

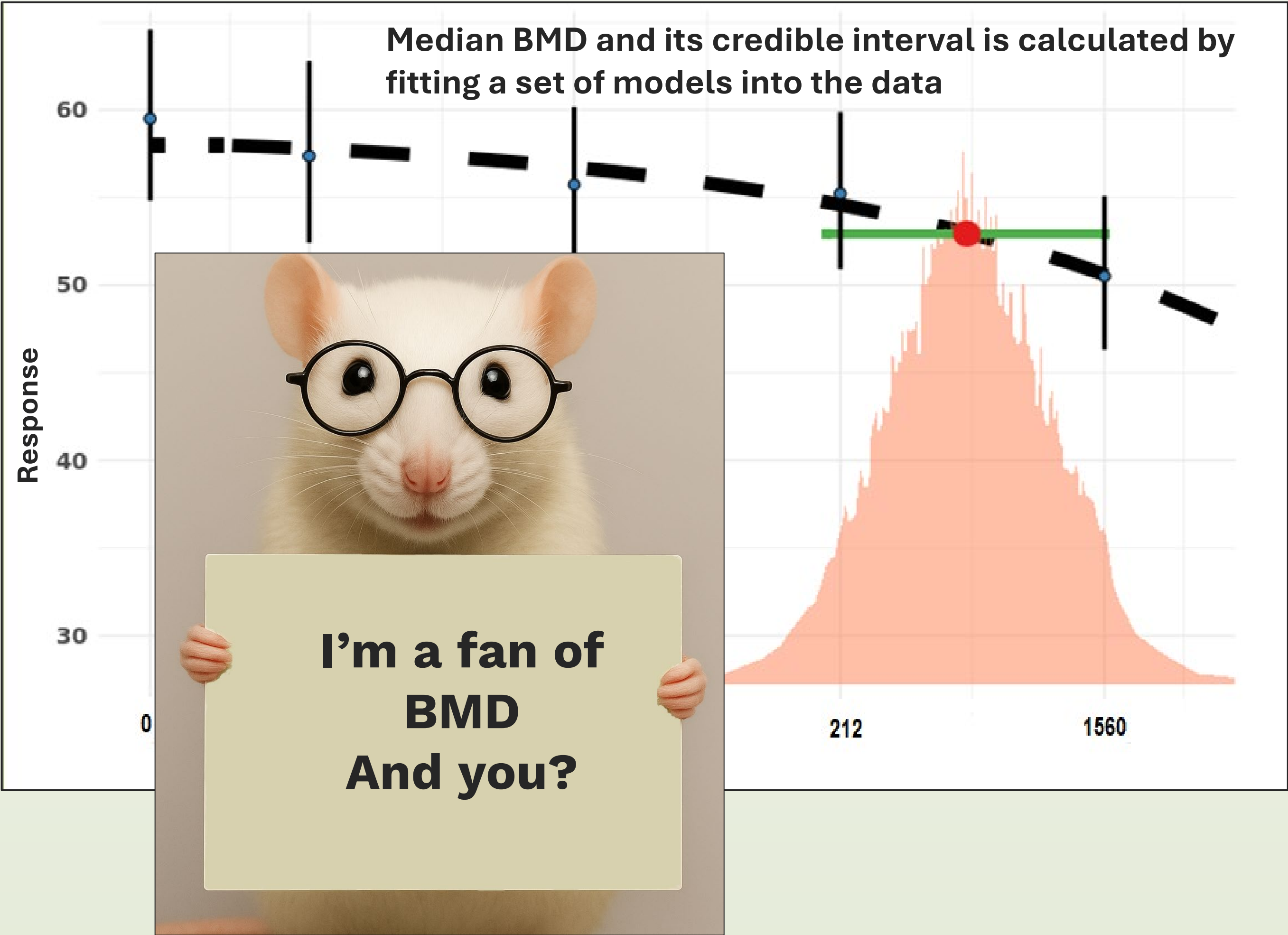
Benchmark Dose modelling for endpoint derivation

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Benchmark Dose (BMD) modelling

- 🐭 Is a statistically advanced approach used in environmental and human risk assessment.
- 🐭 The aim is to determine a dose-level that triggers a measurable change in a relevant toxicological parameter following exposure to a chemical.
- 🐭 In EFSA 2023 Guidance on risk assessment for Birds and Mammals recommends BMD for setting reproductive toxicity endpoints instead of No-Observed-Adverse-Effect-Levels (NOAEL)
- 🐭 The default response level (BMR) for reproductive wildlife risk assessment is 10%.



