Classification of mixtures based on their ecotoxicological properties, - some practical examples

Lilian Törnqvist
May 2015 Belgrade

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

Environmental hazards

Scope

➢ The classification scheme covers both

- short term and
- long term effects

- to both aquatic freshwaters and
- marine ecosystems

Environmental Hazards – 2 classes
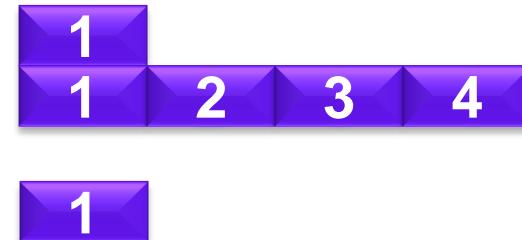
Hazard Class

Hazard Category

Hazardous to the aquatic environment

     Acute hazard

     Chronic (Long-term) hazard

Hazardous to the ozone layer

KEM I
Kemikalieinspektionen
Swedish Chemicals Agency

Basic elements for classification

- Acute aquatic toxicity

- Chronic aquatic toxicity

- Potential for, or actual bioaccumulation

- Degradation (biotic or abiotic) for organic chemicals

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

For aquatic hazard classification, toxicity data is normally needed on three trophic levels


Fish

Crustacean

Alge/aquatic plants
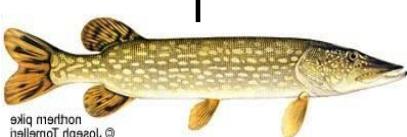
➢ The taxa chosen from three trophic levels represent the "base-set" of toxicity test data; a minimum data-set for a fully valid description of toxicity as part of aquatic hazard.

