Draft Evaluation of Chlorpyrifos as a Toxic Air Contaminant

Department of Pesticide Regulation
Human Health Assessment Branch

Scientific Review Panel Meeting
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Presenting today

Shelley DuTeaux, PhD MPH – Branch Chief, Human Health Assessment

Terrell Barry, PhD – Lead Exposure Assessor

Svetlana Koshlukova, PhD – Senior Toxicologist, Risk Assessment

Eric Kwok, PhD, DABT – Senior Toxicologist, Exposure Assessment

Marylou Verder-Carlos, DVM – Assistant Director

California Environmental Protection Agency
dpr Department of Pesticide Regulation

Today's Presentation

- Opening Statement
- Exposure Assessment Charge Questions 4 &5
- Revisit Previous Charge Questions
- Potential Approach for Next Draft
- Open Discussion

Routes and Duration	DPR TAC 10% RBC AChEI		Published DNT studies		USEPA Nov 2016 HHRA	
	Human		Animal		Human	
	PBPK-PD PoD	RfD or RfC (PoD/UF of 100)	PoD	RfD or RfC (Fold difference compared to DPR value; ↓=lower)	PBPK-PoD (0.004 ug/L CPF in plasma)[d]	RfD or RfC (Fold difference compared to DPR value; ↓=lower)
Uncertainty Factors (UF)		**1 inter 10 intra 10 DNT**		**10 inter 10 intra 1 DNT**		**1 inter 10 intra 1 FQPA 10 LOEL-NOEL**
Acute Oral [µg/kg/day]						
Children 1-2	581	5.81	10	0.1 **(58-fold ↓)**	NA	NA
Females 13-49	467	4.67	NA	NA		
Steady State Oral [µg/kg/day]						
Children 1-2	99	0.99	10	0.1 **(10-fold ↓)**	0.17	0.0017 **(582-fold ↓)**
Females 13-49	78	0.78	NA	NA	0.12	0.0012 **(650-fold ↓)**
Steady State Dermal [µg/kg/day]						
Children 1-2	134250	1342.5	333[#]	3.3[#] **(403-fold ↓)**	14.9	0.149 (**9010 –fold↓**)
Females 13-49	23600	236	NA	NA	3.4	0.034 **(6941 -fold ↓)**
Steady State Inhalation [µg/m^3]						
Children 1-2	2850	28.5	333[#]	3.3[#]**(9-fold ↓)**	1.65	0.0165 **(1727-fold ↓)**
Females 13-49	6150	61.5	NA	NA	5.1	0.0510 **(1206-fold ↓)**

FQPA-Food Quality Protection Act Safety Factor; **NA**-Not available /not measured ; **DNT**-Developmental Neurotoxicity; Reference Dose (**RfD)** or Reference Concentration (**RfC)**: As defined by US EPA (2012), a RfC or RfD is an estimate of the concentration or dose of a substance (with uncertainty spanning perhaps an order of magnitude) to which a human population can be exposed (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime, derived by dividing PoD with total uncertainty factors (UF).

[#] Route to route extrapolation - Inhalation: Route specific inhalation PoD: oral dose mg/kg/day / (BR m^3/h /BW kg); Oral PoD=0.01 µg/kg/day; BR=0.33 m^3/h; BW child k=11 kg
- Dermal: Route specific dermal PoD is based on dermal absorption in rat of 3% (USEPA 2011 HHRA)

[d] Estimated PoDs derived by reverse dosimetry based on a predicted 21 day-time-weighted average (TWA) concentration of chlorpyrifos in blood (USEPA 2016 HHRA)

