Global Plant Advisory Group

Open Meeting Tue 16:15

Issues...

Updated May 2016

Issues with plant tests in the open literature

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Extrapolation

Problems:

- No Dose-response design
- Extrapolation (dose-resp, but ERx outside of range)
- Selection of Effect level (ER_{10}, ER_{20}, ER_{25} ER_{50})
- SSDs and „Greater than-values“

Extrapolation

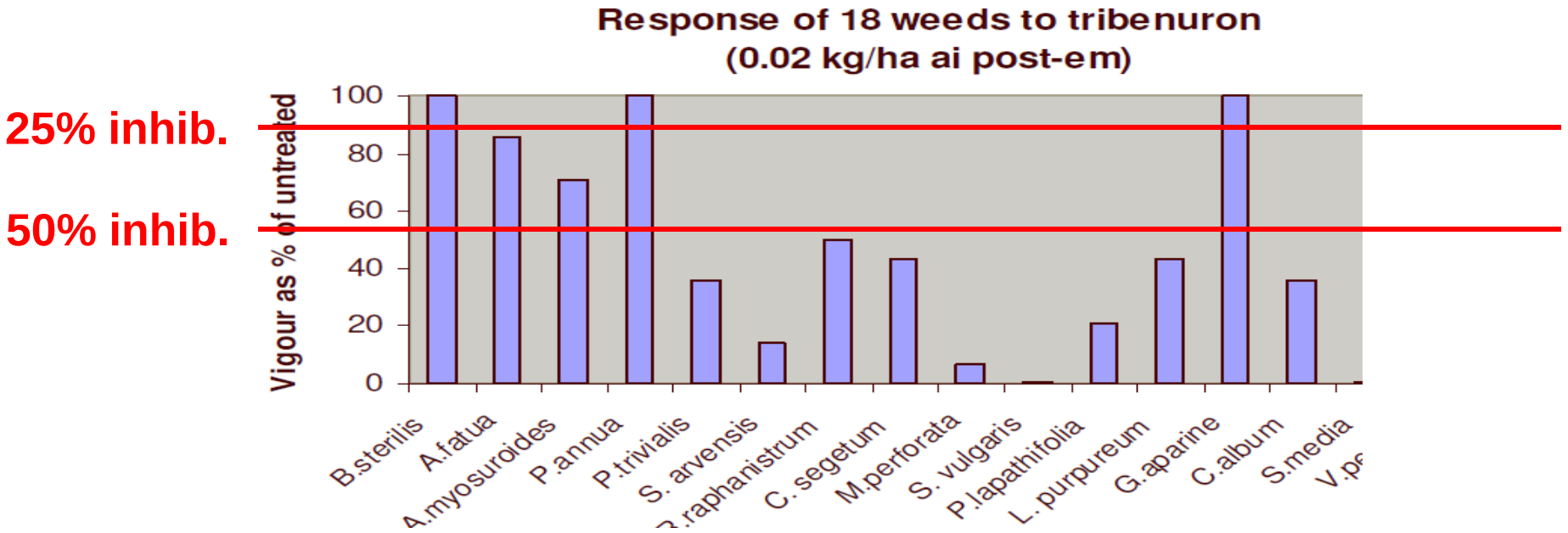
Problem:

No Dose-response design,
ERx wanted, but only
control + one dose tested

No Dose-response design

Problem:

ERx wanted, but only control + one dose (20 g/ha) tested



ER_{50}: >20 >20 >20 >20 <20 <20 **20** **20** <20 <20 <20 **20** >20

ER_{25}: >20 >20 **20** >20 <20 <20 <20 <20 <20 <20 <20 <20 >20

Extrapolation

Problem:

Dose-response design,

but the ERx is outside the range tested

Extrapolation of endpoints

Problem:

