



H1. Herbicide M_a and metabolite

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Aim to illustrate the most important items of the guidance provided in the new AGD

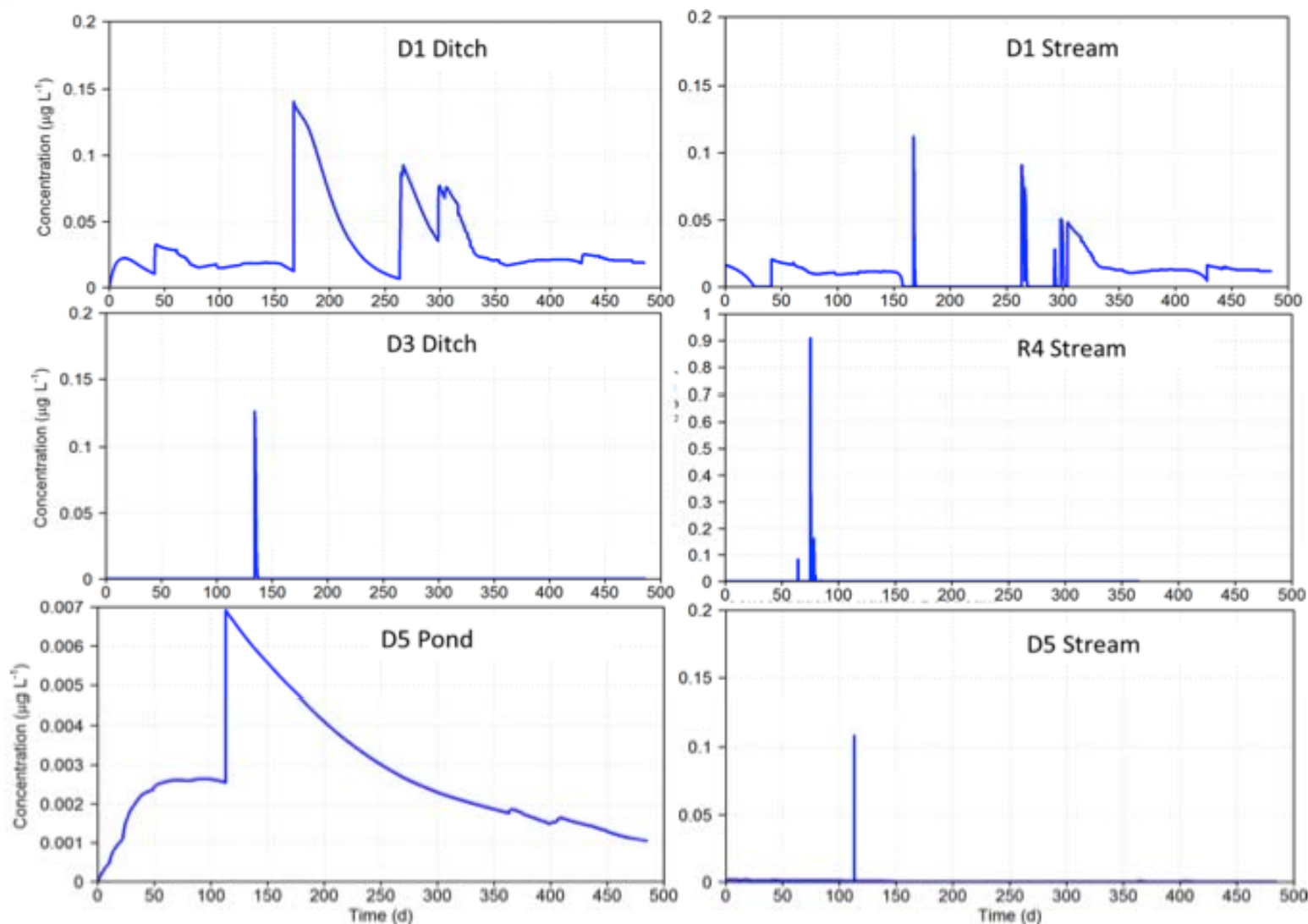
Focus of this presentation on:

- **Herbicides**
- tier 1 to tier 2B effect assessment
- **Metabolite effect assessment**