# Food chain with different trophic levels

Top-
consumers

Secondary
consumers
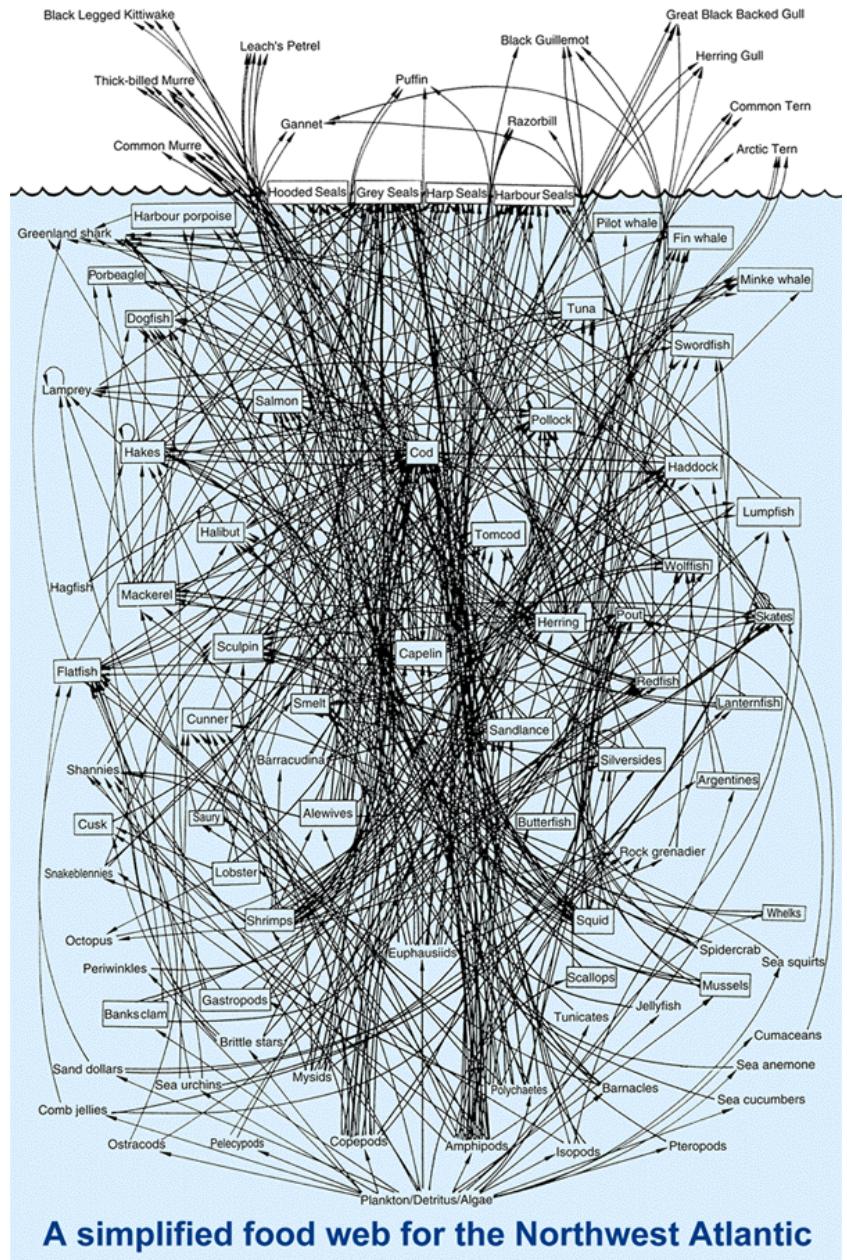
Primary
consumers

Producers

Food web

A simplified food web for the Northwest Atlantic

Labelling elements

➤ Acute (short-term) aquatic hazard - Category Acute 1

Acute 1

Pictogram

Signal
word

Warning

Hazard
Statement

H400: Very toxic
to aquatic life

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

Labelling elements

➤ Long-term aquatic hazard - Categories Chronic 1 to 3

	Chronic 1	Chronic 2	Chronic 3
Pictogram			No Pictogram
Signal word	Warning	No word	No word
Hazard Statement	H410: Very toxic to aquatic life with long-lasting effects	H411: Toxic to aquatic life with long-lasting effects	H412: Harmful to aquatic life with long-lasting effects

Safety net Chronic 4 - H413: May cause long lasting harmful effects to aquatic life.

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

Acute (short-term) aquatic hazard

Highest acute toxicity (lowest value) to
- Fish ● Crustacea or ● Aquatic plant   ➤ Category

LC_{50} or EC_{50} (or IC_{50}) ≤1 mg/l

Acute 1

LC_{50} or EC_{50} (or IC_{50}) >1 to ≤10 mg/l

Acute 2 *

LC_{50} or EC_{50} (or IC_{50}) >10 to ≤100 mg/l

Acute 3 *

* Categories Acute 2 and 3 were mainly meant for transport of bulk-quantities and therefore normally not implemented for Supply & Use

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

Acute aquatic hazard – Example

- Substance A   LC50 = 115 mg/l (fish)   ?
                 EC50 = 1,05 mg/l (crustacea)
                 EC50 = 0,05 mg/l (algea)

- Substance C   LC50 = 0,0003 mg/l   ?
- Substance D   EC50 = 0,02 mg/l   ?
- Substance E   EC50 = 0,99 mg/l   ?

KEM
Kemikalieinspektionen
Swedish Chemicals Agency

Acute aquatic hazard – **Answers** to Exercise 1

- Substance A   LC50 = 115 mg/l (fish)   cat. 1
                   EC50 = 1,05 mg/l (crustacea)
                   EC50 = 0,05 mg/l (algea)

- Substance B   LC50 = 0,0003 mg/l   cat 1
- Substance C   EC50 = 0,02 mg/l   cat 1
- Substance D   EC50 = 0,99 mg/l   cat 1

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

M-factors

➢ 'M-factor' means a multiplying factor. It is applied to substance as part of the <u>substance</u> classification as <u>Categories Acute 1 and/or Chronic 1.</u>

➢ It is used to derive, by the summation method, the classification of a mixture in which the substance is present.

Setting M-factors for highly toxic substances
GHS table 4.1.5   Acute 1 and Chronic 1 (only!)

