

Table 1

Transcriptomic and apical BMDs, in mg/kg. Lowest apical BMDs for both non-neoplastic and neoplastic endpoints are shown. The apical BMD used for comparison to transcriptomic BMDs was the lowest of the non-neoplastic and neoplastic BMDs. That value and the lowest BMDL are in **bold**. MTE is milk thistle extract. Chemicals used in the analysis in the development of the EPA method are underlined.

Chemical	DTT BMD	DTT BMDL	EPA BMD	EPA BMDL	Non-neoplastic			Neoplastic			Note(s)
					Endpoint	BMD	BMDL	Endpoint	BMD	BMDL	
<u>α,β-thujone</u>	125	53.8	10.3	0.892	Kidney mineralization	3.17	2.29	Preputial gland adenoma or carcinoma	22.89	16.57	1
<u>Acrylamide</u>	0.495	0.281	0.499	0.196	Peripheral nerve (sciatic) axon degeneration	0.61	0.43	Thyroid gland follicular cell adenoma or carcinoma	1.45	0.89	1
<u>BDCA</u>	1.41	0.664	1.61	0.799	Bone marrow angiectasis	2.3	1.87	All organs malignant mesothelioma	4.1	3.32	1
BPAF	26.6	5.79	19.2	5.75	F2 absolute dorsolateral prostate weight	39.5	27.8	NA	NA	NA	5
<u>Coumarin</u>	13.5	3.08	4.69	1.57	Liver necrosis	5.85	4.85	Kidney renal tubule adenoma	69.35	44.64	1
<u>DE-71</u>	0.0843	0.0252	0.939	0.496	Liver hepatocyte hypertrophy	0.15	0.11	Pituitary gland (pars distalis) adenoma	6.68	4.53	1
<u>DEHP</u>	10.6	3.41	22.3	14.0	Bone marrow hypercellularity	83.1	39.8	Pancreatic acinar adenoma or carcinoma	31.2	20.3	6

					seminiferous tubules						
<u>EE</u>	2.05 x 10 ⁻⁴	1.51 x 10 ⁻⁴	2.41 x 10 ⁻⁴	2.86 x 10 ⁻⁵	Mammary gland alveolar hyperplasia	0.00069	0.00047	NA	NA	NA	1
Fenofibrate	0.630	0.216	2.01	0.762	78 week Liver weight	0.1	0.052	NA	NA	NA	10
<u>Furan</u>	0.581	0.162	0.546	0.306	Liver cholangiofibrosis	0.1	0.09	Mononuclear cell leukemia	0.47	0.29	1,2
Ginseng	242	114	71.7	46.8	Relative kidney weight	5000	4147	NA	NA	NA	3
<u>HCB</u>	0.209	0.148	0.0994	0.0285	Chronic nephrosis (severe)	0.59	0.35	Adrenal pheochromocytoma	1.23	0.60	1
MTE	842	268	99.3	39.9	Platelet count	745	373	NA	NA	NA	4
<u>Methyleugenol</u>	13.8	5.70	43.7	10.6	Liver eosinophilic focus	13.14	10.01	Liver hepatocellular adenoma or carcinoma	12.02	9.90	1
<u>PFOA</u>	0.0434	0.023	0.0456	0.0133	Liver hepatocyte hypertrophy	0.5	0.41	Pancreas adenoma	0.73	0.57	1
<u>Pulegone</u>	10.7	2.53	23.9	5.04	Nose olfactory epithelium degeneration	14.02	9.47	NA	NA	NA	1
<u>TBBPA</u>	35.5	6.85	13.5	1.76	Total thyroxine	73.0	61.4	NA	NA	NA	8
<u>TCAB</u>	5.14	0.692	9.08	1.56	Forestomach epithelium hyperplasia	2.86	2.13	Lung cystic keratinizing epithelioma	5.10	4.21	1
<u>TCPP</u>	35.0	6.36	33.1	8.23	Lung granulomatous focal inflammation	223.6	58.8	NA	NA	NA	7
Triclosan	2.95	0.413	8.59	3.41	Total thyroxine	14.5	7.23	NA	NA	NA	9