Selective pre- and post-emergence herbicide

- Acetolactate synthase inhibitor
- Affects synthesis of branched amino acids
- used in Spring cereals
- 1 application in spring (0.02 kg/ha)
- FOCUS Step 3 calculations
- One potentially relevant metabolite (met-M_A)
formed in terrestrial soils – enters surface waters

Typical exposure profiles for M_A (FOCUS sw)



Step 3 $\text{PEC}_{\text{sw,max}}$: 0.006–0.569 $\mu\text{g/L}$

Tier 1 effect assessment



	Acute L(E)C ₅₀ (µg a.s./L)	Chronic EC _x /NOEC (µg a.s./L)	endpoint
<i>P. subcapitata</i>	-	119 (72 h E _r C ₅₀)	growth rate
<i>Navicula peliculosa</i>	-	95 (96 h E _r C ₅₀)	growth rate
<i>Lemna minor</i>	-	0.718 (7 d E _r C ₅₀)	growth rate (frond no.)
<i>Myriophyllum spicatum</i>	-	0.280 (14 d E _r C ₅₀)	growth rate (dry weight)
<i>Daphnia magna</i>	>150,000 (48 h)	150,000 (21 d NOEC)	mortality
<i>Oncorhynchus mykiss</i>	100,000 (96 h)	60,000 (21 d NOEC)	mortality

AF of 10 to the lowest toxicity value (0.280 µg/L)

Tier 1 RAC_{sw;ac} = 0.028 µg/L (based on *M. spicatum*)

Tier 1 Risk Assessment

Scenario	Step 3 $PEC_{sw;max}$ ($\mu\text{g/L}$)	Tier 1 RAC_{sw} ($\mu\text{g/L}$)
D1 Ditch	0.189	0.028
D1 Stream	0.140	0.028
D3 Ditch	0.127	0.028
D4 Pond	0.007	0.028
D4 Stream	0.098	0.028
D5 Pond	0.006	0.028
D5 Stream	0.102	0.028
R4 Stream	0.569	0.028

Comparison to step 3
 $PEC_{sw;max}$ values indicates
 potential risks in all scenarios
 - except D4/D5 pond

Aquatic macrophytes more sensitive than

- single celled algae (>10 x)
- Animals (>1000 x)

Higher tier RA focused on aquatic macrophytes

Tier 2A effect assessment (Geomean)

	EC ₅₀ value (µg a.s./L)	endpoint	Taxonomy
Dossier data			
<i>Lemna minor</i>	0.718 (7 d)	growth rate (frond number)	monocot
<i>Lemna gibba</i>	0.850 (7 d)	growth rate (frond number)	monocot
<i>Myriophyllum spicatum</i>	0.280 (14 d)	growth rate (dry wt. - newly formed tissue)	dicot
<i>Ceratophyllum demersum</i>	0.320 (21 d)	growth rate (dry wt. - newly formed tissue)	dicot
Open Literature data			
<i>Elodea canadensis</i>	0.116 (21 d)	growth rate (recalculated from yield, new shoot length)	monocot
<i>Batrachium trichophyllum</i>	0.180 (28 d)	growth rate (recalculated from yield, new shoot length)	dicot

Geomean = 0.323

Geom-RAC_{sw} of 0.0323 µg/L (aquatic macrophytes AF of 10)