Acute toxicity	M factor	Chronic toxicity	M factor	
$L(E)C_{50}$ value		NOEC value	NRD[a] components	RD[b] components
$0.1 < L(E)C_{50} \leq 1$	1	$0.01 < NOEC \leq 0.1$	1	-
$0.01 < L(E)C_{50} \leq 0.1$	10	$0.001 < NOEC \leq 0.01$	10	1
$0.001 < L(E)C_{50} \leq 0.01$	100	$0.0001 < NOEC \leq 0.001$	100	10
$0.0001 < L(E)C_{50} \leq 0.001$	1000	$0.00001 < NOEC \leq 0.0001$	1000	100
$0.00001 < L(E)C_{50} \leq 0.0001$	10000	$0.000001 < NOEC \leq 0.00001$	10000	1000
(continue in factor 10 intervals)		(continue in factor 10 intervals)		

($L(E)C_{50}$ and NOEC (or EC_x) in mg/l)

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

M factors for acute toxicology

- Substance C   LC50 = 0,0003 mg/l cat 1   **M = 1000**
- Substance D   EC50 = 0,02 mg/l   cat 1   **M = 10**
- Substance E   EC50 = 0,99 mg/l   cat 1   **M = 1**

Degradation

and

Bioaccumulation

assessment

for classification purposes

Rapid degradation

- ➤ biotic or abiotic
  - degradation of organic substances; or
  - transformation of inorganic substances

- ➤ Either
  - full mineralisation or
  - primary degradation / transformation to <u>non hazardous species</u> (t½ < 16 days)

Criteria for Long-term hazard

Adequate chronic toxicity data available		In absence of adequate chronic toxicity data
Non-rapidly degradable (NRD) substance	**Rapidly degradable (RD) substances**	**ACUTE TOXICITY** **+** **NON-RAPIDLY DEGRADABLE** **and/or** **BIOACCUMULATIVE**
Category: **Chronic 1** NOEC or $EC_x \leq 0.1$	Category: **Chronic 1** NOEC or $EC_x \leq 0.01$	
Category: **Chronic 2** $0.1 <$ NOEC or $EC_x \leq 1$	Category: **Chronic 2** $0.01 <$ NOEC or $EC_x \leq 0.1$	
	Category: **Chronic 3** $0.1 <$ NOEC or $EC_x \leq 1$	

➢ Toxicity + degradation and/or bioaccumulation

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

Chronic toxicity – example chronic data for substance "X"

- **Fish**
  Danio rerio: NOEC 1,2 mg/l

- **Crustacea**
  Daphnia magna: NOEC 1,1 mg/l

- **Algea/aquatic plants**
  Scenedesmus subspicatus: NOEC 0,03 mg/l

Classification ?

CHRONIC CAT 1 (if RD then Chronic cat 2)

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

Substance example A:

➢ Hydrophilic substance, straightforward classification based on acute and chronic toxicity data.

Substance example A, *cont.*

ELEMENTS	Value
Physico-chemical properties	
Water solubility / Log Kow:	1200 mg/l / 2.75
Acute aquatic toxicity	
Fish: *Oncorhynchus mykiss*: *Lepomis macrochirus*:	12 mg/l (96 h LC_{50}) 2.7 mg/l (96 h LC_{50})
Crustacea *Daphnia magna*:	18 mg/l (48 h EC_{50})
Algae/aquatic plants *Scenedesmus subspicatus*: *Lemna gibba*:	0.056 mg/l (96 h ErC_{50}) 0.031 mg/l (7 d ErC_{50})
Chronic aquatic toxicity	
Fish: *Danio rerio*:	1.2 mg/l (21 d NOEC)
Crustacea: *Daphnia magna*:	1.1 mg/l (21 d NOEC)
Algae/aquatic plants: *Scenedesmus subspicatus*:	0.01 mg/l (96 h NOEC)
Degradation (evidence of rapid degradation)	
Biotic degradation: Abiotic degradation, hydrolysis: (half-life (d)):	86 % in 28 days → **RD** No data
Bioaccumulation	
Bioconcentration factor (BCF) in fish	No data

Acute aquatic hazard

Acute toxicity: **?**

≤ 1 mg/l

between 0.01 and 0.1 mg/l

Acute 1, M = 10

Long-term aquatic hazard

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

Setting M-factors for highly toxic substances GHS table 4.1.5 Acute 1 and Chronic 1 (only!)

