Five dithiocarbamates (mancozeb, maneb, metiram, ziram, and thiram) were found to belong to a CMG based on the production of a common neurotoxic metabolite, carbon disulfide (USEPA, 2001c). No RPFs were calculated in this document. However, on December 19, 2001, OPP produced a memorandum stating that, based on the recommendations of the SAP and comments from the public, OPP re-evaluated the data and concluded that the available evidence does not support a common mechanism for neuropathology (USEPA, 2001d). Currently, USEPA does not support the use of RPFs for dithiocarbamates (USEPA, 2015).

4.5 Triazines

OPP included five triazines (atrazine, simazine, desethyl-s-atrazine, desisopropyl-s-atrazine, and diaminochlorotriazine) into the same CMG. Triazines were evaluated based on neuroendocrine effects. The common mechanism of toxicity involves the disruption of the hypothalamic-pituitary-gonadal axis. The hypothalamic-pituitary axis is involved in the development and maintenance of the reproductive system, bone formation, and immune, CNS, and cardiovascular functions. Therefore, disruption can lead to a variety of adverse health effects. Atrazine was chosen as the index chemical. Evaluation of endocrine-related data demonstrated potencies for chemicals in the CMG were equal or slightly less than atrazine. Therefore, an RPF of 1 was used for all chemicals in the CMG (USEPA, 2006a). Oral RPFs for triazines can be found in Table 7.

4.6 Pyrethrins and Pyrethroids

OPP included a total of 15 naturally occurring pyrethrins (including pyrethrins I and pyrethrins II) and synthetic pyrethroids that belong to the same CMG. The common mechanism grouping is based on 1) shared structural characteristics, 2) shared ability to interact with the voltage-gated sodium channels, which results in disruption of membrane excitability in the nervous system, and 3) neurotoxicity characterized by two different toxicity syndromes. OPP's CMG science policy paper (USEPA, 2011a) discusses how behavioral responses, particularly in the rat, can be used as sensitive indicators of pyrethroid toxicity. Rat behavior studies from Weiner et al. (2009) and Herberth (2010) were selected for benchmark dose modeling. A BMD_{20} was calculated based on a 20% change from controls. Behavioral data tends to have a higher level of variability compared to other biomarkers of toxicity. Due to the high variability and smaller sample size of the pyrethrin behavioral data, the BMD_{20} is the lowest dose for which a significant change can be detected from control values. It is consistent with the threshold used in other pyrethroid behavior studies (USEPA, 2011b). Deltamethrin was chosen as the index chemical because it has the most robust database of guideline and literature studies and is of sufficient quality to minimize error and uncertainty in cumulative risk assessments. Oral RPFs for pyrethrins and pyrethroids can be found in Table 8.

4.7 Chloroacetanilides

OPP included two pesticides (alachlor and acetochlor) in the same CMG. Both compounds produce nasal olfactory epithelium tumors in rats by a common mechanism including cytotoxicity of the olfactory epithelium, followed by regenerative cell proliferation of the nasal epithelium, and neoplasia if cytotoxicity and proliferation are sustained. Additionally, both compounds produce thyroid follicular cell tumors in rats by

UDPGT induction, increased TSH, alterations in T3/T4 hormone production, and thyroid hyperplasia (USEPA, 2006b). Because tumor development for these chemicals has a non-linear mode of action, tumor incidences were used to derive NOAELs for nasal tumors in male and female rats. Alachlor was chosen as the index chemical (USEPA, 2006b). The RPF was calculated using the ratio of the NOAEL for alachlor to the NOAEL for acetochlor. The oral RPF for acetochlor can be found in Table 9.

5. Application of Dose Additivity for Pesticides

As detailed in Section 2.1 (Dose Additivity), when multiple pesticides belonging to a CMG are found at a site, the individual concentrations of the pesticides are multiplied by their respective RPF values to get an ICED. All ICEDs are then summed to get the total ICED.

