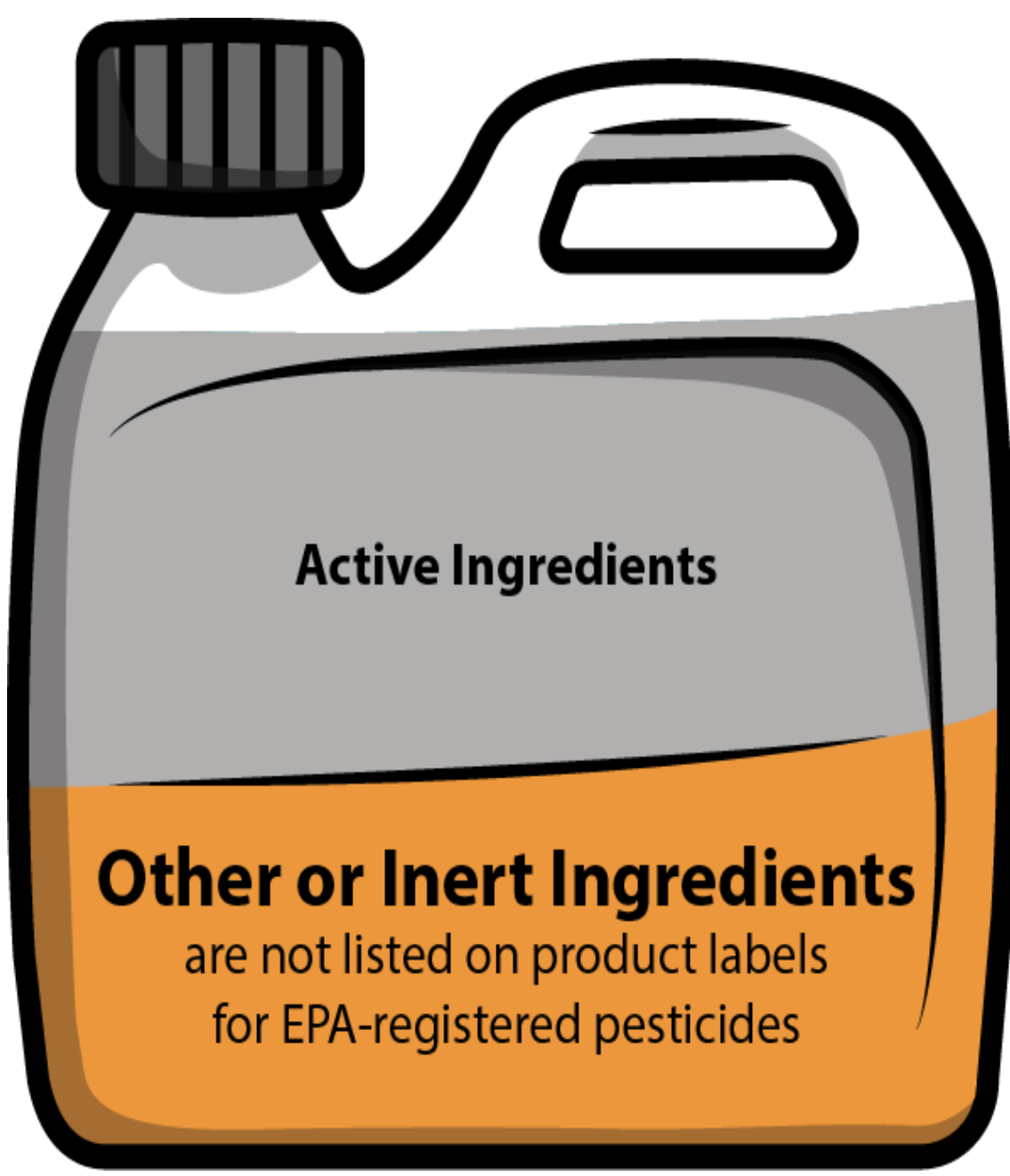


Tiered Approach for Exposure and Risk Assessment of Inert Ingredients in Pesticide Product Formulations

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EPA defines inert ingredients as *everything except the active ingredient(s)*

Inert ingredients (AKA co-formulants) include attractants, stabilizers, emulsifiers, surfactants, solvents, carriers, propellants, fragrances, dyes, etc.