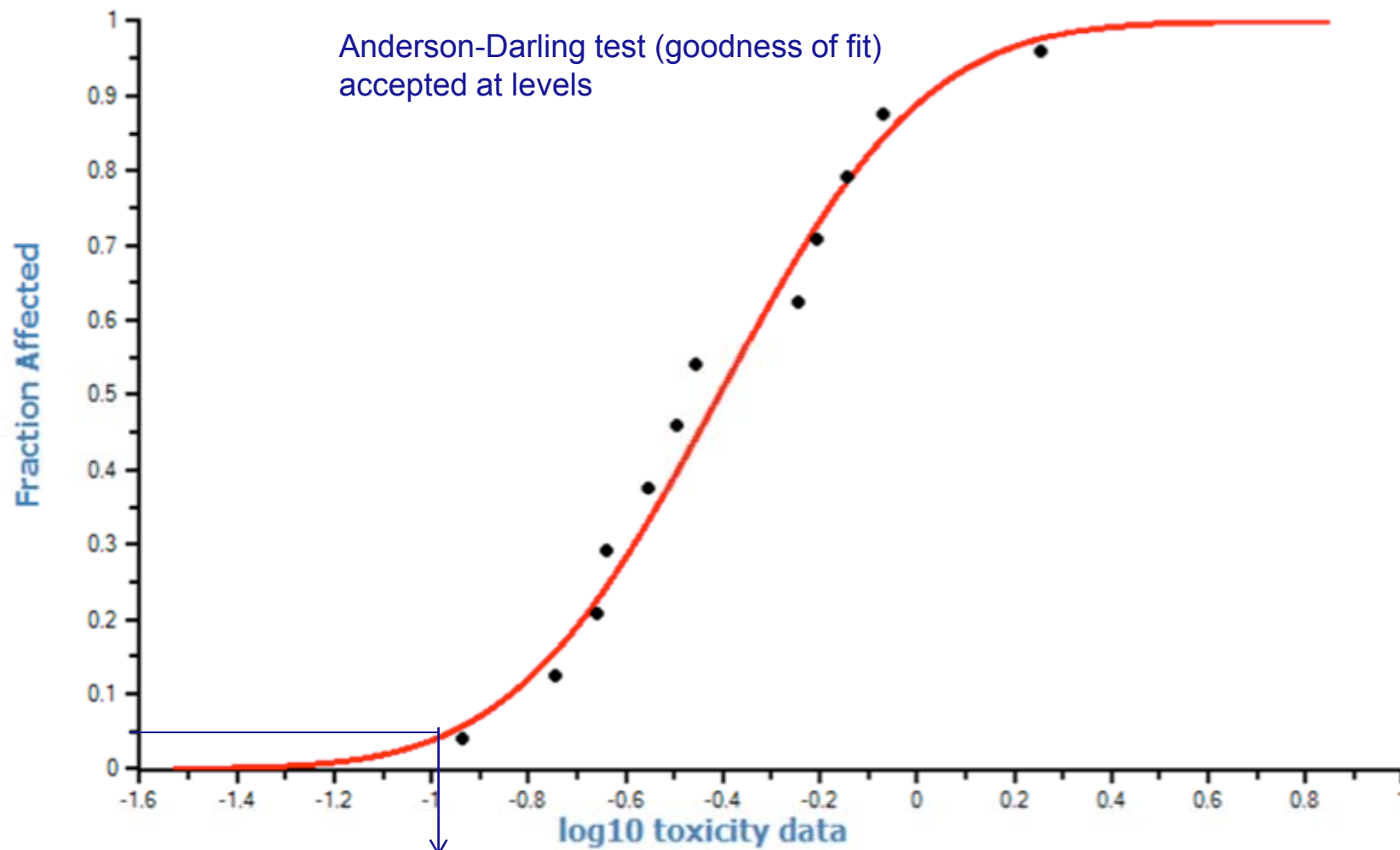
Tier 2B effect assessment

	EC ₅₀ value (µg a.s./L)	endpoint	Taxonomy
Specific growth rate available/recalculated			
Dossier data			
<i>Lemna minor</i>	0.718 (7 d)	E _r C ₅₀	monocot
<i>Lemna gibba</i>	0.850 (7 d)	E _r C ₅₀	monocot
<i>Myriophyllum spicatum</i>	0.280 (14 d)	E _r C ₅₀	dicot
<i>Ceratophyllum demersum</i>	0.320 (21 d)	E _r C ₅₀	dicot
Open Literature data			
<i>Elodea canadensis</i>	0.116 (21 d)	E _r C ₅₀ (recalculated)	monocot
<i>Batrachium trichophyllum</i>	0.180 (28 d)	E _r C ₅₀ (recalculated)	dicot
<i>Myriophyllum aquaticum</i>	0.220 (14 d)	E _y C ₅₀	dicot
<i>Spirodela polyrhiza</i>	0.230 (14 d)	E _y C ₅₀	monocot
<i>Potamogeton crispus</i>	0.350 (21 d)	E _y C ₅₀	monocot
<i>Elodea canadensis</i>	0.570 (21 d)	E _y C ₅₀	monocot
<i>Ceratophyllum submersum</i>	0.620 (21 d)	E _y C ₅₀	dicot
<i>Lemna trisulca</i>	1.800 (7 d)	E _y C ₅₀	monocot