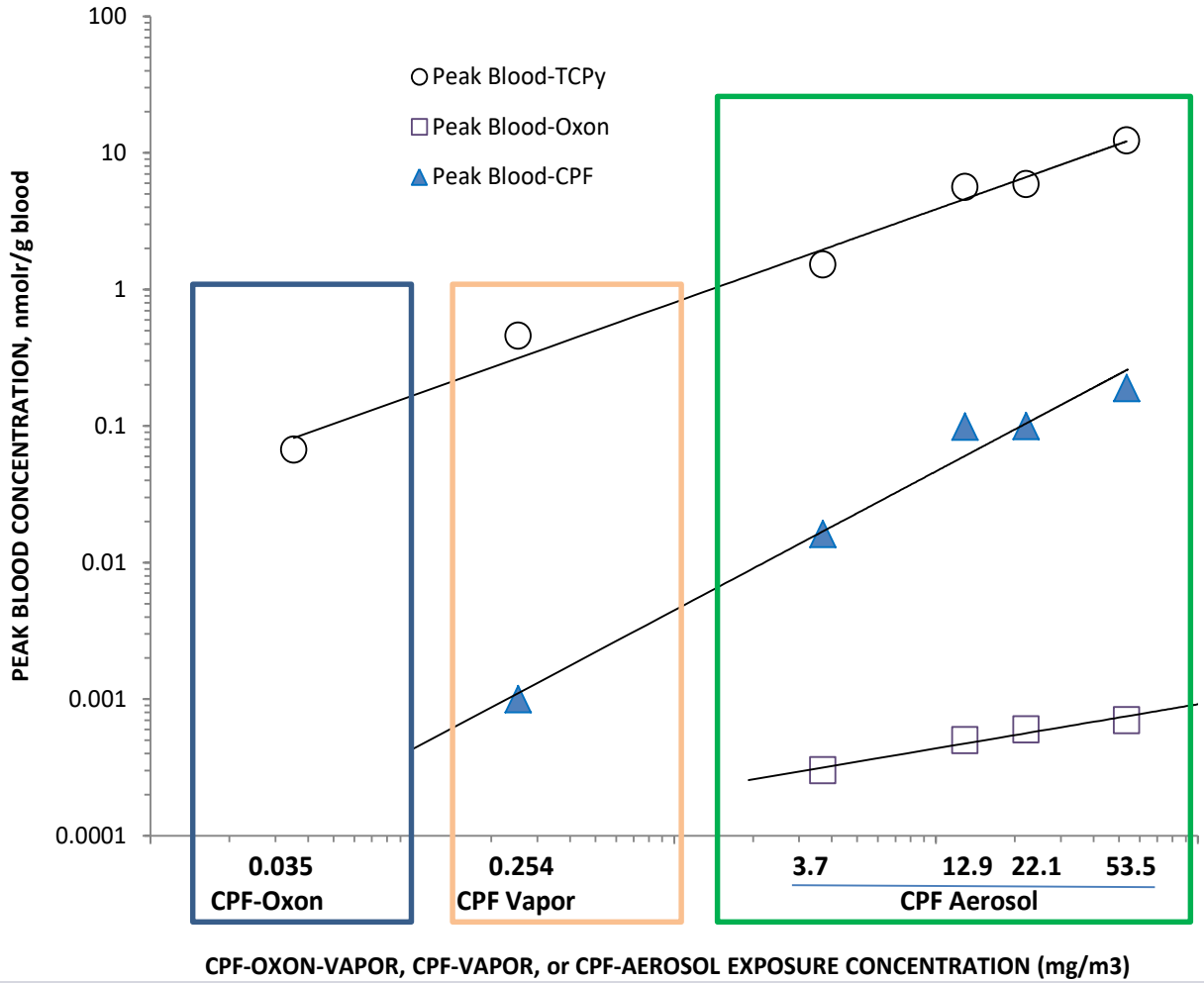