Source/notes

1. BMDs and BMDLs are from Gwinn et al. 2020 Supplemental Material: Table 5 (non-neoplastic) and Table 6 (neoplastic). Values shown are the lowest BMD in each table for the chemical and its associated BMDL. Chronic (or subchronic) Study Maximum Dose are from Gwinn 20 Table 3.
2. Gwinn 2020 reports 2 different studies for furan, with maximum doses 2 and 8 mg/kg.
3. NTP 90-day gavage study of ginseng, NTP TR 567. BMDs were calculated using EPA BMDS online (<https://bmdsonline.epa.gov/>). BMD is > maximum dose. BMD is BMD₁₀ (10% change in response). BMD was over the maximum dose and was set to the maximum dose for comparison with transcriptomic BMDs.
4. NTP 3-month feed study of milk thistle extract, NTP TR 565. BMDs were calculated using EPA BMDS online (<https://bmdsonline.epa.gov/>). Doses were derived from feed dose in ppm and data on feed consumption. BMD is BMD₁₀ (10% change in response).
5. NTP modified one-generation study of bisphenol AF, NTP DART 08. BMDs were calculated using EPA BMDS online (<https://bmdsonline.epa.gov/>). Doses were derived from feed dose in ppm and data on feed consumption. Maximum dose given is the highest dose for which there were confirmed pregnant females. BMD is BMD₁₀ (10% change in response).
6. Non-neoplastic BMD is from NTP Technical Report on the Toxicology and Carcinogenesis Studies of Di(2-ethylhexyl) Phthalate (CASRN 117-81-7) Administered in Feed to Sprague Dawley (Hsd:Sprague Dawley® SD®) Rats: Technical Report 601. (<https://www.ncbi.nlm.nih.gov/books/NBK579343/> doi: 10.22427/NTP-TR-601). Neoplastic BMD is from analysis of NTP data in Table 6-4 of EPA document 'Scientific Studies Supporting Development of Transcriptomic Points of Departure for EPA Transcriptomic Assessment Products', [ps://doi.org/10.23645/epacomptox.25365550](https://doi.org/10.23645/epacomptox.25365550) March 2024. Maximum dose 602 is from EPA document, 674 from Gwinn 2020. BMD is BMD for 10% extra risk.

7. From analysis of NTP data in Table 6-2 of EPA document ‘Scientific Studies Supporting Development of Transcriptomic Points of Departure for EPA Transcriptomic Assessment Products’, [ps://doi.org/10.23645/epacomptox.25365550](https://doi.org/10.23645/epacomptox.25365550) March 2024. BMD is BMD for 10% extra risk.
8. NTP TR-587, 3-month gavage study of TBBPA, table F1. BMDs were calculated using EPA BMDS online (<https://bmdsonline.epa.gov/>). BMD is BMD₁₀ (10% change in response).
9. Zorrilla 2009, TOXICOLOGICAL SCIENCES 107(1), 56–64 (2009), doi:10.1093/toxsci/kfn225. BMD is BMD₂₀ (20% change in response).
10. Price SC, Hinton RH, Mitchell FE, Hall DE, Grasso P, Blane GF, Bridges JW. Time and dose study on the response of rats to the hypolipidaemic drug fenofibrate. Toxicology. 1986 Oct;41(2):169-91. doi: 10.1016/0300-483x(86)90198-8. PMID: 3764941.

Table 2. Number of GO terms with BMDs ranked ≤ 150 .

Chemical	Replicate	Tissue	DTT method	EPA method
BDCA	1	Kidney	150	147
BDCA	1	Liver	150	149
BDCA	2	Kidney	80	150
BDCA	2	Liver	21	150
BDCA	3	Kidney	14	150
BDCA	3	Liver	64	148
Furan	1	Kidney	150	151
Furan	1	Liver	151	150
Furan	2	Kidney	150	149
Furan	2	Liver	149	151
Furan	3	Kidney	11	151
Furan	3	Liver	150	152
PFOA	1	Kidney	150	150
PFOA	1	Liver	150	153
PFOA	2	Kidney	150	150
PFOA	2	Liver	150	147
PFOA	3	Kidney	150	149
PFOA	3	Liver	150	155
TBBPA	2	Kidney	33	147
TBBPA	2	Liver	149	148
TBBPA	3	Kidney	0	142
TBBPA	3	Liver	150	150

Table 3. Concordance metrics for comparison of apical and transcriptomic BMDs. Metrics are as described in Table 2 of Weitekamp et al. 2025. Metrics were calculated using log10 of the apical and transcriptomic BMDs.

Method	Chemical set	Mean Absolute Difference	RMSD	Residual RMSE	Correlation	Rank Correlation	R ²	Mean Signed Difference
DTT	All chemicals	0.56	0.72	0.68	0.89	0.87	0.80	-0.22
EPA	All chemicals	0.61	0.75	0.74	0.87	0.88	0.76	-0.15
DTT	Chemicals from EPA analysis	0.43	0.57	0.53	0.91	0.86	0.84	-0.13
EPA	Chemicals from EPA analysis	0.51	0.59	0.56	0.90	0.89	0.82	-0.07