Combining growth- and yield-based endpoints
provides enough data points (ie > 8) for SSD

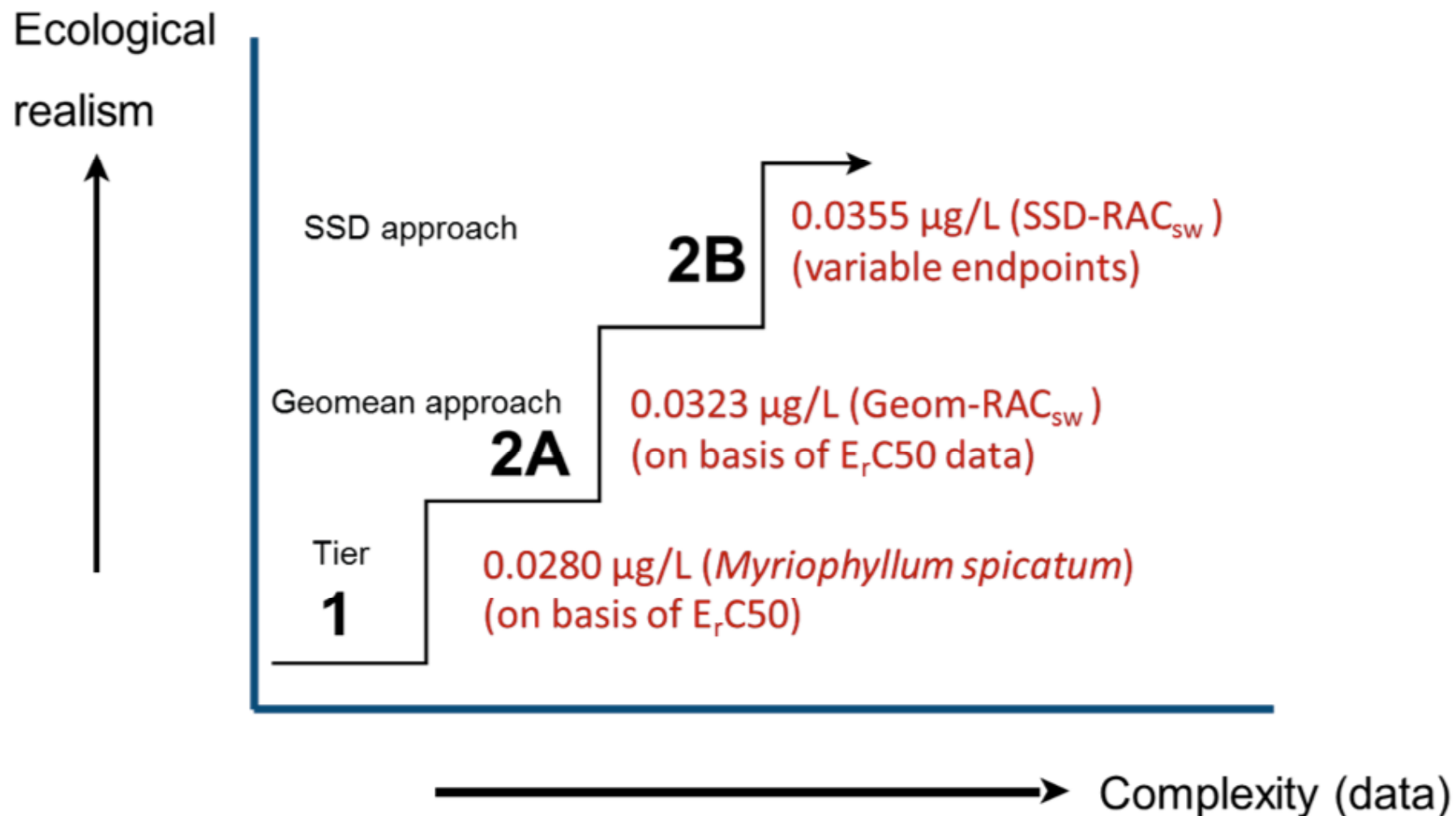


Tier 2B effect assessment - SSD



median HC5 = 0.1065 / 3 (primary producers) **SSD-RAC_{sw} = 0.0355 (µg a.s./L) 9**