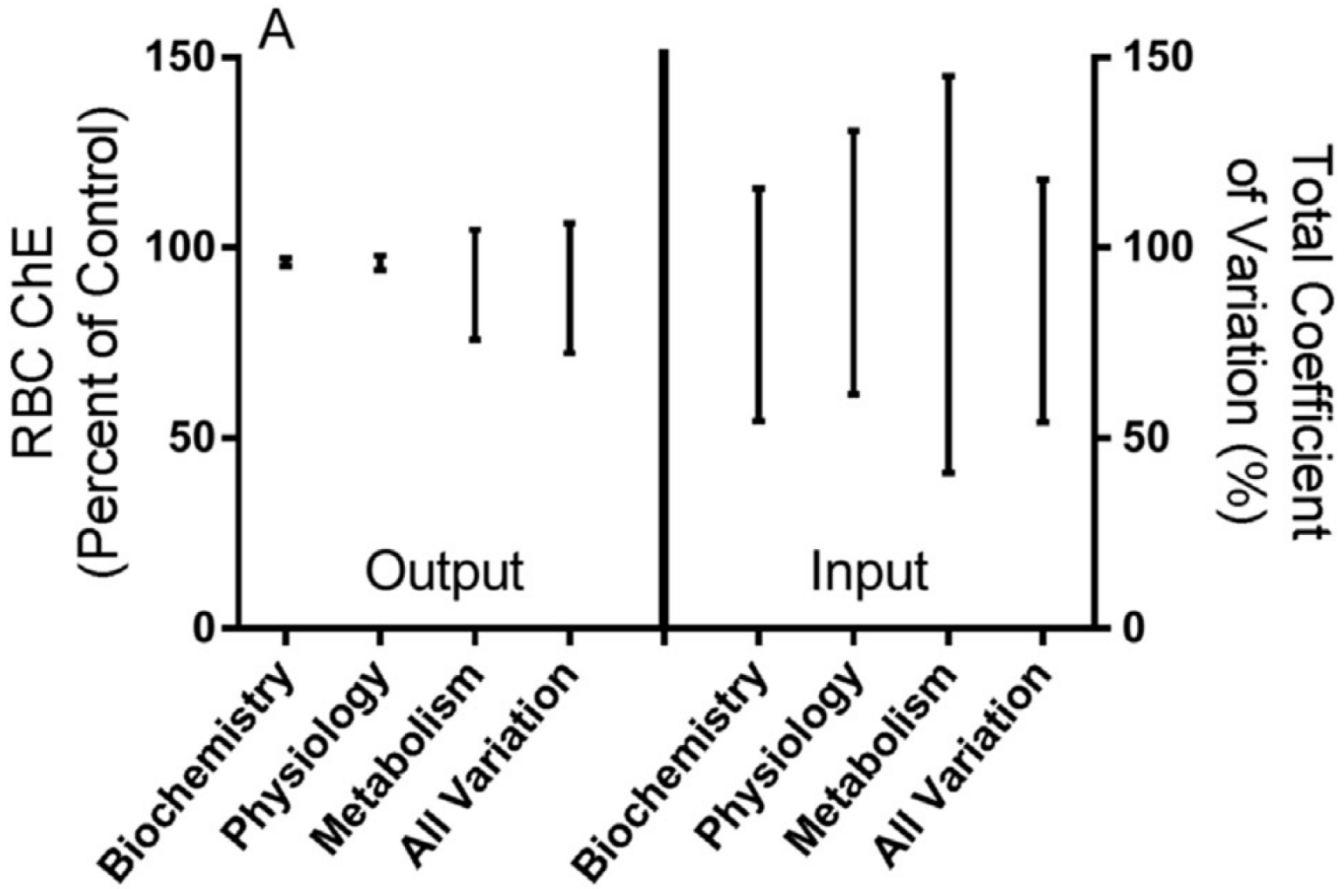