Acute toxicity	M factor	Chronic toxicity	M factor	
L(E)C$_{50}$ value		NOEC value	NRD[a] components	RD[b] components
0.1 < L(E)C$_{50}$ ≤ 1	1	0.01 < NOEC ≤ 0.1	1	-
0.01 < L(E)C$_{50}$ ≤ 0.1	**10**	0.001 < NOEC ≤ 0.01	10	1
0.001 < L(E)C$_{50}$ ≤ 0.01	100	0.0001 < NOEC ≤ 0.001	100	10
0.0001 < L(E)C$_{50}$ ≤ 0.001	1000	0.00001 < NOEC ≤ 0.0001	1000	100
0.00001 < L(E)C$_{50}$ ≤ 0.0001	10000	0.000001 < NOEC ≤ 0.00001	10000	1000
(continue in factor 10 intervals)		(continue in factor 10 intervals)		

(L(E)C$_{50}$ and NOEC (or EC$_x$) in mg/l)

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

Substance example A, *cont.*

ELEMENTS	Value
Physico-chemical properties	
Water solubility / Log Kow:	1200 mg/l / 2.75
Acute aquatic toxicity	
Fish: *Oncorhynchus mykiss*: *Lepomis macrochirus*:	 12 mg/l (96 h LC_{50}) 2.7 mg/l (96 h LC_{50})
Crustacea *Daphnia magna*:	 18 mg/l (48 h EC_{50})
Algae/aquatic plants *Scenedesmus subspicatus*: *Lemna gibba*:	 0.056 mg/l (96 h ErC_{50}) 0.031 mg/l (7 d ErC_{50})
Chronic aquatic toxicity	
Fish: *Danio rerio*:	 1.2 mg/l (21 d NOEC)
Crustacea: *Daphnia magna*:	 1.1 mg/l (21 d NOEC)
Algae/aquatic plants: *Scenedesmus subspicatus*:	 0.01 mg/l (96 h NOEC)
Degradation (evidence of rapid degradation)	
Biotic degradation: Abiotic degradation, hydrolysis: (half-life (d)):	86 % in 28 days → **RD** No data
Bioaccumulation	
Bioconcentration factor (BCF) in fish	No data

Acute aquatic hazard

Acute toxicity:

≤ 1 mg/l

between 0.01 and 0.1 mg/l

Acute 1, M = 10

Long-term aquatic hazard

Chronic toxicity: **?**

≤ 1 mg/l

between 0.001 and 0.01 mg/l

Degradation:

Rapidly degradable

Chronic

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

Criteria for Long-term hazard (categories Chronic 1-3)

Adequate **chronic** toxicity data available	
Non-rapidly degradable (NRD) substance	**Rapidly** degradable (RD) substances
Category: **Chronic 1** NOEC or $EC_x \leq 0.1$	Category: **Chronic 1** NOEC or $EC_x \leq 0.01$
Category: **Chronic 2** $0.1 <$ NOEC or $EC_x \leq 1$	Category: **Chronic 2** $0.01 <$ NOEC or $EC_x \leq 0.1$
	Category: **Chronic 3** $0.1 <$ NOEC or $EC_x \leq 1$