5.1 Which pesticides to include

Because pesticides are specialized for both the type of organism (insecticide versus herbicide) and the location of application (e.g., agricultural versus residential), colocation of pesticides within and among CMGs is not assumed. Pesticides are applied in many scenarios (application to food crops, use in residential and commercial buildings, and lawn care) over various spatial areas making predicting potential exposures difficult (USEPA, 2003). While assessment of human health risk is necessary when multiple chemicals from a CMG are present, the detection of one or more pesticides does not confirm or imply the presence of others. The dose additivity approach should be used only for those pesticides that are detected at a site. An example calculation is shown in Table 10.

5.2 Route specific RPFs

The TEFs for PCDDs/PCDFs, PCBs, and PAHs are intended to be applicable for all routes of exposure. For pesticides, USEPA made an attempt to develop route-specific RPFs. Thus, some pesticides have separate RPFs for oral, dermal, and inhalation routes of exposure, some have RPFs for two routes, while other pesticides have only oral route RPFs. The existence of route-specific RPFs, and their availability for some but not other pesticides, complicates their use in calculating risks and developing risk-based CTLs. One approach to include all RPFs when available would be to create a weighted RPF based upon the relative contribution of oral, dermal, and inhalation exposure to total exposure. This weighted RPF could be used with standard risk and CTL equations in the same way that calculations are performed for PCDDs/PCDFs, PCBs, and PAHs. However, the weighting would depend upon the specific exposure assumptions selected for the three routes and chemical/physical properties of the pesticide. Therefore, it would have to be derived for each chemical, exposure scenario, and with any site-specific deviations for default assumptions. This makes this approach cumbersome as a general method for implementing dose additivity for pesticides. Another approach would be to use different risk and CTL equations where oral, dermal, and inhalation risks are calculated separately, each with its own concentration term, and then summed. This would require a separate set of risk equations for pesticides, which may be confusing and difficult to implement as a general method. The simplest approach, which is recommended, is to create ICED values using the oral RPF [only] and use the standard equations for calculating risk and developing

risk-based CTLs. Generally, dermal and inhalation exposures for these chemicals from environmental media are low compared with oral exposure, and the error produced by using the oral RPF for all routes should be small. If there is a site-specific situation in which dermal or inhalation exposure is expected to be substantial relative to oral exposure, then either of the two other approaches discussed above can be used to more accurately estimate the contribution of these exposure routes to total risk.

5.3 Comparison with CTLs

Often the objective of evaluating dose-additivity is to determine whether the combined effects of the chemicals cause them to exceed a CTL. For the pesticides, this process is somewhat more complicated than for PCDDs/PCDFs, PCBs, and PAHs. The complication arises from the fact that the pesticides may have toxic effects that need to be addressed other than the effects that form the basis for the CMGs. A clear example is carcinogenicity. All of the CMGs are based upon non-cancer effects, while some of the pesticides in these CMGs are carcinogens. [A list of pesticides in the five CMGs that are carcinogens is shown in Table 11.] Consequently, in addition to additive non-cancer effects among the class of pesticides, potential carcinogenic effects also need to be addressed through comparison of concentrations of these pesticides with their individual CTLs derived based upon cancer risk. An example comparison can be found in Table 12. These CTLs appear in Chapter 62-777, FAC or are derived on a site-specific basis. With respect to non-cancer effects, some pesticides have non-cancer effects in addition to those reflected in their CMG. Consideration of these effects is also accomplished by comparing concentrations of the pesticides with their individual CTLs derived based upon non-cancer risk. Dose additivity should be evaluated separately by comparing the total ICED for the CMG with a CTL for the index chemical derived specifically based upon the common toxic effect. That CTL is based on a reference dose derived from the CMG analysis conducted by the USEPA, and may be different from the CTL based upon a reference dose from another source such as IRIS. To minimize confusion, a separate set of CTLs for the index chemicals appears in Chapter 62-777, FAC for the purpose of determining dose-additivity of pesticides.

For the purposes of cleanup under 62-780, F.A.C., a chemical must be addressed as part of the risk management strategy for the site if any of the applicable CTLs are exceeded.