BMD analyses in real cases

The median BMD10 were calculated for the ecologically relevant parameters of several active substances. The Guidance on the Use of the Benchmark Dose Approach in Risk Assessment (EFSA, 2022) was followed, and the results were obtained using EFSA's web tool for Bayesian BMD analysis. Results show:

Risk assessment for humans

- 🐭 In the case of human risk assessment, the BMR level must be justified
- 🐭 The lower limit of the credible interval should be used instead of the median

Risk assessment for wild birds and mammals

- 🐭 Many toxicological studies are designed only to derive NOAELs
- 📊 Not all extracted data sets were suitable for the BMD approach but in most of the cases we were able to calculate BMDs that were higher than the NOAELs
- 📊 In some cases, informative priors have been used to derive our results, as permitted by the Bayesian approach.
- 📊 Based on scientific literature, the 10% default BMR could be discussed

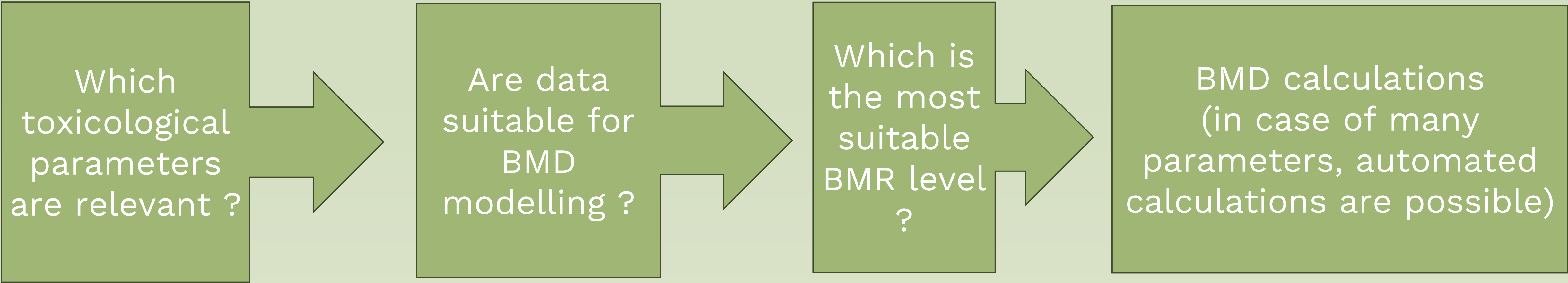
Results

Active substance	EU agreed endpoint (mg a.s/kg bw/d)	Toxicological parameter	BMD10L*	BMD10**
A	NOAEL= 6.2	Body weight of pups	43	49.2
		Total number of pups born	46.6	91
		Number of pups born alive	45	97.2
		Number of pups per litter	26.9	53.6
B	NOAEL= 19.5	Body weight of males (P generation)	705	1237
		Body weight of females (P generation)	645	1326
		Body weight males (F1 generation)	267.2	632.1
C	NOAEL= 23	Body weight of pups (F1a generation)	99.7	160.4
		Body weight of pups (F1b generation)	133.2	246.1
		Body weight of pups (F2a generation)	95.1	205.4
		Body weight of pups (F2b generation)	121.4	246.3
D	NOAEL=4.2	Body weight of pups (F2 generation)	17.6	19.2

***BMD10L**: The lower bound of the Benchmark Dose credible interval
Units: mg a.s./kg bw/d

****BMD10**: The median Benchmark Dose for a 10% change in the response
Units: mg a.s./kg bw/d

Conclusion



If you have any questions, are interested in calculating BMDs for your substance portfolio, or need help, please feel free to contact us

