Tutorial for CEBS Benchmark Dose Tool

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Function

The Benchmark Dose application enables users to review dose response relationships in NTP studies with statistically significant neoplastic and non-neoplastic findings. The analysis uses the multistage model for benchmark dose (BMD) analysis of dichotomous data. Original and poly3 adjusted (weighted) datasets are analyzed for studies containing 3 or more dose groups fitted both with and without the highest dose group.

The CEBS Benchmark Dose Tool has 3 steps:

- Select study
- Select histopathology finding
- Review results

From the CEBS Homepage (http://tools.niehs.nih.gov/cebs3/ui/), select the Look Up BMD Values button.

1) Select Study

- Browse list of studies for which BMD has been calculated
- Search / Filter the study selection table using the study parameter search boxes at the top of each column
  Note: *The filter uses exact match search criteria and is therefore case sensitive.*
- Click the 'View' button to review results

- Sort columns by clicking on the parameter of interest in the header row
- Resize columns by dragging the borders

View	CAS Number	Chemical Name	Route	NTP Study Number	Study Length	Species
	100-01-6	p-Nitroaniline	GAVAGE	C60786B	CHRONIC	Mouse
	100-02-7	p-Nitrophenol	DERMAL_SOLUTION	C55992B	CHRONIC	Mouse
	100-41-4	Ethylbenzene	RESPIRATORY EXPOSURE WH...	C56393B	CHRONIC	Mouse
	100-41-4	Ethylbenzene	RESPIRATORY EXPOSURE WH...	C56393B	CHRONIC	Rat
	100-52-7	Benzaldehyde	GAVAGE	C56133	CHRONIC	Mouse
	100-52-7	Benzaldehyde	GAVAGE	C56133	CHRONIC	Rat
	10026-24-1	Cobalt sulfate heptahydrate	RESPIRATORY EXPOSURE WH...	C61530B	CHRONIC	Mouse

2) Select Histopathology Findings

Review neoplastic and non-neoplastic findings for the selected study. Number of doses administered, number of models available and the number of models fitted to the data are shown.

- Click on a row with the finding of interest to review results
- Sort columns by clicking on the header row
- Resize columns by dragging the borders

Findings

Sex	Organ	Morphology	No. Doses	Models Ava	Models Fitt
FEMALE	Thyroid Gland: C-C	Adenoma	3	2	1
FEMALE	Thyroid Gland: C-C	Carcinoma	3	2	0
FEMALE	Thyroid Gland: C-C	Carcinoma or Aden	3	2	1
FEMALE	Thyroid Gland: Foll	Cyst	3	2	0
FEMALE	Thyroid Gland: Foll	Adenoma	3	2	2
FEMALE	Thyroid Gland: Foll	Carcinoma	3	2	2
FEMALE	Thyroid Gland: Foll	Carcinoma or Aden	3	2	2
FEMALE	Trachea	Inflammation Chroni	3	2	0
FEMALE	Urinary Bladder: Mu	Hyperplasia	3	2	0
FEMALE	Uterus	Cyst	3	2	2
FEMALE	Uterus	Hemorrhage	3	2	2
FEMALE	Uterus	Hydrometra	3	2	0
FEMALE	Uterus	Hyperplasia Cystic	3	2	0
FEMALE	Uterus	Polyp Stromal	3	2	2
FEMALE	Uterus	Sarcoma Stromal or	3	2	2
FEMALE	Zymbal's Gland	Squamous Cell Care	3	0	0
MALE	Adrenal Cortex	Adenoma	3	2	0
MALE	Adrenal Gland: Cor	Accessory Adrena	3	2	2

Note: Findings are displayed regardless of the number of fitted models.

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4) Review Results

For the selected finding review the Incidence Data table:

- Doses administered
- Number of subjects (unweighted) in the dose group
- Number of subjects (unweighted) with the selected finding
- Poly3 adjusted (weighted) number of subjects in the dose group
- Poly3 adjusted (weighted) number of subjects with the selected finding

Incidence Data				
Doses (mg/kg)	No. Subjects	No. Findings	No. Subjects:	No. Findings:
0	50	0	44.13	0
200.	4	2	4.00	2
400.	50	1	38.88	1

For the selected finding, review the Model Parameter table containing parameters for both unweighted and poly3 adjusted data.

Model Parameters		
Parameter	Unweighted	Poly3 Adjusted
Dose Groups	3	3
Fit P-value	0.0928	0.1294
AIC	49.665	46.9393
log Likelihood	-22.8325	-21.4696
BMD	-9999	971.557
BMDL	-9999	250.868
BMR	0	0.14666
Scaled Residual	-9999	-0.322
Background	0.0461445	0.0518484
Beta1	0.0000612	0.0001084
Beta2	0.0	0.0
Valid Model	False	True
View Graph	Unweighted	Poly3 Adjusted

- Select desired graph in 'View Graph' to view graphical representation of the fitted model
  Note: *'View Graph' is available for selection regardless of whether a benchmark dose was calculated*
- Graph can be resized by dragging the corner of the window

5) Example Section

This example should demonstrate the type of questions that can be answered using tis workflow. For this example, we will ask: What is the calculated benchmark dose for uterine endometrium inflammation for Toluene in mice?

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a) Select Study

First, search for 'Toluene' in the Chemical name field. This field is case sensitive. Of the two options, select the mouse study, by clicking on the View button.

b) Select Histopathology Findings

Because we are interested for findings in the endometrium, we will need to locate the Uterus in the Organ column. Scroll down to locate the Uterus: Endometrium, or sort the Organ column in reverse alphabetical order by clicking the Organ header twice. Click to select the Uterus: Endometrium row with the morphology of Inflammation Acute. There are 4 fitted models for that finding.

c) Review Findings

Once that finding has been selected, Incidence data and model parameters will be displayed. Details of note for this finding could include: none of the models have a significant fit, the benchmark dose of the models is very different with and without the high dose, and the model with the best fit and lowest AIC is the unweighted no high dose model.

6) Additional Instructions/Information

1) Flash movie running flex code for CEBS indicates a software platform is being used to create graphics or texts for CEBS

2) CEBS data may be cited by navigating to the CEBS Support page, and selecting the Citing CEBS document under FAQs. Here, instructions can be found on citing NTP Data as well as non-NTP data in CEBS.