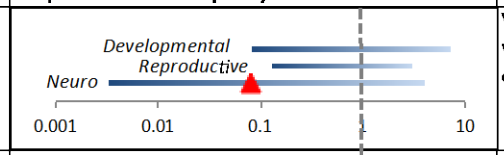
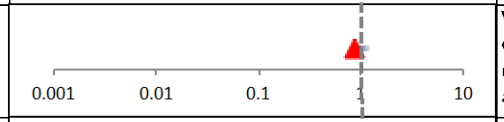
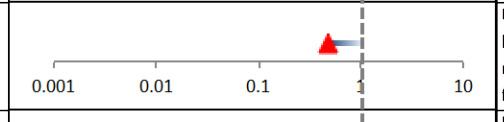
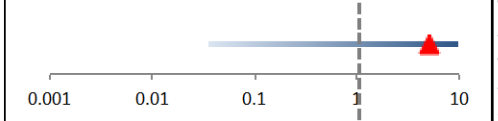
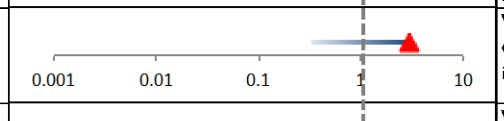
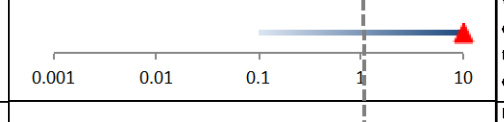
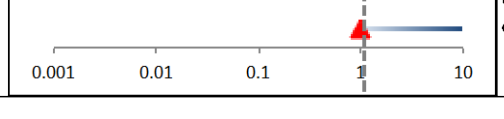
Table 1. Summary of Decisions Made for the Acrylamide Oral RfD Assessment

Decision Point	Range of Options[a] Fraction of Central Tendency Value (indicated by dashed line for quantitative decision points)	Range Reflects Uncertainty or Variability	Basis for Normalizing Values (e.g., central tendency or highest confidence value)	Decided Option	Confidence in Decision (Science- or Policy-based)
Data Set/Endpoint Selection[b]		Variation in the effective chronic NOAEL values (minimum and maximum values calculated from EPA Table 5-1)[c]	Mean effective chronic NOAEL value across candidate studies (6.1 mg/kg-day, based on data provided in EPA Table 5-1)	NOAEL for peripheral nerve effects (0.5 mg/kg-day; Johnson et al., 1986)	Medium/High confidence in key study. Selection of a sensitive endpoint and study reflects a policy decision to be protective
Causative Agent Determination (MOA)[b]	1) Neurotoxicity is attributed to acrylamide 2) Neurotoxicity is attributed to glycidamide	Uncertainty in MOA regarding causative agent	NA	Neurotoxicity is attributed to acrylamide	Not explicitly stated by EPA
Dose-Response Model Selection[b]		Variation in POD across models, based on minimum (1.2 mg/kg-day) and maximum (1.8 mg/kg-day) for alternative BMD values	Mean POD of acceptable models (1.4 mg/kg-day; EPA Table C-2)	Log-logistic model (1.2 mg/kg-day; EPA Table C-2)	High confidence (EPA Section 5.3.1.3). Selecting the best fitting model reflects a science-based decision to be predictive
Confidence Limit Selection		Uncertainty in model parameters for log-logistic model, based on BMDL10 (0.57 mg/kg-day) and BMD10 (1.2 mg/kg-day) from EPA Table C-2	POD = BMD (1.2 mg/kg-day; central tendency)	POD = BMDL (0.6 mg/kg-day; 95% lower confidence limit)	Not explicitly stated by EPA, however selecting lower confidence limit reflects a policy-based decision to be protective
Benchmark Response Rate Selection		Uncertainty in POD response, based on range defined by the BMDL01 (0.05 mg/kg-day) and BMDL10 (0.57 mg/kg-day) from EPA Table 5-3	BMR = 10% (BMDL10 = 0.57 mg/kg-day) for the default response rate for dichotomous data	BMR = 5% (BMDL05 = 0.27 mg/kg-day)	Not explicitly stated by EPA, however selecting a BMR value (5%) that is below the default value (10%) appears to reflect a policy-based decision to be protective
Interspecies Extrapolation (rat dose:HED)[b]		Variation across measured/ estimated adduct rates in rats and humans, based on the range rat dose:HED ratios for acrylamide (0.035-16.4) from EPA Table 5-6	Based on assumption of equivalent dose (i.e., rat dose:HED = 1)	Based on relative rates of AAVal formation in rats (27.4 uM-hr per mg) and humans (140.1 uM-hr per mg) the rat dose:HED = 5.1	Not explicitly state by EPA
Interspecies Variation (UFa)		Variation across species, based on a default range for toxicodynamics (3-fold in each direction, or 0.33-3)	UFa=1 (assume humans and rats are equally sensitive)	3 (assume that humans are 3x more sensitive than rats based on toxicodynamic factors)	Not explicity states by EPA, however selecting a value greater than 1 reflects a policy decision to be protective
Intraspecies Variation (UFh)		Variation across individuals, based on a default range of for toxicokinetics and toxicodynamics (10-fold in each direction, or 0.1-10)	UFh=1 (for average individual)	10 (assume some individuals are 10x more sensitive)	Not explicity states by EPA, however selecting a value greater than 1 reflects a policy decision to be protective
Duration Extrapolation (UFs); LOAEL-to-NOAEL Extrapolation (UFl); Database Uncertainty		Uncertainty in additional factors, based on default range (1-10)	UFs=1; UFl=1; UFd=1	1 for each (key study is chronic; BMD methods used; database is complete)	Medium/High confidence places in the toxicity database
Results			***Central Tendency Value = 3 mg/kg-day***	***RfD = 0.002 mg/kg-day***	***Medium/High confidence in RfD***