The signal word on the label indicates the toxicity or hazard category of the formulated product, which refers to the active and all inert ingredients combined

If residues in food or feed are expected, either a tolerance or a tolerance exemption must be granted

TIER 1: EPA "I-DEEM" Approach

EPA's Inert Ingredient Assessment Branch (IIAB) has developed the I-DEEM approach for the assessment of inerts

Uses EPA's DEEM™ software Version 3.16 (R08) or 4.02 (R10)

All food residues (ppm) are pre-populated with the highest established tolerance value for registered pesticides

Adjustment Factor #2 (0.02x) must be calculated for the inert of interest depending upon Percent Inclusion in the formulation...

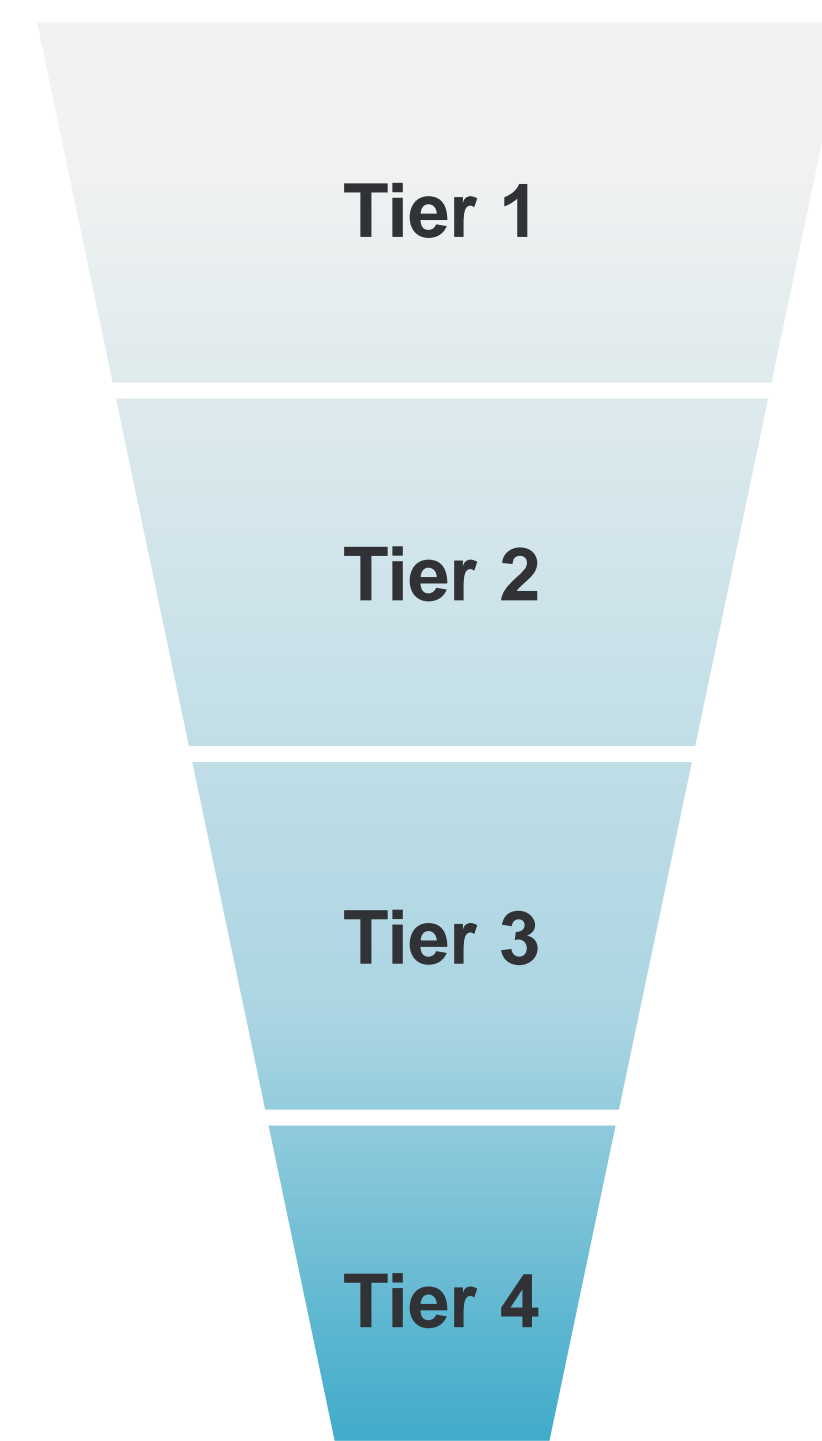
TIER 2: Upper-Bound Residue Estimates based upon crop yield