Tested treatment levels do not cover desired endpoint

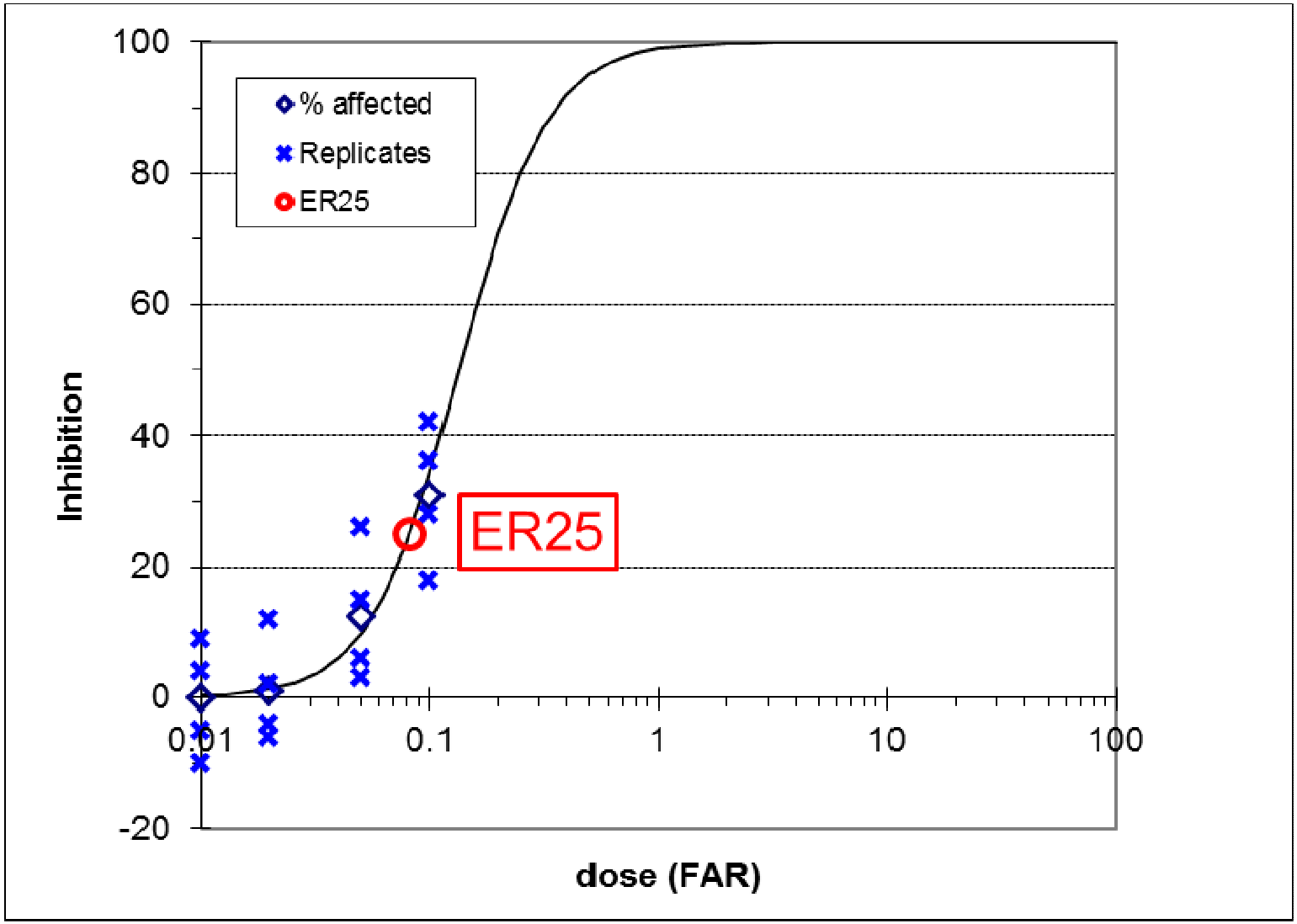
Wanted: ER_{25}

Tested levels 0.02, 0.05, 0.1 * FAR

ER25 of different species range
between 0.02 and 4.0 FAR

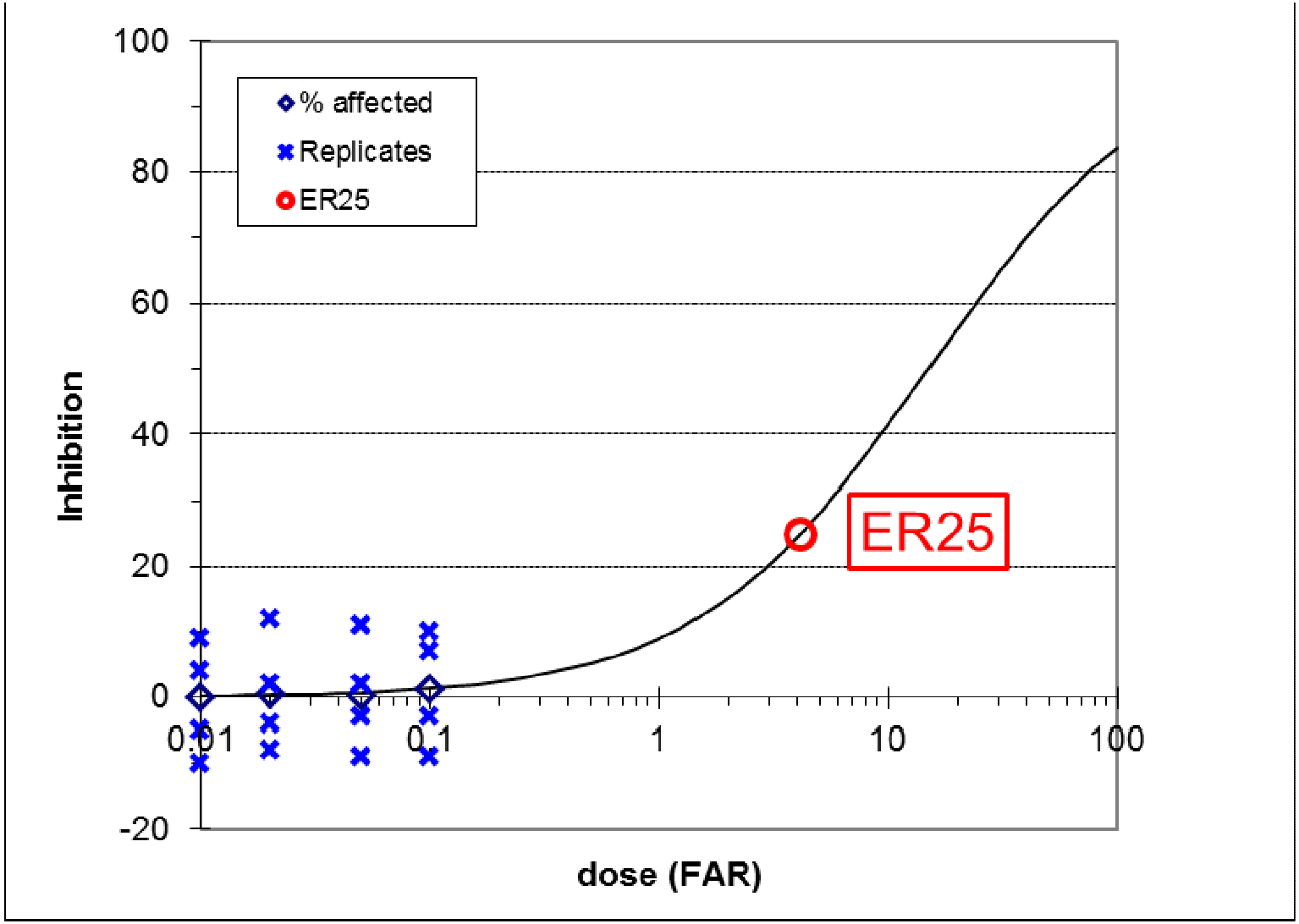
Extrapolation

Reproductive endpoint 0.08 FAR



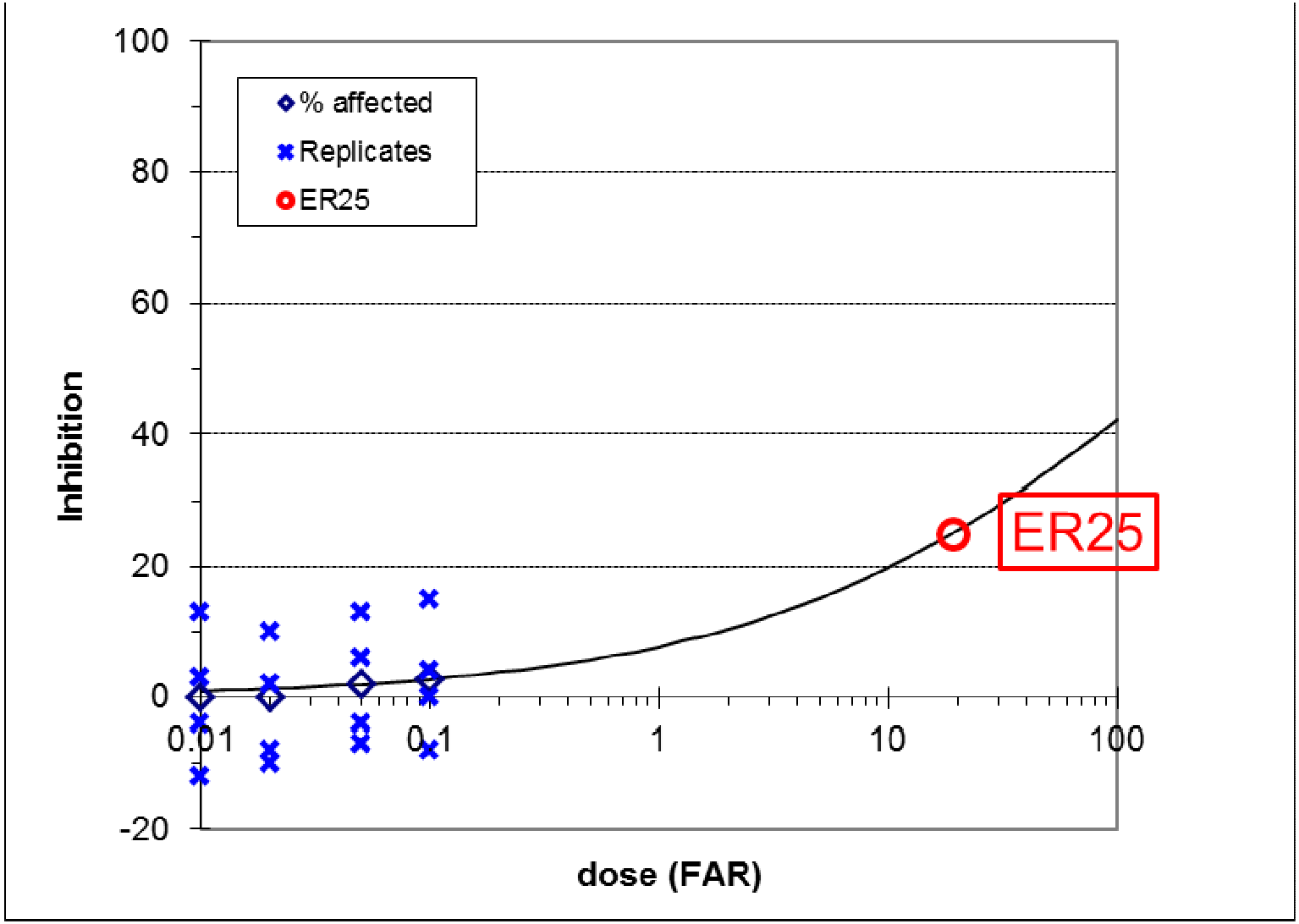
Extrapolation

Vegetative endpoint: **4 FAR**.