Figure 1. Peak Blood Concentration of TCPy, CPF-Oxon, and CPF from Inhaled CPF vapor, CPF aerosol, or CPF Oxon in Rats (modified from Hotchkiss, 2010 and Poet et al., 2015)



Reference – Poet, 2017

Table 2
Ratios of the maximum value to minimum value in the raw data, model output and bootstrap model simulations for the critical enzyme activities.

	CYP450 to TCPy	CYP450 to Oxon	Hepatic PON1	Plasma PON1
Range in *in vitro* data (Smith et al., 2011)	12	28	11	6
Range in parametric distribution	26	34	33[a]	33[a]
Range in 20 parametric bootstraps	74	98	58[a]	58[a]

[a] PON1 in liver and plasma were assumed to be correlated and thus have the same variation.

Table 3
Data use in deriving the values of the Data Derived Extrapolation Factors for intra-species extrapolation ($DDEF_{HD}$).

	Adult male and female		Infants		Non-pregnant female		Pregnant female[a]	
	Median (50th percentile)	1st percentile	Median (50th percentile)	1st percentile	Median (50th percentile)	1st percentile	Median (50th percentile)	1st percentile
ED_{10} (mg/kg)	0.47	0.14	0.52	0.13	0.46	0.14	0.39	0.16
$DDEF_{HD}$		3.4		3.6		3.4		2.9

[a] Pregnant cohort is 3rd trimester, based on most sensitive group.

Reference – Poet, 2017

Charge Question #4

Use of a surrogate approach to estimate spray drift aerosol inhalation exposures due to ground boom and orchard airblast spray

- The inhalation exposures of concern for ground boom and orchard airblast presented by EPA (2012) were calculated using surrogate air concentrations estimated using fixed wing scenario air concentrations
- So, the use of fixed wing estimated air concentrations as surrogates for ground boom and orchard airblast is not without precedent

Charge Question #5

The current exposure assessment assumes that 100% of the droplet cloud is absorbed by the subject

- A spray drift cloud is comprised of aerosol droplets of varying sizes that continually change as the cloud travels away from the application target
- The air concentration estimate produced by the AGDISP model is comprised of an aerosol cloud of varying droplet sizes depending upon the distance downwind of the application (the flux plane) and the height above ground where the air concentration is measured
- In the current risk assessment, HHA does not adjust for inhalable fraction

AGDISP 8.28

- AGDISP models the behavior of the droplet cloud released from nozzles on aircraft
- A well-vetted First Principles Lagrangian Model
  - Comparisons with field data indicate that the model tends to over estimate, particularly in the far field
- The AGDISP code has a long history, beginning in the 1960's
- The original code was developed by the US Army and US Forest Service
  - Gaussian Plume
- The Lagrangian AGDISP code was developed under contract to NASA
- AGDISP has been validated with many field studies including:
  - The Spray Drift Task Force (SDTF) in 1992-1993
  - Reviewed by the USEPA SAP in 1997
- The AGDISP 8.26 model algorithm is included in the AgDRIFT model
- AGDISP 8.28 implemented improvements to droplet evaporation

AgDRIFT 2.1.1

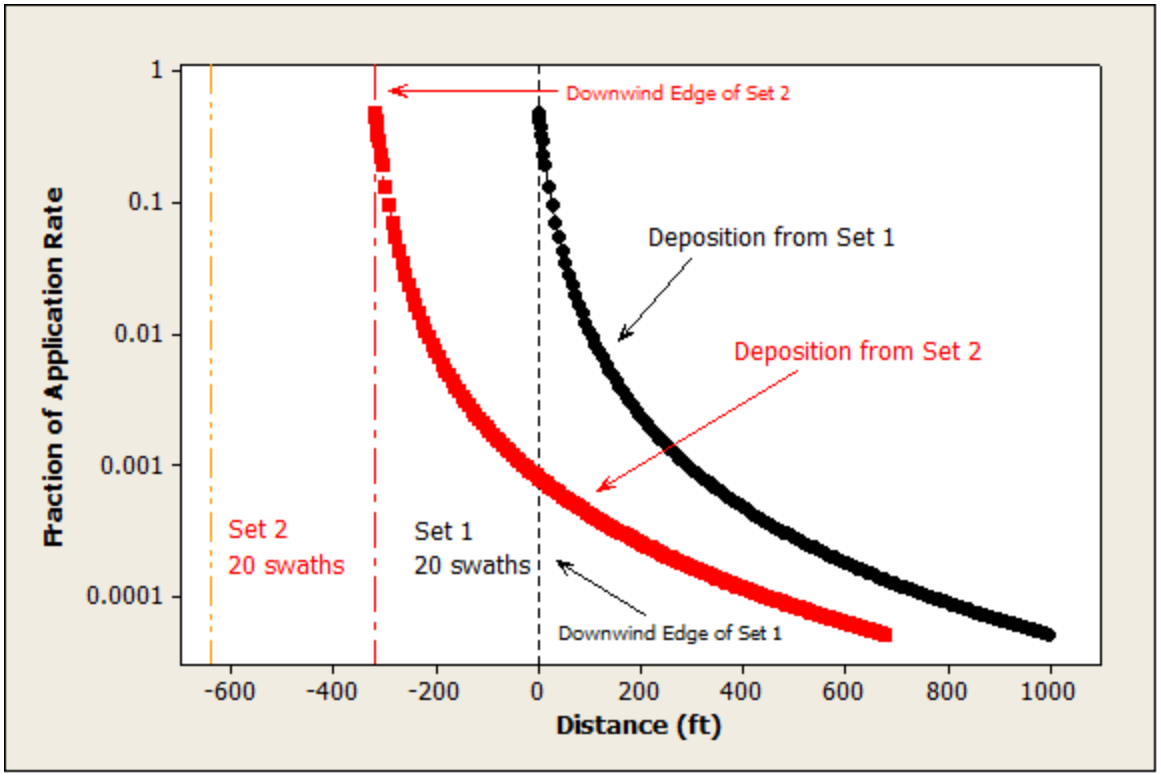
- AgDRIFT 2.1.1 is the US EPA OPP regulatory model
- The horizontal deposition curves are based upon sound field data and are well vetted
- The Spray Drift Task Force conducted the field studies under a CRADA with US EPA ORD
- A US EPA OPP peer review panel and several SAP reviews have been completed