Crop	formulation No. appls.	rate (oz/A)	appt rate (lb/A)	A-245 Inert (wt%)	A-245 (lb/A)	USDA NASS Crop Yield (lbs/A)	Estimated A-245 mg/kg (ppm)		
cherry	fruit	3	4.8	0.90	1.0%	0.009	7,800	1.15	
artichoke	globe	3	4.8	0.9	1.0%	0.009	14,500	0.62	
herbs	basil	3	4.8	0.9	1.0%	0.009	no data	use celery	
herbs	chives	3	4.8	0.9	1.0%	0.009	no data	use celery	
brassica	broccoli	4	4.8	1.2	1.0%	0.012	15,780	0.76	
brassica	cauliflower	4	4.8	1.2	1.0%	0.012	19,940	0.60	
brassica	cabbage	4	4.8	1.2	1.0%	0.012	40,010	0.30	
brassica	mustard greens	3	4.8	0.9	1.0%	0.009	no data	use spinach	
fruiting veg	pepper	3	4.8	0.9	1.0%	0.009	33,990	0.26	
fruiting veg	tomato	3	4.8	0.9	1.0%	0.009	81,140	0.11	
cucurbits	squash	3	4.8	0.9	1.0%	0.009	17,600	0.51	
cucurbits	cantaloupe	3	4.8	0.9	1.0%	0.009	no data	use cuke	
cucurbits	cucumber	3	4.8	0.9	1.0%	0.009	15,030	0.60	
wine (import)	wine								
leafy veg	celery	3	4.8	0.9	1.0%	0.009	68,100	0.13	
leafy veg	head lettuce	3	4.8	0.9	1.0%	0.009	37,630	0.24	
leafy veg	leaf lettuce	3	4.8	0.9	1.0%	0.009	37,630	0.24	
leafy veg	spinach	3	4.8	0.9	1.0%	0.009	14,960	0.60	
pome fruit	apple	3	4.8	0.9	1.0%	0.009	28,500	0.32	
pome fruit	pear	3	4.8	0.9	1.0%	0.009	36,000	0.25	
tree nuts	almond nutmeat	3	4.8	0.9	1.0%	0.009	2,280	3.95	over-estimate (whole nut)
tree nuts	pecan	3	4.8	0.9	1.0%	0.009	no data	use almond	

Tiered Approach to Estimating Residues

Four approaches were used to provide a range of Inert Ingredient residue estimates for use in the dietary assessments

- I-DEEM (EPA):** Most conservative. Provides screening-level estimates for inerts based upon industry "percent inclusion" statistics
- Crop Yield:** assumes that all inert ingredient applied to an acre of crop land is taken up into all of the crop harvested from that acre
- MRL proportional:** assumes that inert residues would be proportional to an active ingredient MRL
- Refined residue estimate:** assumes the inert ingredient residue would be proportional to active ingredient residues