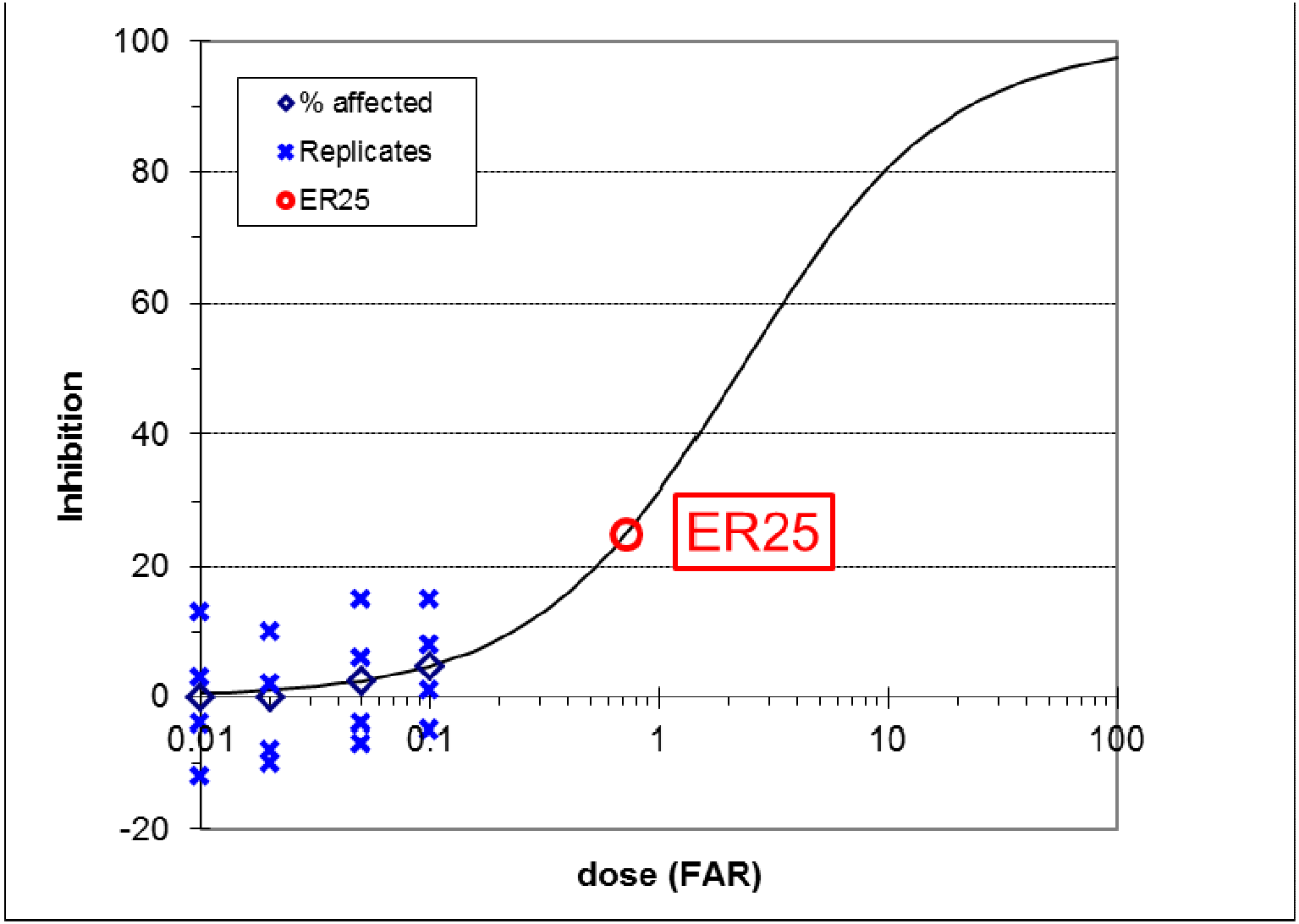
Extrapolation

Vegetative endpoint – random change of replicates



Extrapolation

Vegetative endpoint – random change of replicates



Extrapolation

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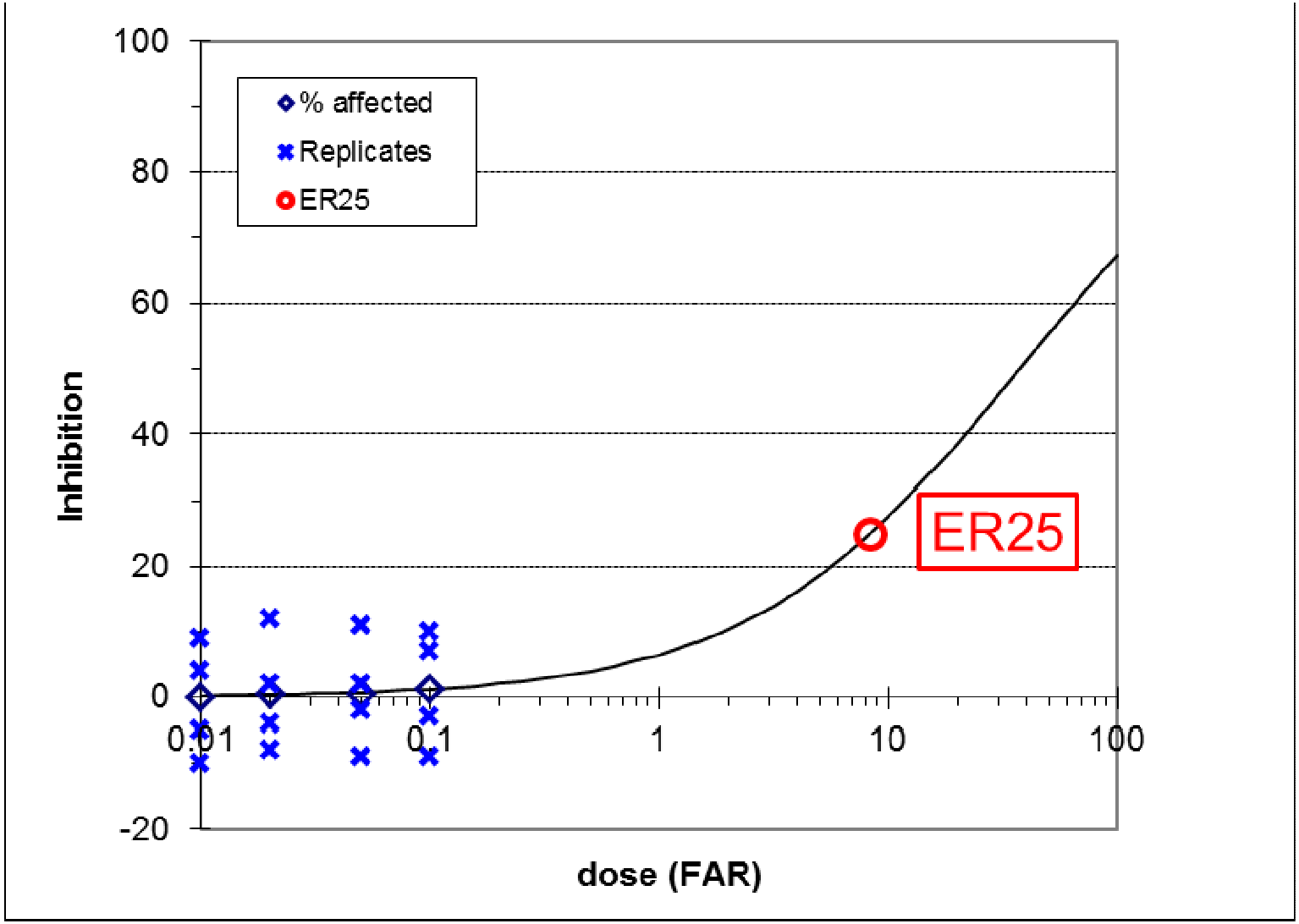
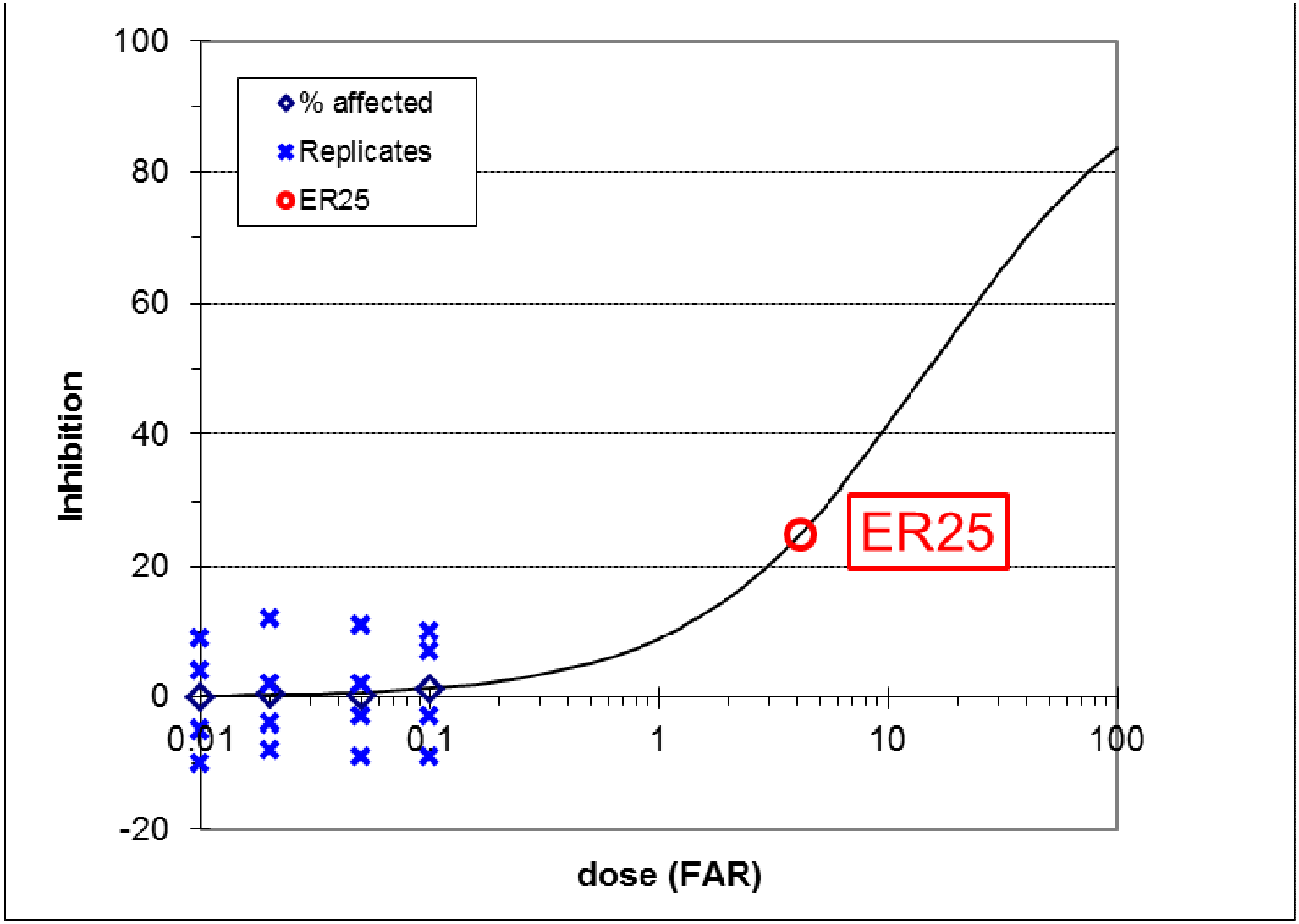