Mass Released for 6 lb/ac Scenario

- Fixed-wing aircraft
  - Swath width 60ft
  - 50 swaths (3000 ft wide)
  - 206.6 acres
  - 1236 lbs
  - Approximately 11 min at 145 mph

- Orchard airblast
  - Swath width 16 ft
  - 60 swaths (640 ft wide)
  - 21.2 acres
  - 127 lbs
  - Approximately 4 hrs at 3 mph

Relationship of Successive Swath Deposition



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Averaging Time Concepts

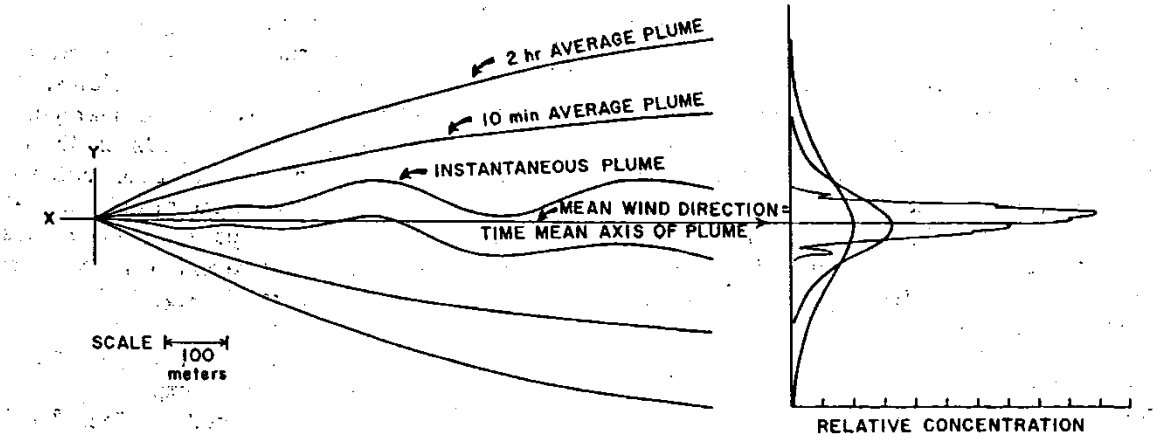


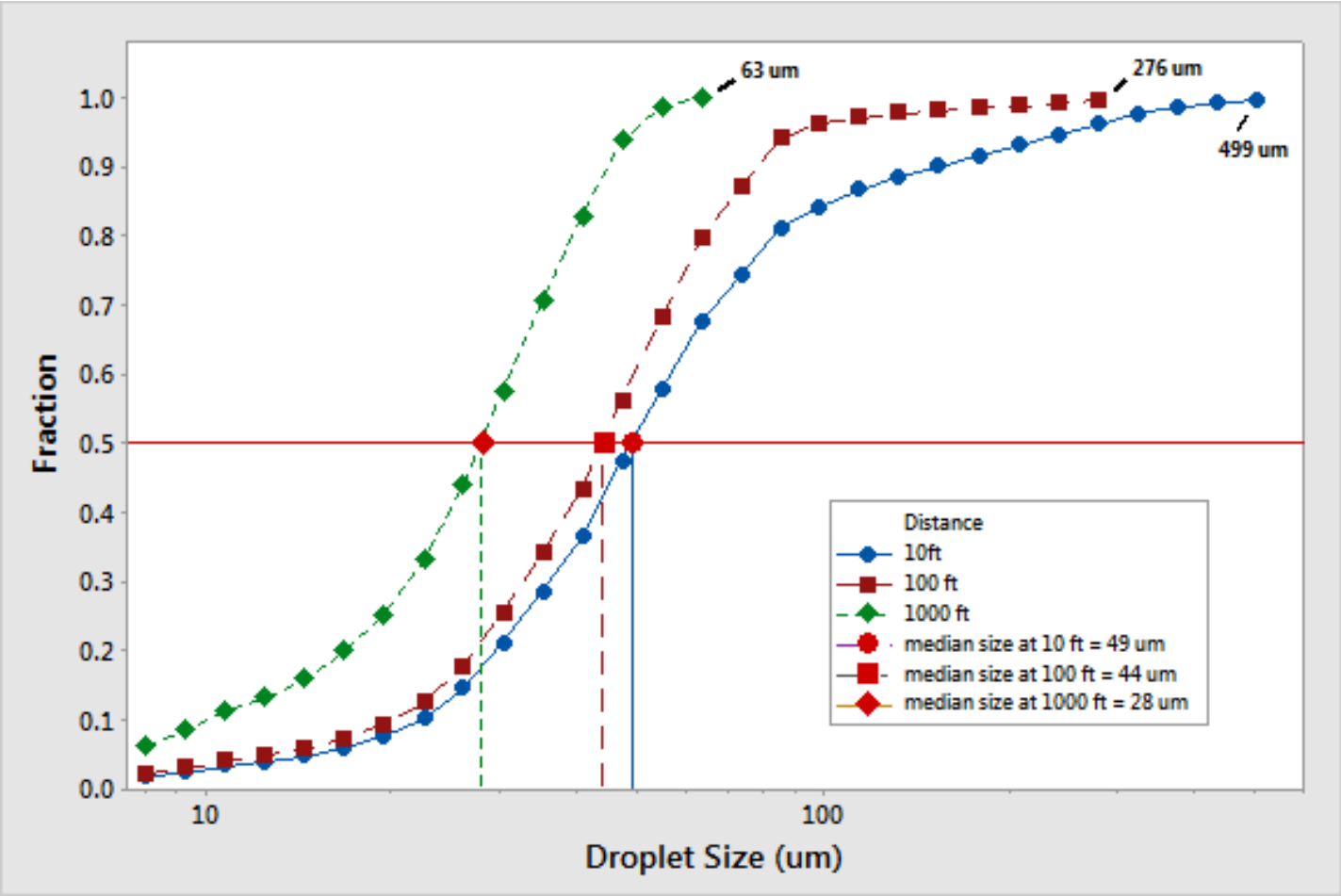
Fig. 2.38—The diagram on the left represents the approximate outlines of a smoke plume observed instantaneously and of plumes averaged over 10 min and 2 hr. The diagram on the right shows the corresponding cross-plume distribution patterns.

- For a fixed point –
  - While the field is being treated both the position of the release and the wind direction changes causes changes in the position of the plume centerline to deviate from that fixed point

- This lateral plume movement reduces the time weighted average air concentrations with increasing averaging times at that fixed point

Figure from Slade (1968) Meteorology and Atomic Energy 1968.

Cumulative Droplet Spectra at Increasing Distance Downwind



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