TIER 3: Estimated MRL-level residues

Crop	Active Ingrid. MRL (ppm)	Inert:Active (ratio)	estimated Inert MRL (ppm)	<0.01 ppm ?	
cherry	fruit	0.100	0.20	0.020	no
artichoke	globe	0.060	0.20	0.012	no
herbs	basil	0.070	0.20	0.014	no
herbs	chives	0.020	0.20	0.004	yes
brassica	broccoli	0.050	0.20	0.010	no
brassica	cauliflower	0.050	0.20	0.010	no
brassica	cabbage	0.050	0.20	0.010	no
brassica	mustard greens	0.050	0.20	0.010	no
fruiting veg	pepper	0.020	0.20	0.004	yes
fruiting veg	tomato	0.020	0.20	0.004	yes
cucurbits	squash	0.020	0.20	0.004	yes
cucurbits	cantaloupe	0.020	0.20	0.004	yes
cucurbits	cucumber	0.020	0.20	0.004	yes
wine (import only)	wine	0.030	0.20	0.006	yes
leafy veg	celery	0.100	0.20	0.020	no
leafy veg	head lettuce	0.100	0.20	0.020	no
leafy veg	leaf lettuce	0.100	0.20	0.020	no
leafy veg	spinach	0.100	0.20	0.020	no
pome fruit	apple	0.025	0.20	0.005	yes
pome fruit	pear	0.025	0.20	0.005	yes
tree nuts	almond hull	0.200	0.20	0.040	no
tree nuts	almond nutmeat	0.020	0.20	0.004	yes
tree nuts	pecan	0.020	0.20	0.004	yes

Estimated inert residues would be proportional to active ingredient MRLs:
 $1.0\% / 5.0\% = 0.2x \text{ ratio}$

Inert residues of >0.01 ppm would not be exempted from the establishment of a tolerance

TIER 4: Lower-Bound Residue Estimates

Crop	Maximum Active Ingrid. Residue (ppm)	Inert:Active ratio	Maximum Estim. Inert Residue (ppm)	<0.01 ppm ?	
cherry	fruit	0.068	0.20	0.014	no
artichoke	globe	0.037	0.20	0.007	yes
herbs	basil	0.047	0.20	0.009	yes
herbs	chives	0.009	0.20	0.002	yes
brassica	broccoli	0.027	0.20	0.005	yes
brassica	cauliflower	0.015	0.20	0.003	yes
brassica	cabbage	0.137	0.20	0.027	no
brassica	mustard greens	0.084	0.20	0.017	no
fruiting veg	pepper	0.005	0.20	0.001	yes
fruiting veg	tomato	0.005	0.20	0.001	yes
cucurbits	squash	0.020	0.20	0.004	yes
cucurbits	cantaloupe	0.008	0.20	0.002	yes
cucurbits	cucumber	0.021	0.20	0.004	yes
wine (import only)	wine	0.019	0.20	0.004	yes
leafy veg	celery	0.161	0.20	0.032	no
leafy veg	head lettuce	0.173	0.20	0.035	no
leafy veg	leaf lettuce	0.078	0.20	0.016	no
leafy veg	spinach	0.033	0.20	0.007	yes
pome fruit	apple	0.009	0.20	0.002	yes
pome fruit	pear	0.008	0.20	0.002	yes
tree nuts	almond hull	0.105	0.20	0.021	no
tree nuts	almond nutmeat	0.003	0.20	0.001	yes
tree nuts	pecan	0.003	0.20	0.001	yes