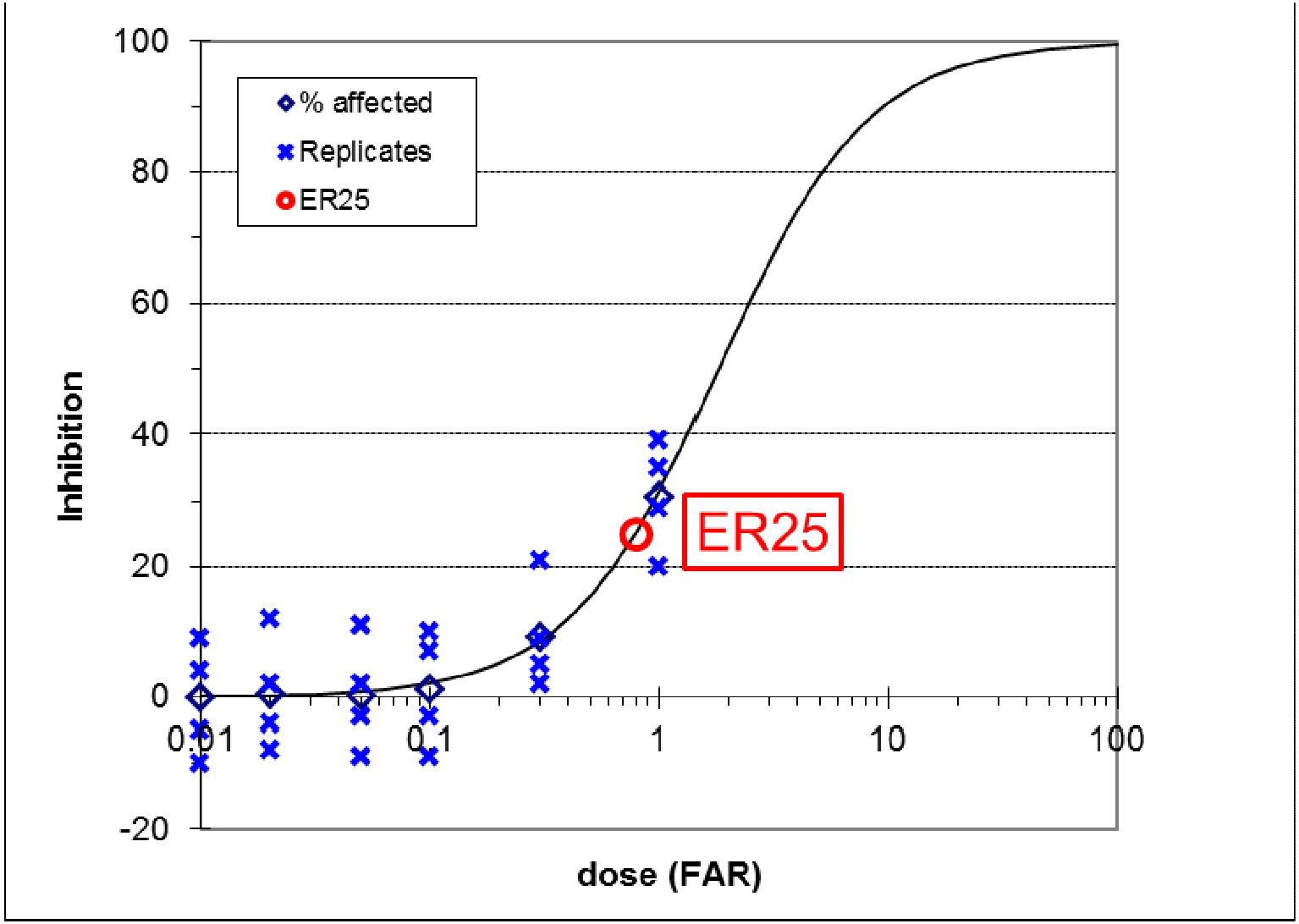
Extrapolation

Vegetative endpoint – random change of replicates



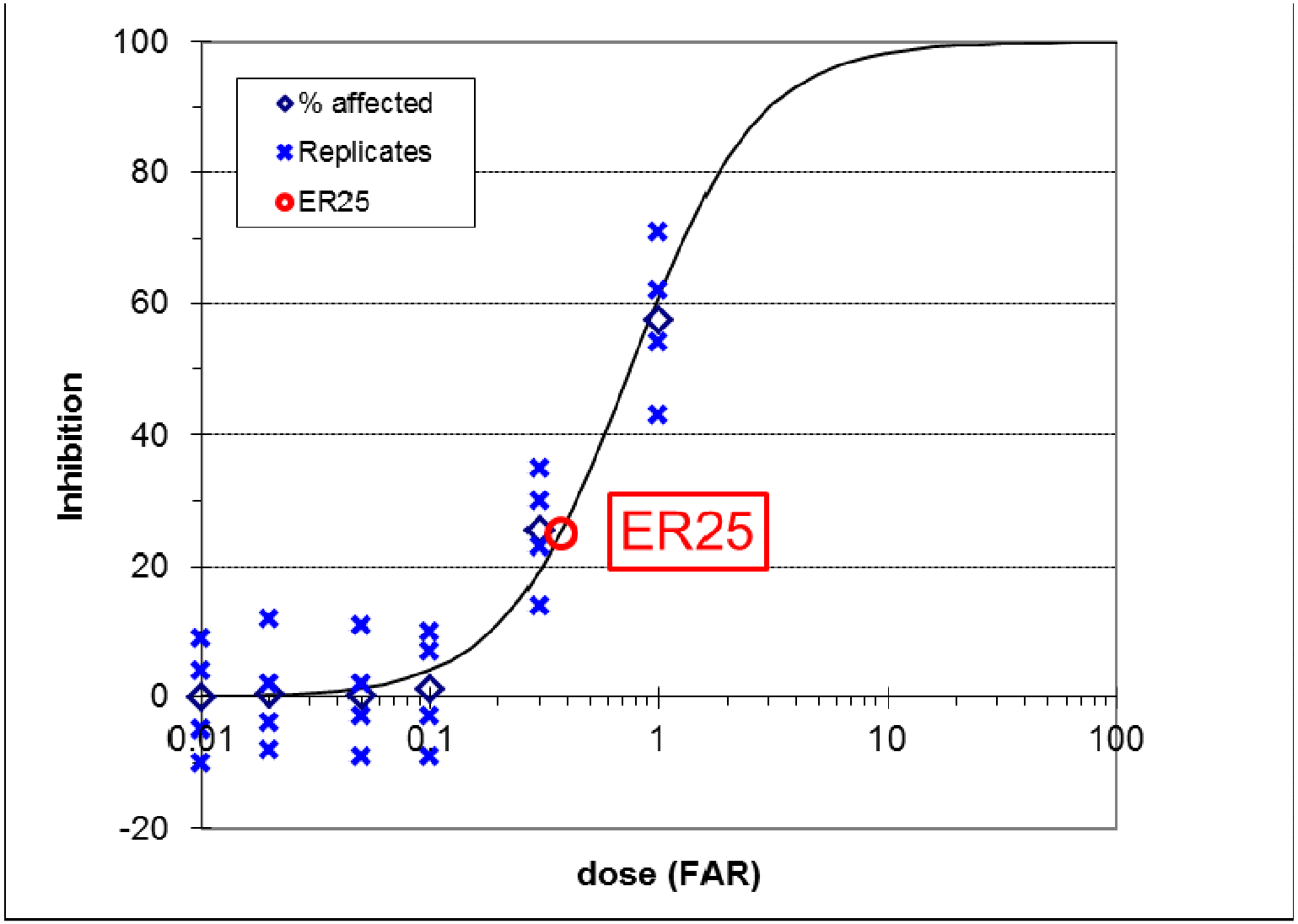
Extrapolation

Vegetative endpoints with sufficient test rates...



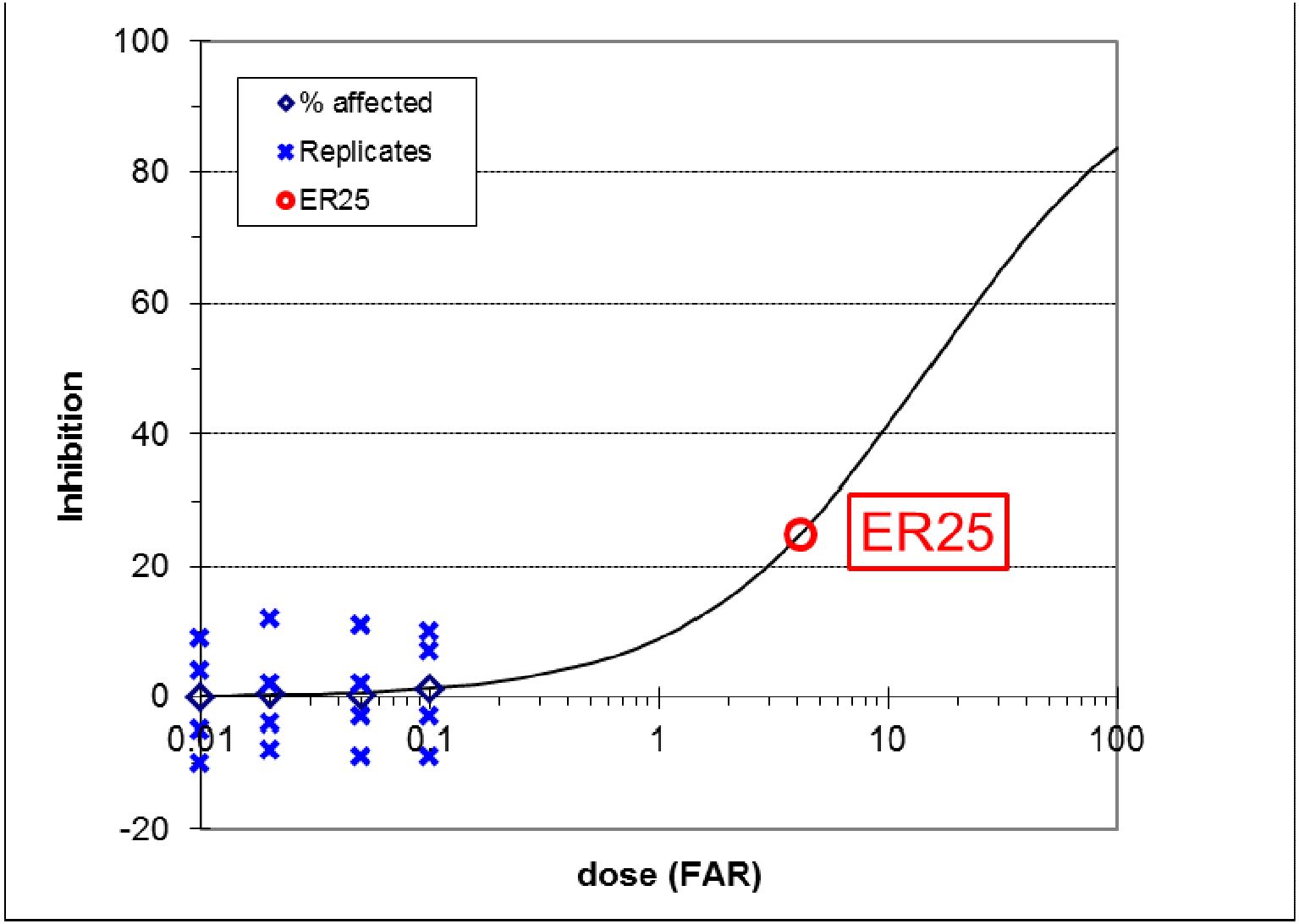
Extrapolation

Vegetative endpoints with sufficient test rates...



Extrapolation

...but these vegetative **extrapolations** were reported.



Extrapolation

After spotting this, we checked with one of the Authors, who confirmed that these were indeed mathematical extrapolations, not just a typo.

What would you do with these values?