➤ Toxicity + degradation

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

Substance example A, *cont.*

ELEMENTS	Value
Physico-chemical properties	
Water solubility / Log Kow:	1200 mg/l / 2.75
Acute aquatic toxicity	
Fish: *Oncorhynchus mykiss*: *Lepomis macrochirus*:	 12 mg/l (96 h LC_{50}) 2.7 mg/l (96 h LC_{50})
Crustacea *Daphnia magna*:	 18 mg/l (48 h EC_{50})
Algae/aquatic plants *Scenedesmus subspicatus*: *Lemna gibba*:	 0.056 mg/l (96 h ErC_{50}) 0.031 mg/l (7 d ErC_{50})
Chronic aquatic toxicity	
Fish: *Danio rerio*:	 1.2 mg/l (21 d NOEC)
Crustacea: *Daphnia magna*:	 1.1 mg/l (21 d NOEC)
Algae/aquatic plants: *Scenedesmus subspicatus*:	 0.01 mg/l (96 h NOEC)
Degradation (evidence of rapid degradation)	
Biotic degradation: Abiotic degradation, hydrolysis: (half-life (d)):	86 % in 28 days No data
Bioaccumulation	
Bioconcentration factor (BCF) in fish	No data

Acute aquatic hazard

Acute toxicity:

≤ 1 mg/l

between 0.01 and 0.1 mg/l

Acute 1, M = 10

Long-term aquatic hazard

Chronic toxicity:

≤ 1 mg/l

between 0.001 and 0.01 mg/l

Degradation:

Rapidly degradable

Chronic 1, M = 1

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

Setting M-factors for highly toxic substances
(Acute 1 and Chronic 1)

Acute toxicity	M factor	Chronic toxicity	M factor	
L(E)C$_{50}$ value		NOEC value	NRD[a] components	RD[b] components
$0.1 < L(E)C_{50} \leq 1$	1	$0.01 < NOEC \leq 0.1$	1	-
$0.01 < L(E)C_{50} \leq 0.1$	10	**$0.001 < NOEC \leq 0.01$**	10	**1**
$0.001 < L(E)C_{50} \leq 0.01$	100	$0.0001 < NOEC \leq 0.001$	100	10
$0.0001 < L(E)C_{50} \leq 0.001$	1000	$0.00001 < NOEC \leq 0.0001$	1000	100
$0.00001 < L(E)C_{50} \leq 0.0001$	10000	$0.000001 < NOEC \leq 0.00001$	10000	1000
(continue in factor 10 intervals)		(continue in factor 10 intervals)		

(L(E)C$_{50}$ and NOEC (or EC$_x$) in mg/l)

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

Substance ingredients

➢ It is important to get a clear picture on which substances are contained in a mixture.

➢ Basic information would include:
(i) the <u>substance</u> identity,
(ii) its classification
(iii) any applied M-factor, and
(iv) concentration in the mixture.

➢ Where an ingredient in a mixture is itself a mixture, it is generally necessary to get information on the ingredient substances of the first mixture.

Summation method

➤ It is generally the summation of the quantities of the hazardous components that should be used to determine a specific hazard classification of the mixture.

➤ Short-term (acute) hazard:

Summation of components:	Mixture is classified as:
∑(Acute 1 x M) ≥ 25 %	Acute 1
Categories Acute 2 and 3 are mainly for transport of bulk-quantities and therefore normally not implemented for Supply & Use	

Classification of mixture – aquatic acute

Substance	Conc. (%)	Classification	M-factor
A	1,5	Acute cat 1	1
B	15	Acute cat 1	1
Water	84	Not classified	-

1. Classification of mixture?
2. Change M-factor for substance A to 10. Classification?

Use summation formula

$$\sum(\text{Acute } 1 \times M)$$

1. M=1.

$(1,5 \times \mathbf{1}) + (15 \times 1) = 16,5 < 25\ \%$,

the mixture is NOT classified as Acute cat 1.