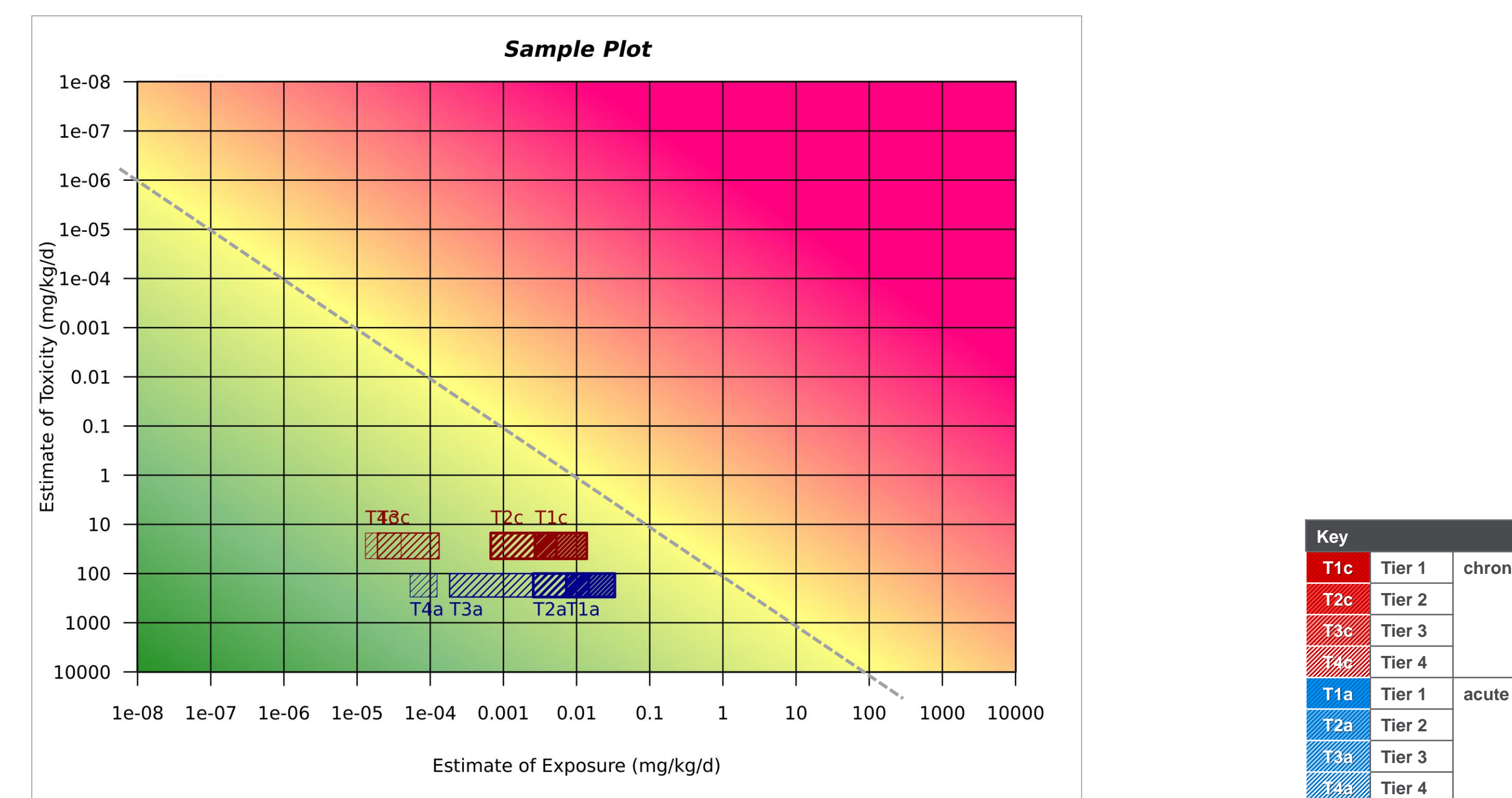
Assumes that inert residues would be proportional to field trial residues for the active ingredient:
 $0.2x \text{ ratio}$

Again, it is unlikely that inert residues exceeding 0.01 ppm for a given crop would be considered for exemption from a tolerance

Case Study and Background

- Company XYZ, Inc. intends to add a new inert ingredient called "A-245" at up to 1.0% by weight to an already registered crop protection product, which contains an active ingredient (a.i.) at up to 5.0% by weight
- There are no residue data for A-245 on any food crop
- The inert-to-active ratio (1:5) can be used to develop "tiered" residue estimates
- Because it has many non-food uses, A-245 has an extensive, publicly available toxicology database (i.e., SDS)

All scenarios, combined – 100X UF



All scenarios, combined – 1000X UF (i.e., lack of a NOAEL)