[a] The shading gradient of the lines indicates the direction of higher or lower conservatism. Values in the dark blue region result in lower RfDs than the light blue region.

[b] Decision points that are impacted by MOA conclusions are designated with an "*". Adopting of a different MOA conclusion may yield alternative results for these decision points

[c] Range of effective chronic NOAEL values for each endpoint: neurotoxicity (0.02-25 mg/kg-day); reproductive (0.79-18.7 mg/kg-day); developmental (0.5-45 mg/kg-day). Effective chronic NOAEL values reflect that application of default uncertainty factors of 10 each for use of a LOAEL and/or subchronic study for comparison purposes.

Table 2. Summary of Confidence and Importance of the Decisions Made in the RfD Assessment for Acrylamide

		Confidence in Decision[b]				
		High	**Medium**	**Low**	**Not Specified in EPA (2010)**	**Prioritization of Data Needs (Section Discussed)**
Importance of Decision to Assessment[a]	**High**	*Data set/endpoint selection*			*Causative agent determination (MOA)* *Interspecies extrapolation (rat dose:HED)* *Intraspecies variation (UFh)*	*1) Causative agent determination[c] (EPA Section 4.7.3.1.4)* *2) Data set (EPA Section 5.3.1.1)* *3) Interspecies extrapolation (EPA Section 5.3.1.4)*
	Medium				*Benchmark response rate selection* *Interspecies variation (UFa)* *Addition uncertainty factors (UFs, UFl, UFd)*	None identified by EPA
	Low	*Dose-response model selection*			*Confidence limit selection*	Not applicable

[a]Relative importance of decision to the assessment characterized using the range of options defined in Table 1, Column 2: High (>10-fold range defined by min and max); Medium (3- to 10-fold range); Low (<3-fold range).

[b]Confidence based on the designation in the last column of Table 1.

[c]Considered high since this decision impacts multiple steps in the assessment.

Shaded region of the table can be used to identify priority data needs for additional research/refined assessment