Herbicide MA – summary effects



Checking SSD-RAC against lower tiers

	Acute L(E)C ₅₀ (µg a.s./L)	Chronic EC _x /NOEC (µg a.s./L)	endpoint	
<i>P. subcapitata</i>	-	119 (72 h E _r C ₅₀)	growth rate	✓
<i>Navicula peliculosa</i>	-	95 (96 h E _r C ₅₀)	growth rate	
<i>Lemna minor</i>	-	0.718 (7 d E _r C ₅₀)	growth rate (frond no.)	
<i>Myriophyllum spicatum</i>	-	0.280 (14 d E _r C ₅₀)	growth rate (dry weight)	
<i>Daphnia magna</i>	>150,000 (48 h)	150,000 (21 d NOEC)	mortality	✓
<i>Oncorhynchus mykiss</i>	100,000 (96 h)	60,000 (21 d NOEC)	mortality	✓

Linking effects to exposure: TWA

Scenario	PEC _{sw;max} of herbicide M _A (µg/L)	
	Step 3	Step 4: 90 % drift reduction
D1 Ditch	0.189	0.115
D1 Stream	0.140	0.092
D3 Ditch	0.127	0.013
D4 Pond	0.007	0.007
D4 Stream	0.098	0.010
D5 Pond	0.006	0.002
D5 Stream	0.102	0.011
R4 Stream	0.569	0.569



Scenario	PEC _{sw;7d-twa} of herbicide M _A (µg/L)	
	Step 3	Step 4: 90 % drift reduction
D1 Ditch	0.115	0.111
D1 Stream	0.069	0.069
D3 Ditch	0.017	0.002
D4 Pond	0.007	0.007
D4 Stream	0.005	0.005
D5 Pond	0.006	0.002
D5 Stream	0.001	0.001
R4 Stream	0.079	0.079

Effects and Risk assessment - metabolite

Soil metabolite Met-M_A formed (>10% AR)
in laboratory soil degradation studies

Toxophore is lost

Assume Met-MA has same toxicity as parent molecule

Convert tier 1 toxicity values to molar equivalents of the
parent

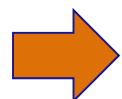
Met-M_A – estimation of Tier 1 effects

	Endpoint	M _A (µg/L)	Met-M _A assuming equal toxicity as parent	AF	RAC Met-MA (µg/L)
Acute					
<i>O. mykiss</i>	96 h LC ₅₀	100 000	93 333	100	933
<i>D. magna</i>	48 h EC ₅₀	>150 000	140 000	100	1 400
Chronic					
<i>P. subcapitata</i>	96 h E _r C ₅₀	119	111	10	11.1
<i>N. peliculosa</i>	96 h E _r C ₅₀	95	89	10	8.9
<i>Lemna minor</i>	7 d E _r C ₅₀	0.718	0.670	10	0.067
<i>M. spicatum</i>	14 d E _r C ₅₀	0.28	0.26	10	0.026
<i>O. mykiss</i>	21 d NOEC	60 000	56 000	10	5 600
<i>D. magna</i>	21 d NOEC	150 000	140 00	10	14 000

Met-M_A Tier 1 Risk Assessment

Comparing RAC_{sw} (aquatic macrophytes)
to FOCUS step 2 values for Met-M_A:

Scenario	STEP 2 PEC _{sw;max} (µg/L)	STEP 2 PEC _{sw;7d-twa} (µg/L)	RAC _{sw} (µg/L)
Northern Europe	0.16	0.15	0.026
Southern Europe	0.32	0.31	0.026



Potential risk for aquatic macrophytes

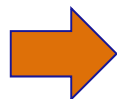
Next steps..

Standard laboratory test of Met-M_A with potentially most sensitive species - from Tier 1 testing of parent (*Myriophyllum*)

14 d E_rC₅₀ (dry weight of newly formed tissue) = 1600 µg/L / AF 10

$$\text{RAC}_{\text{sw}} (\text{Met-M}_A) = 160 \text{ } \mu\text{g/L}$$

Scenario	STEP 2 PEC _{sw;max} (µg/L)	STEP 2 PEC _{sw;7d-twa} (µg/L)	RAC _{sw} (µg/L)
Northern Europe	0.16	0.15	160
Southern Europe	0.32	0.31	160



NO potential risks from Met-M_A identified