2. M=10

$(1,5 \times \mathbf{10}) + (15 \times 1) = 30 > 25\ \%$,

the mixture IS classified as Acute cat.1

M=1 or 10 => different label information

- M = 1
  NOT classified

  <u>NO</u> hazard information
  at all in label

- M = 10
  classified Acute cat 1

  Warning

  Very toxic
  to aquatic life

Summation method

➢ **Short-term (acute) hazard:**

Summation of components:	Mixture is classified as:
$\sum$(Acute 1 x M) ≥ 25 %	Acute 1
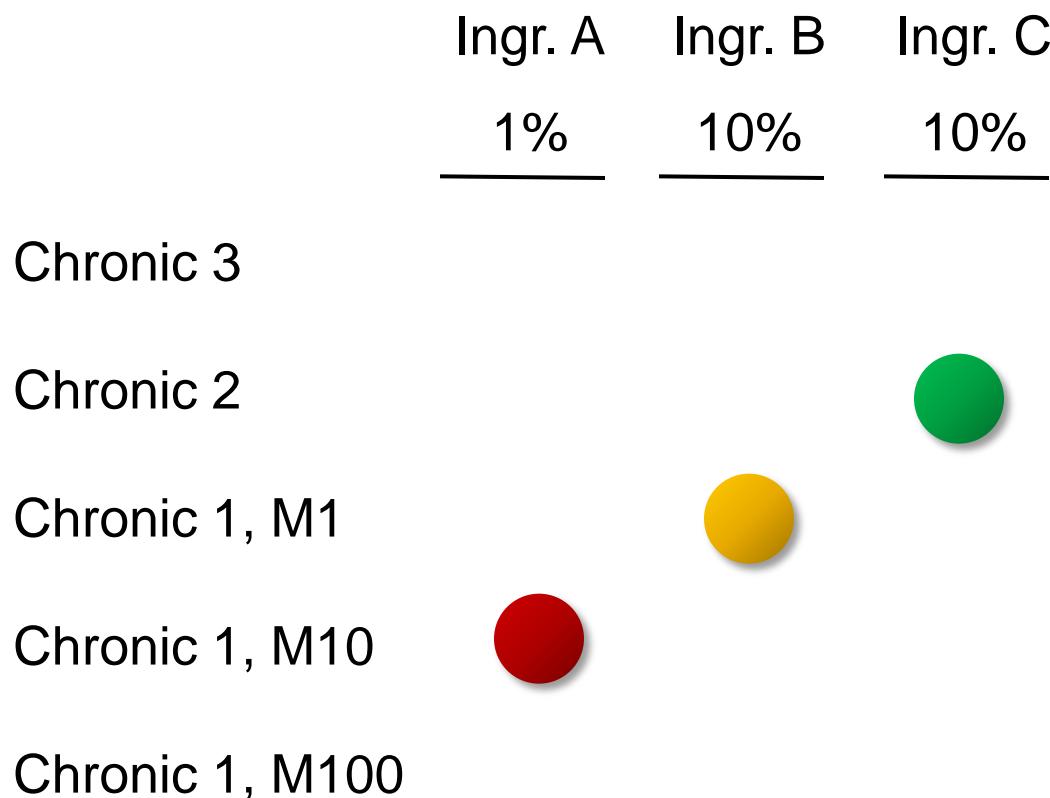
➢ **Long-term aquatic hazard (a stepwise procedure):**