We decided to include them,

but only as greater-than values...

extrapolations ≤ 2 considered to be acceptable

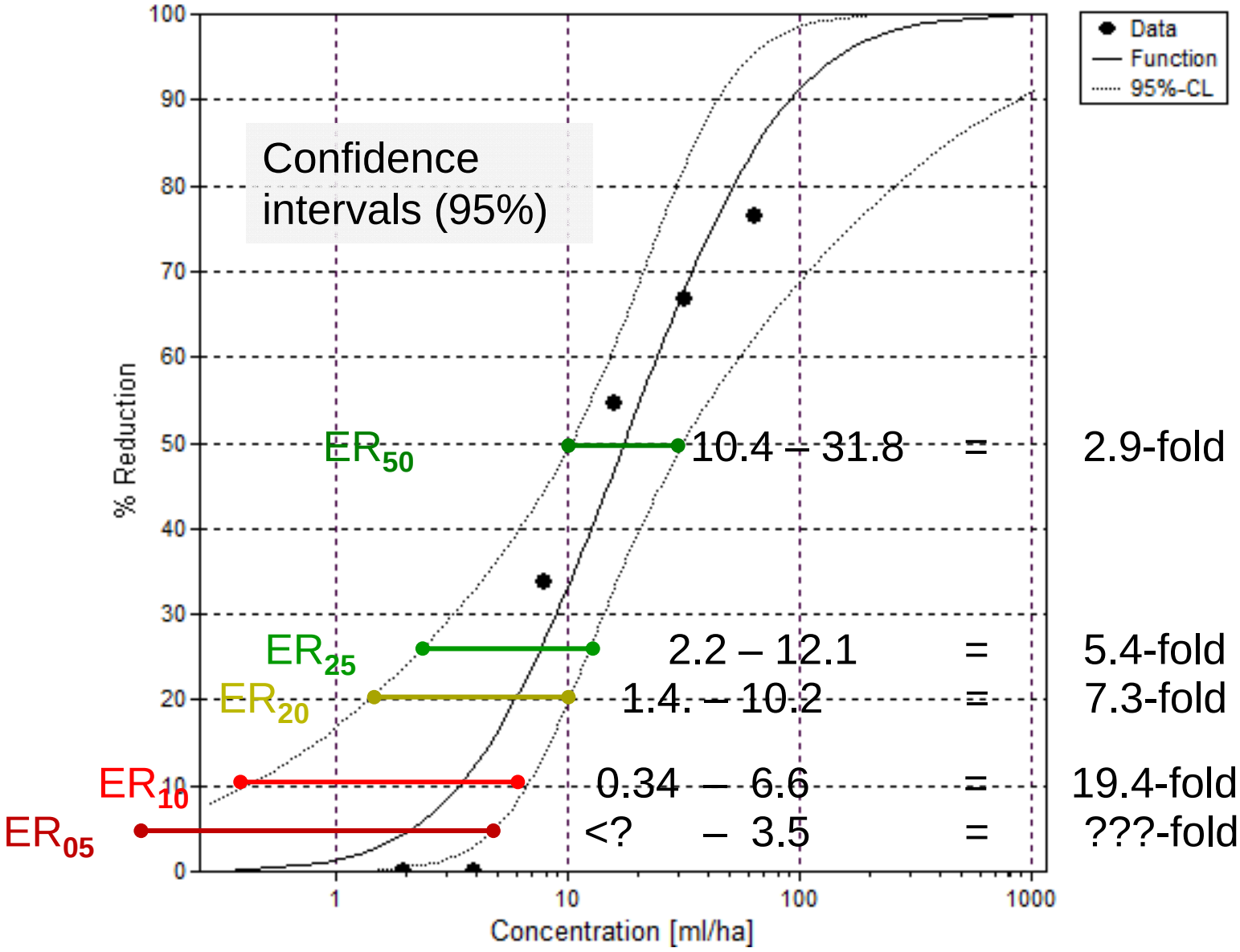
Selection of Effect level (ER_{10}, ER_{20}, ER_{25}...)

Problem:

Reliability of endpoints varies with effect level

Central estimates always more reliable than estimates at the tails of a distribution

Selection of Effect level (ER_{10}, ER_{20}, ER_{25}...)



Selection of Effect level (ER_{10}, ER_{20}, ER_{25}...)

Problem:

Reliability of endpoints varies with effect level

Endpoint	Confidence interval (95%)	Factor
ER_{50}	10.4 – 31.8	**2.9** - fold
ER_{25}	2.2 – 12.1	**5.4** - fold
ER_{20}	1.4 – 10.2	7.3 - fold
ER_{10}	0.34 – 6.6	**19.4** - fold
ER_{05}	< ? – 3.5	**> ??** - fold

Use ER_{50} (with assessment factor), or ER_{25} & AF
(also this would make US-EPA data available),
but any lower ERx would be unreasonably uncertain

SSDs and „Greater than-values“

Problem:

Endpoints with “>“ or “<“

5 options to handle data:

a) Exclude the species with censored endpoints
b) Include censored data, ignoring the “>“
c) Include censored data with a correction factor e.g. f = 2 (UBA 2014???)
d) Consider censored data for n, but discard numeric values (HC 2008)
e) Consider censored data with a MLE-method (bootstrapping, e.g. MOSAIC script 2014)

SSDs and „Greater than-values“

Data: (AMRAP Case C)