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Table 1. Toxic Equivalency Factors for PCDDs/PCDFs

Chemical	TEF
Polychlorinated dibenzo-p-dioxins (PCDDs)	
2,3,7,8-TCDD*	1
1,2,3,7,8-PeCDD	1
1,2,3,4,7,8-HxCDD	0.1
1,2,3,6,7,8-HxCDD	0.1
1,2,3,7,8,9-HxCDD	0.1
1,2,3,4,6,7,8-HpCDD	0.01
OCDD	0.0003
Polychlorinated dibenzofurans (PCDFs)	
2,3,7,8-TCDF	0.1
1,2,3,7,8-PeCDF	0.03
2,3,4,7,8-PeCDF	0.3
1,2,3,4,7,8-HxCDF	0.1
1,2,3,6,7,8-HxCDF	0.1
1,2,3,7,8,9-HxCDF	0.1
2,3,4,6,7,8-HxCDF	0.1
1,2,3,4,6,7,8-HpCDF	0.01
1,2,3,4,7,8,9-HpCDF	0.01
OCDF	0.0003
Polychlorinated biphenyls (PCBs)	
3,3',4,4'-TCB (77)	0.0001
3,4,4',5-TCB (81)	0.0003
3,3',4,4',5-PeCB (126)	0.1
3,3',4,4',5,5'-HxCB (169)	0.03
2,3,3',4,4'-PeCB (105)	0.00003
2,3,4,4',5-PeCB (114)	0.00003
2,3',4,4',5-PeCB (118)	0.00003
2',3,4,4',5-PeCB (123)	0.00003
2,3,3',4,4',5-HxCB (156)	0.00003
2,3,3',4,4',5'-HxCB (157)	0.00003
2,3',4,4',5,5'-HxCB (167)	0.00003
2,3,3',4,4',5,5'-HpCB (189)	0.00003

* Index chemical

Table 2. Example Calculation of Total TCDD Equivalents for Polychlorinated Dioxins and Furans

Polychlorinated dibenzodioxins				
Congener	Analytical Result (mg/kg)	Concentration (mg/kg)	TEFs	2,3,7,8-TCDD Equivalents (mg/kg)
2,3,7,8-TCDD	0.0000000062	0.0000000062	1	0.000000006
1,2,3,7,8-PeCDD	0.00000053 U	0.00000027	1	0.0000003
1,2,3,4,7,8-HxCDD	0.0000000042	0.0000000042	0.1	0.0000000004
1,2,3,6,7,8-HxCDD	0.00000088 U	0.00000044	0.1	0.00000004
1,2,3,7,8,9-HxCDD	0.0000000031	0.0000000031	0.1	0.0000000003
1,2,3,4,6,7,8-HpCDD	0.0000099 U	0.000005	0.01	0.00000005
OCDD	0.000068	0.000068	0.0003	0.00000002
			Total Dioxin Equivalents=	0.0000004

Polychlorinated dibenzofurans				
Congener	Analytical Result (mg/kg)	Concentration (mg/kg)	TEFs	2,3,7,8-TCDD Equivalents (mg/kg)
2,3,7,8-TCDF	0.0000072 U	0.0000036	0.1	0.0000004
1,2,3,7,8-PeCDF	0.00000094	0.00000094	0.03	0.00000003
2,3,4,7,8-PeCDF	0.0000046 U	0.0000023	0.3	0.0000007
1,2,3,4,7,8-HxCDF	0.000000089	0.000000089	0.1	0.000000009
1,2,3,6,7,8-HxCDF	0.0000055 U	0.0000028	0.1	0.0000003
1,2,3,7,8,9-HxCDF	0.00056 U	0.00028	0.1	0.000028
2,3,4,6,7,8-HxCDF	0.00000092	0.00000092	0.1	0.00000009
1,2,3,4,6,7,8-HpCDF	0.0000085	0.0000085	0.01	0.00000009
1,2,3,4,7,8,9-HpCDF	0.00000000066	0.0000000007	0.01	0.000000000007
OCDF	0.00000049 U	0.00000025	0.0003	0.00000000008
			Total Furan Equivalents =	0.000030