Summation of components:	Mixture is classified as:
$\sum$(Chronic 1 x M) ≥ 25 %	Chronic 1
$\sum$(Chronic 1 x M x 10) + $\sum$(Chronic 2) ≥ 25 %	Chronic 2
$\sum$(Chronic 1 x M x 100) + $\sum$(Chronic 2 x 10) + $\sum$(Chronic 3) ≥ 25 %	Chronic 3
$\sum$(Chronic 1) + $\sum$(Chronic 2) + $\sum$(Chronic 3) + $\sum$(Chronic 4) ≥ 25 %	Chronic 4 (Safety-net)
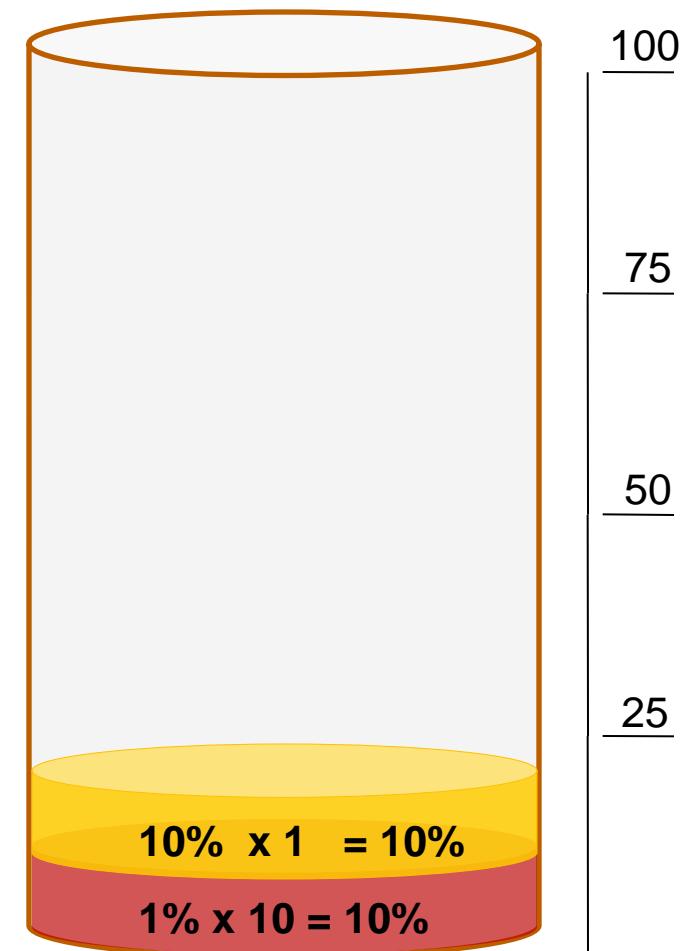
Summation method, example on Long term effects step 2:

Mixture classified as Category Chronic 2 if
∑(Category Chronic 1 x M x 10) + ∑(Category Chronic 2) ≥ 25%