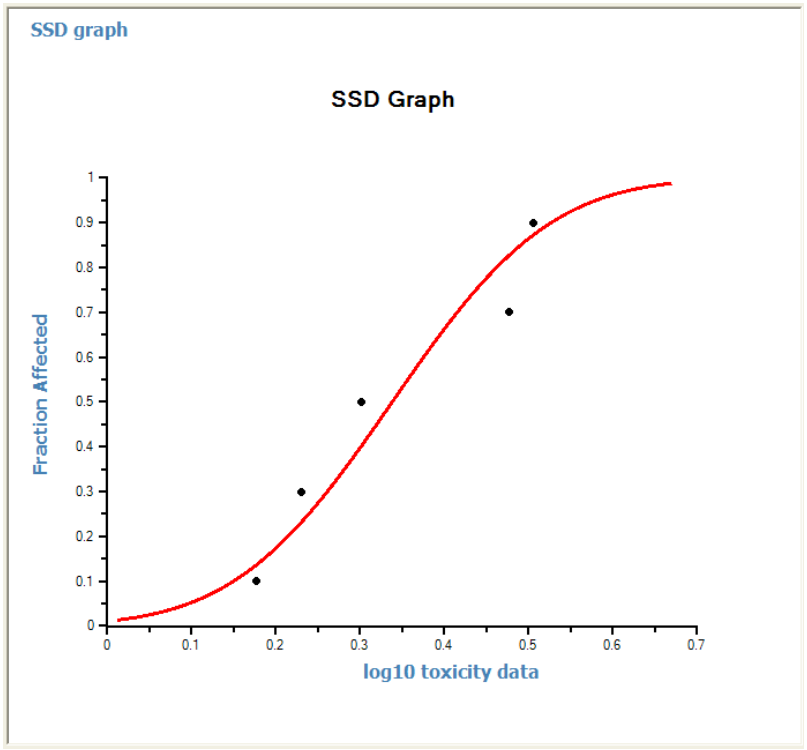
Input toxicity data

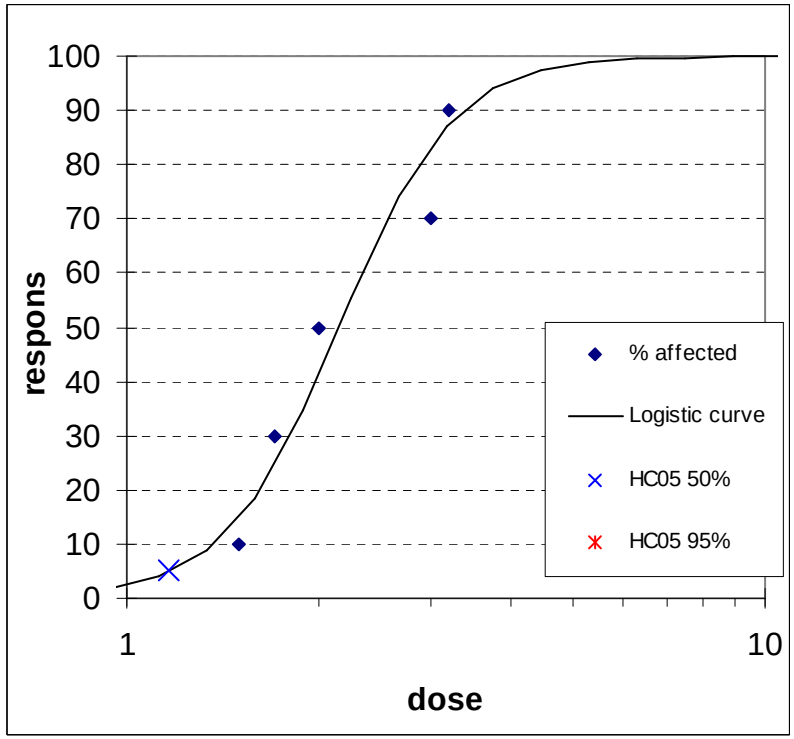
Data no.	Toxicity data	Label
1	1.5	Lemna gibba
2	1.7	Lagarosiphon major
3	2	Myriophyllum heterophyllu
4	3	Ceratophyllum demersum
5	3.2	Potamogeton pectinatus
6	3.4	Mentha aquatica
7	3.8	Valisneria americana
8	5	Elodea canadensis
9	5.1	Ranunculus lingula
10	5.3	Glyceria maxima

1.5	*Lemna gibba*
1.7	*Lagarosiphon major*
2	*Myriophyllum heterophyllur*
3	*Ceratophyllum demersum*
3.2	*Potamogeton pectinatus*
>3.4	*Mentha aquatica*
>3.8	*Valisneria americana*
>5.0	*Elodea canadensis*
>5.1	*Ranunculus lingula*
>5.3	*Glyceria maxima*

SSDs and „Greater than-values“

a) Exclude the species

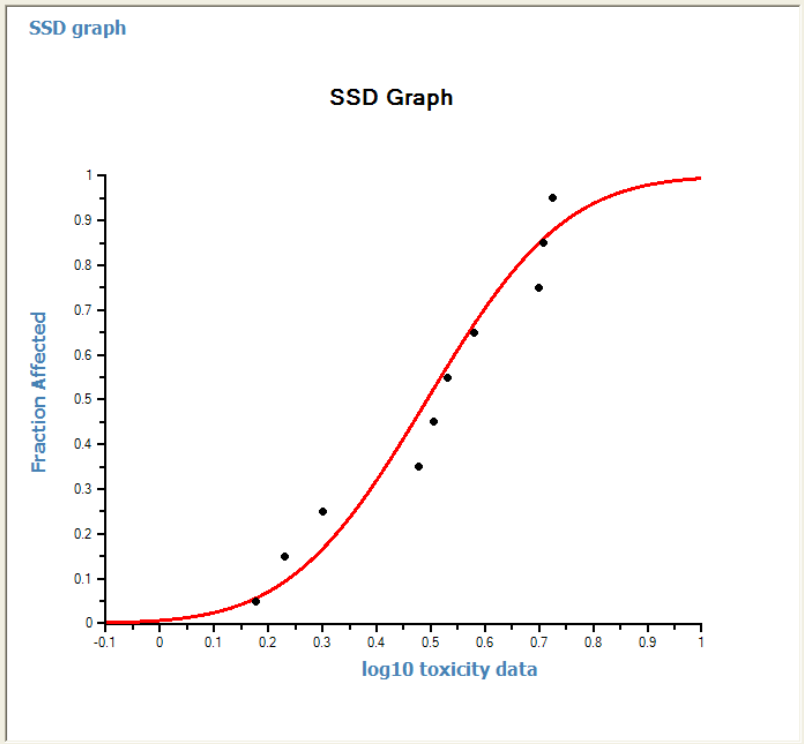


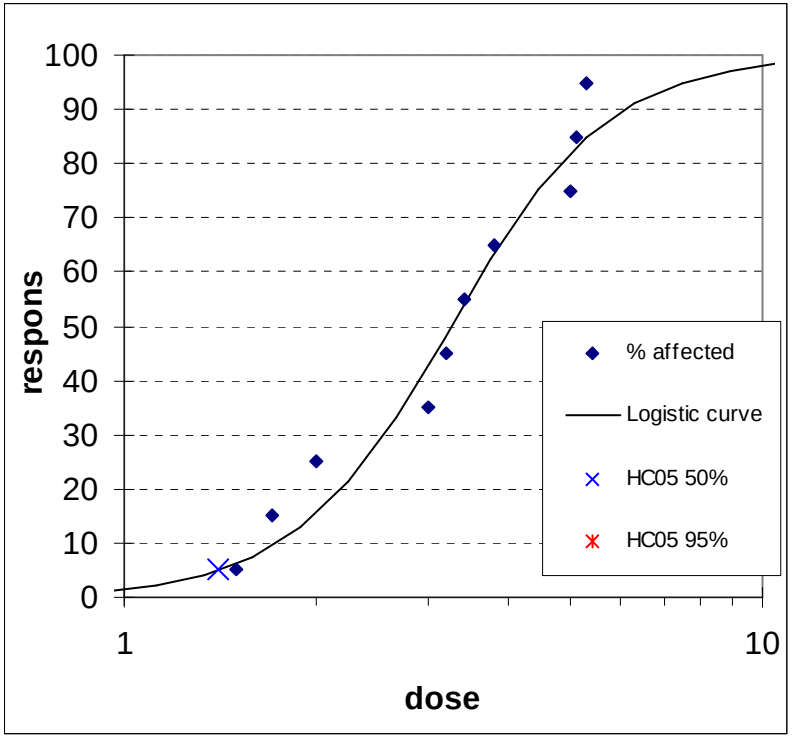


(no good idea)

SSDs and „Greater than-values“

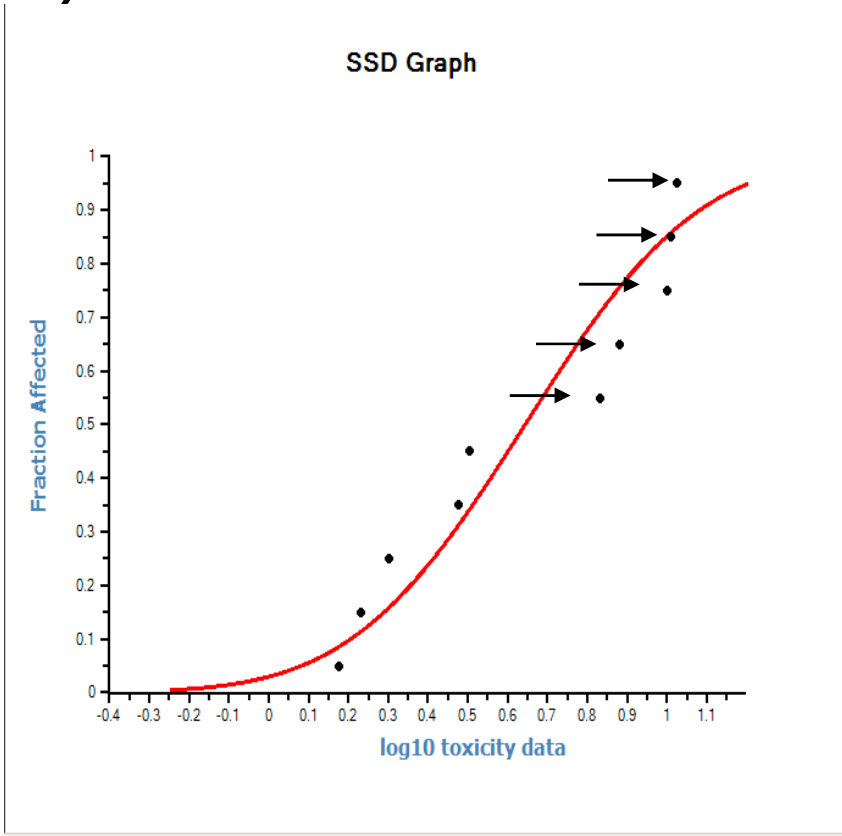
b) Include censored data, ignoring the “>“

