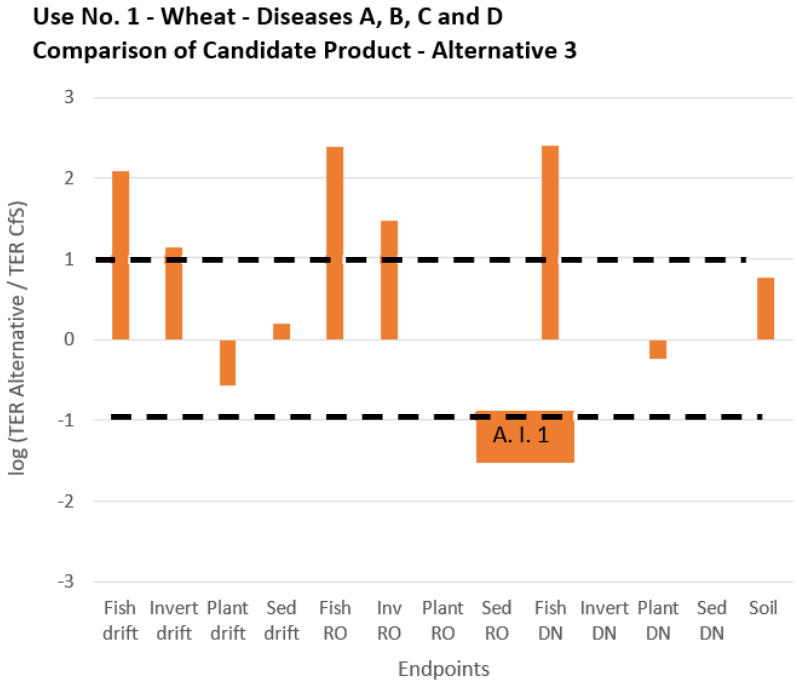
< -1
alternative **significantly worse**

> +1
alternative **significantly better**

(significant difference → factor 10)

Step 4: Possible Outcome





→ **significantly higher** risks with Alternative 1 due to active ingredient 2

→ **significantly lower** risks with Alternative 3

Decision Taking

		Alternatives				
	Candidate product	1	2	3	4	Substitution
	FRAC 4	FRAC 4	FRAC 5	FRAC 6	FRAC 7	
Case 1		++	irrelev.	irrelev.	irrelev.	Yes
Case 2			+	+	-	No
Case 3			++	+	-	Yes
Case 4			++	--	+	Yes/No?
x						

+ , - = better, worse
++ , -- = significantly better, significantly worse

How to decide in case 4?

- One safer alternative → substitution
- **But:** Substitution would increase the probability of use of products with significantly higher risks?