Total TEQs; Dioxins + Furans=	0.0000304

Table 3. Toxic Equivalency Factors for PAHs

Chemical	TEF
Benzo(a)pyrene*	1
Benzo(a)anthracene	0.1
Benzo(b)fluoranthene	0.1
Benzo(k)fluoranthene	0.01
Chrysene	0.001
Dibenz(a,h)anthracene	1
Indeno(1,2,3-cd)pyrene	0.1

* Index chemical

Table 4. Example Calculation of Total BaP Equivalents for Polycyclic Aromatic Hydrocarbons

Contaminant	Analytical Result (mg/kg)	Concentration (mg/kg)	TEFs	Benzo(a)pyrene Equivalents (mg/kg)
Benzo(a)pyrene	0.051	0.051	1.0	0.0510
Benzo(a)anthracene	0.25 U	0.125	0.1	0.0125
Benzo(b)fluoranthene	0.0012	0.0012	0.1	0.0001
Benzo(k)fluoranthene	0.89	0.89	0.01	0.0089
Chrysene	0.37	0.37	0.001	0.0004
Dibenz(a,h)anthracene	0.0064 U	0.0032	1.0	0.0032
Indeno(1,2,3-cd)pyrene	0.003 U	0.0015	0.1	0.0002

Total Benzo(a)pyrene Equivalents = 0.0762

(Note: For comparing to the soil direct exposure CTL in 62-777, the B(a)P equivalents are rounded to one decimal place. In the example above, the rounded result would be 0.1 mg/kg B(a)P TEQs.)

Table 5. Organophosphate Relative Potency Factors

Chemical	Oral RPF	Dermal RPF	Inhalation RPF
Acephate	0.08	0.0025	0.208
Azinphos-methyl	0.10		
Bensulide	0.003	0.0015	
Chlorethoxyfos	0.13		
Chlorpyrifos	0.06		
Chlorpyrifos-methyl	0.005		
Diazinon	0.01		
Dichlorvos	0.03		0.677
Dicrotophos	1.91		
Dimethoate	0.32		
Disulfoton	1.26	0.47	6.596
Ethoprop	0.06		
Fenamiphos	0.04	1.5	0.315
Fenthion	0.33	0.015	
Fosthiazate	0.07		
Malathion	0.0003	0.015	0.003
Methamidophos*	**1.00**	**1.00**	**1.00**
Methidathion	0.32		
Methyl-parathion	0.12		
Mevinphos	0.76		
Naled	0.08	0.075	0.82
Omethoate	0.93		
Oxydemeton-methyl	0.86		
Phorate	0.39		
Phosalone	0.01		
Phosmet	0.02		
Phostebupirim	0.22		
Pirimiphos-methyl	0.04		
Profenofos	0.004		
Terbufos	0.85		
Tetrachlorvinphos	0.001	0.00075	
Tribufos	0.02		
Trichlorfon	0.003	0.0075	0.087

* Index Chemical

Table 6. N-Methyl Carbamate Relative Potency Factors

Chemical	Oral RPF	Dermal RPF	Inhalation RPF
Aldicarb	4.00		
Aldicarb sulfone	3.44		
Aldicarb sulfoxide	3.68		
Carbaryl	0.15	0.71	0.51
Carbofuran	2.4		
3- and 5-Hydroxycarbofuran	2.4		
Formetanate HCL	2.18		
Methiocarb	0.18	0.09	0.62
Methomyl	0.67		
Oxamyl*	**1.00**	**1.00**	**1.00**
Pirimicarb	0.02		
Propoxur	0.11	0.03	0.18
Thiodicarb	0.89		

* Index chemical

Table 7. Triazine Relative Potency Factors

Chemical	Oral RPF
Atrazine*	**1**
Simazine	1
Desethyl-s-atrazine	1
Desisopropyl-s-atrazine	1
Diaminochlorotriazine	1