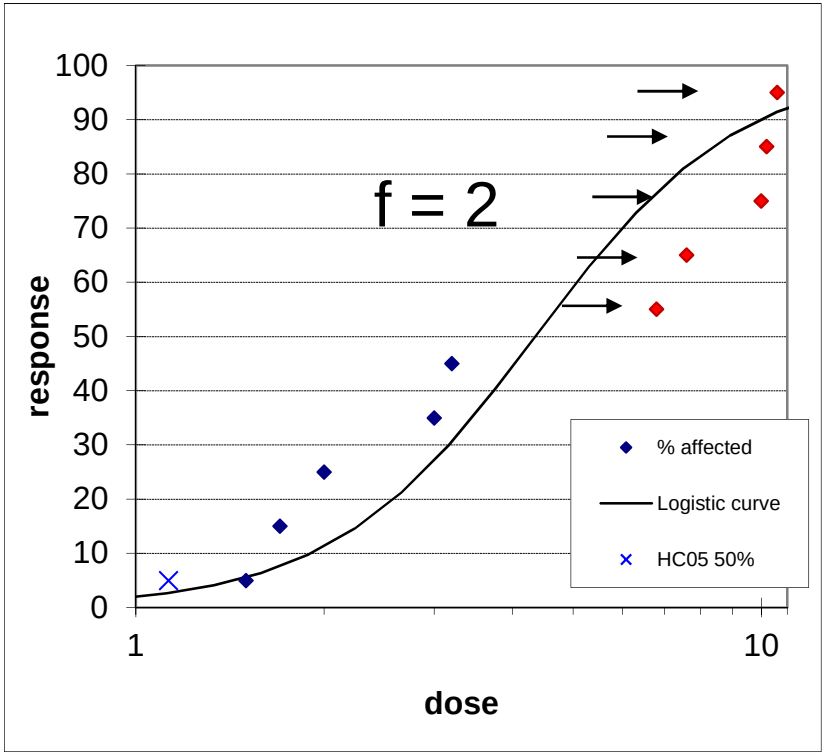




SSDs and „Greater than-values“

c) include data with a correction factor, e.g. f = 2



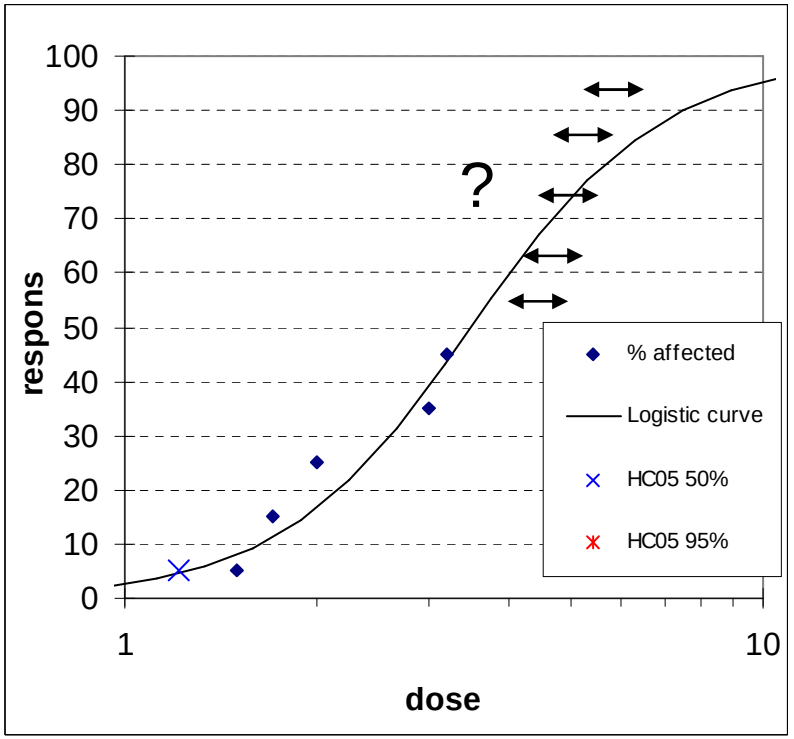


SSDs and „Greater than-values“

d) Consider data for n, but discard numeric value

?

Fundamentally not possible with ETX 2.0



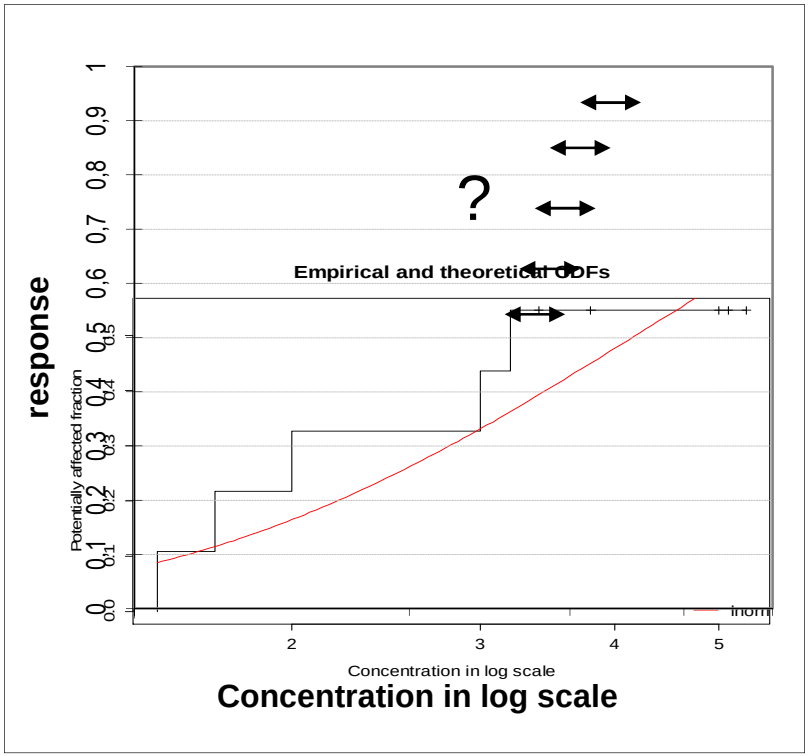
SSDs and „Greater than-values“

e) Consider censored data with maximum likelihood

e.g. MOSAIC script in R

again not

possible with ETX 2.0



MOSAIC-Online version and R-script (University Lyon)
using two custom libraries (fitdistrplus), (actuar)

Kon Kam King et al. (2014) MOSAIC_SSD: A new Web tool for SSD - Environ Toxicol Chem 33 (9) pp. 2133–2139

SSDs and „Greater than-values‘

Results:

Option	HC_{05} (50% prob)	HC_{50} (50% prob)
a) (5 species)	1.18	2.14
b) (10 species <> as values)	1.43	3.08
c) (10 species, <> with correction factor, e.g. f = 2	1.15 (ETX) 1.44 (LSQ)	4.40 (ETX) 4.35 (LSQ)
d) (10 species, 5 used for fitting)	1.25	3.49
e) (MLE bootstrap; 10 spec, 5 censored) (MOSAIC)	1.24	4.15

SSDs and „Greater than-values“

Recommendation?

a) and b): Ignore censored data, or include, ignoring < >:
most commonly used, (simplest, but least satisfying)

c): Consider censored data with a correction factor (f = 2)
also simplistic, but not generally accepted (UBA?)

d): Consider censored data for n, but discard numeric values (relatively straightforward, no tool available yet)

e): Consider via MLE-method, censored data affect distribution (MOSAIC, bootstrap), (complex, still not perfect: Treatment of less-than values problematic; HC_5 may get unreasonably low)

Fin...

Thank you!