Ingr. A   Ingr. B   Ingr. C   →   CHRONIC 2
1%   10%   10%

Chronic 3

Chronic 2

Chronic 1, M1

Chronic 1, M10

Chronic 1, M100

300

200

100

10%

10% x 1 x 10 = 100%

1% x 10 x 10 = 100%
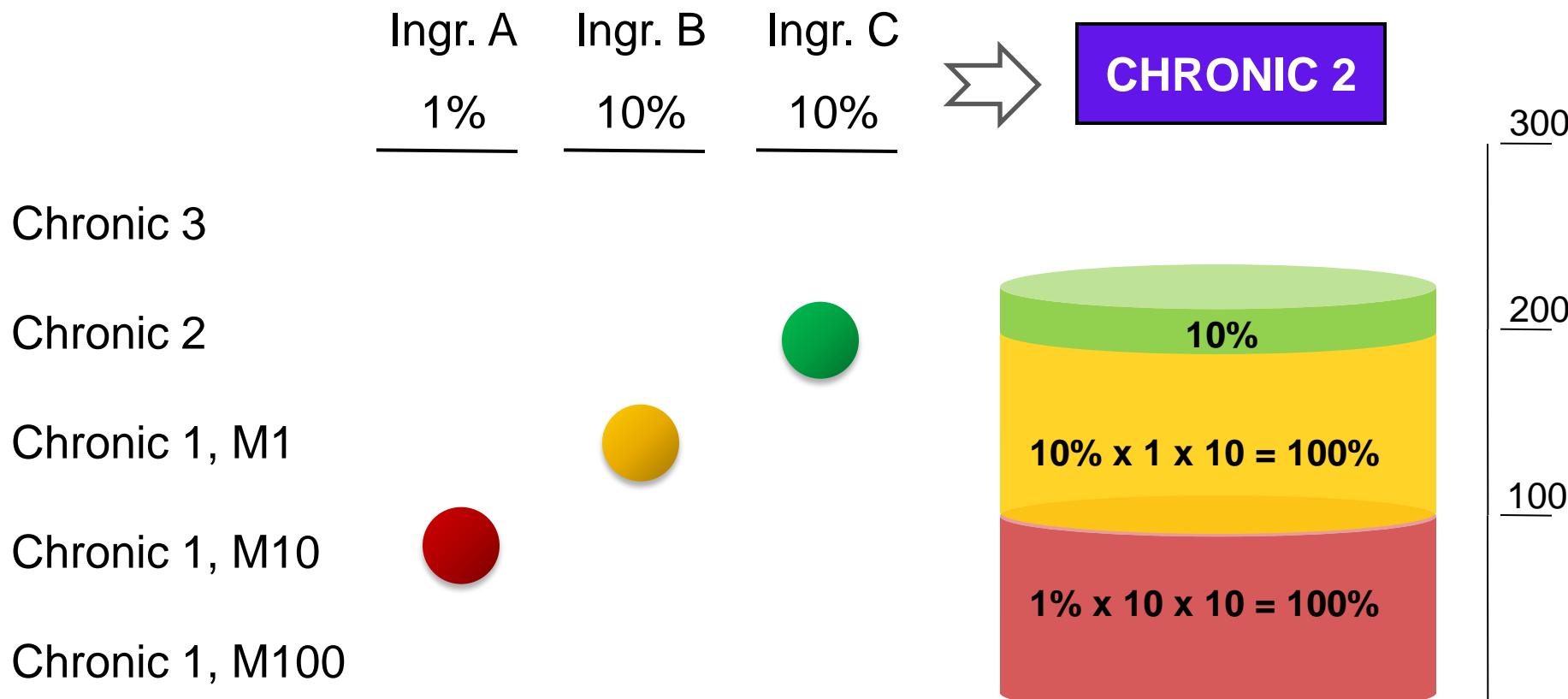
100% + 100% + 10% = 210%, which is ≥ 25%.
Hence, mixture classified as Chronic 2.

Importance of M factors for classification and information given in labels

- Substance C LC50 = 0,0003 mg/l   cat 1   **M = 1000**
- Substance D EC50 = 0,02 mg/l   cat 1   **M = 10**
- Substance E EC50 = 0,99 mg/l   cat 1   **M = 1**

Substance C, D & E are all Acute Cat 1, but how much can you have of the individual substances within a mixture before the mixtures becomes classified as Cat 1? Use summation formula!

- C   **0,025 %** * 1000 ≥ 25%
- D   **2,5%** *10 ≥ 25%
- E   **25 %** * 1 ≥ 25%

KEM

Kemikalieinspektionen
Swedish Chemicals Agency

Exercise – summation method

Substance	Acute Aq.	M	Chronic Aq.	M	Conc. (%)
Astralamid	1	10	1	10	1
Bastralamid	1	1	Not classified	-	3
Castralamid	Not classified	-	2	-	10
Dastralamid	Not classified	-	Not classified	-	10
Estralamid	Not classified	-	Not classified	-	76

Classification of mixture

Acute cat 1

$(1\times10)+(3\times1)=13 < 25\ \%,$

NOT classified as Acute cat. 1

Chronic cat 1

$(1\times10)=10 < 25\ \%,$

NOT classified as Chronic cat. 1

Chronic cat 2

$(1\times10\times10)+10=110 > 25\ \%,$

Classified as Chronic cat 2

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

Labelling elements

➤ Long-term aquatic hazard - Categories Chronic 1 to 3

	Chronic 1	Chronic 2	Chronic 3
Pictogram			No Pictogram
Signal word	Warning	No word	No word
Hazard Statement	H410: Very toxic to aquatic life with long-lasting effects	H411: Toxic to aquatic life with long-lasting effects	H412: Harmful to aquatic life with long-lasting effects

Safety net Chronic 4 - H413: May cause long lasting harmful effects to aquatic life.

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

Thank You for Your Attention