* Index chemical

Table 8. Pyrethroid (Including Pyrethrins) Relative Potency Factors

Chemical	Oral RPF
Allethrin	0.11
Bifenthrin	1.01
Cyfluthrin	1.15
Lambda-Cyhalothrin	1.63
Cyphenothrin	0.15
Cypermethrin	0.19
Deltamethrin*	**1.00**
Esfenvalerate	0.36
Fenpropathrin	0.50
Tau-Fluvalinate	1.00
Imiprothrin	0.02
Permethrin	0.09
Prallethrin	0.10
Pyrethrins	0.02
Resmethrin	0.05

* Index chemical

Table 9. Chloroacetanilide Relative Potency Factors

Chemical	Oral RPF
Alachlor*	**1.00**
Acetochlor	0.05

* Index chemical

Table 10. Example Calculation of Total Oxamyl Equivalents for N-Methyl Carbamates (Note that only detected pesticides are included in the calculation)

N-Methyl Carbamates				
Pesticide	Analytical Result (mg/kg)	Concentration (mg/kg)	Oral RPF	Oxamyl Equivalents (mg/kg)
Aldicarb	56	56	4	224
Aldicarb sulfone	150	150	3.44	516
Aldicarb sulfoxide	33	33	3.68	121
Carbaryl	87 U		0.15	
Carbofuran	41 U		2.4	
3- and 5-Hydroxycarbofuran	5 U		2.4	
Formetanate HCL	11 U		2.18	
Methiocarb	320	320	0.18	58
Methomyl	68	68	0.67	46
Oxamyl	460	460	1	460
Pirimicarb	15 U		0.02	
Propoxur	78	78	0.11	8.6
Thiodicarb	32 U		0.89	
			Total Oxamyl Equivalents=	1434

Table 11. Carcinogenic Pesticides

Chemical*
Acephate
Alachlor
Atrazine
Dichlorvos
Ethoprop
Permethrin
Resmethrin
Simazine
Tetrachlorvinphos

*Carbaryl, pirimicarb, propoxur, and thiodicarb are also classified as probable carcinogens or likely to be carcinogenic but were not included in this list because no cancer slope factors or inhalation unit risks exist for these pesticides. As such, a CTL based on a cancer endpoint cannot be calculated.

Table 12. Example SCTL comparison for a pesticide (acephate) which has both non-cancer and cancer effects

Pesticide	Analytical Result (mg/kg)	Oral RPF	Methamidophos equivalents	Methamidophos residential SCTL based on non-cancer effects (Ch. 62-777, F.A.C, 2005)	Exceeds non-cancer SCTL?
Acephate	50	0.08	4.0	3.1	Yes

Pesticide	Analytical Result (mg/kg)	Acephate residential SCTL based on cancer effects (mg/kg) (Ch. 62-777, F.A.C, 2005)	Exceeds cancer SCTL?
Acephate	50	120	No

Acephate is a member of the organophosphate CMG. The basis for grouping the organophosphates together is shared neurotoxic non-carcinogenic effects. Thus, when acephate is present at a contaminated site, it should be evaluated for its non-carcinogenic effects, i.e. concentrations of acephate should be converted to methamidophos equivalents, as in the first table above. If any other pesticide in the organophosphate CMG is present, they too should be converted to methamidophos equivalents and added together to get the total ICED (see Table 10 for example calculation). The ICED should then be compared to the SCTL for the index chemical when the SCTL is derived for the same target effect (e.g. neurotoxicity). In this example, acephate is the only organophosphate present at the site; therefore, the analytical result is converted to methamidophos equivalents, which can then be directly compared to the residential SCTL derived to be protective of methamidophos effects of neurotoxicity. In this example, the acephate is in exceedance of the methamidophos residential SCTL.

However, acephate is known to also produce carcinogenic effects. To assess the cancer risk from acephate, concentrations at a site should be directly compared to the acephate residential SCTL derived to be protective of carcinogenic effects. In this example, the analytical result falls below the acephate residential SCTL for cancer effects.

For the purposes of cleanup under 62-780, acephate would need to be addressed as a chemical of concern because the total methamidophos equivalents exceed the methamidophos SCTL based on non-cancer effects.