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SUBJECT: Guidance for Evaluating Cases of Detection of DDT (1,1,1-trichloro-2,2-bis(4-chlorophenyl)ethane) on Commodities that are not Covered by Food and Drug Administration (FDA) Action

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DDT (1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane) is an organochlorine pesticide that was banned in the US and worldwide in the 1970s due to concerns regarding effects on wildlife, effects on the reproductive and developing nervous system in humans, carcinogenicity potential, environmental persistence, and bioaccumulation in the food chain. Before its ban, human exposure to DDT happened directly from its insecticidal use. Today, human exposure mainly derives from environmental persistence resulting in residues in soil and foods. Action levels for DDT in food were established by the Food and Drug Administration (FDA) in 2002 to address unavoidable environmental contamination. Residues in foods higher than expected persistence could be due to illegal agricultural uses of this banned pesticide.

The Department of Pesticide Regulation (DPR) Enforcement Branch requested guidance from the Human Health Assessment Branch (HHAB) for evaluating cases of detection of both DDT and related isomers and metabolites (DDTr) on commodities that are not covered by FDA action levels.

This memorandum consists of two parts:

Part 1: Establishes action levels on commodities that are not covered by FDA action levels.
Part 2: Summarizes relevant toxicology data for DDT/DDE and establishes the acute no-observed-effect level (NOEL) and reference dose (RfD) for evaluation of illegal DDT residues on fresh produce.

Recommendations:

1. Action levels for the following commodities are:
   - Cilantro (Chinese parsley, coriander leaves) – 0.5 ppm
   - Yam- 1 ppm
   - Broccoli (rapa, Italian turnip, rapini) – 0.5 ppm
   - Burdock (gobo, harlock- clotbur) – 0.2 ppm
   - Onion (green) – 0.2 ppm
   - Sesame (seed and pod vegetable) – 0.1 ppm
   - Taro – 0.2 ppm

2. For cases referred to HHAB for risk assessment, an acute reference dose (aRfD) of 0.0017 mg/kg will be used to evaluate risk.

PART 1. GUIDANCE FOR EVALUATING CASES OF DDT DETECTS ON COMMODITIES THAT ARE NOT COVERED BY FDA ACTION LEVELS

The Department of Pesticide Regulation Enforcement Branch requested guidance from the Human Health Assessment Branch (HHAB) for evaluating cases of the detection of DDT (1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane) and related isomers and metabolites (DDTr) on commodities that are not covered by the Food and Drug Administration (FDA) action levels, specifically, maximum residues that would not be expected to result in an acute health concern. HHAB reviewed current FDA action levels, toxicity data for DDTr, and residue data from USDA's PDP program and DPR's residue monitoring program. We made the following conclusions regarding the evaluation of potentially illegal DDTr residues on fresh produce, that is, residues that exceed the FDA action level or residues detected on commodities that do not have action levels:

- California soils and soils around the world where crops are grown for the California market contain legacy residues due to previous use of DDT as an insecticide on food crops and the long half-life of the chemical in the environment.
- The California Department of Food and Agriculture (CDFA) published a report in 1985 (updated in 1996) that investigated possible illegal use of DDT in California. It concluded that DDT residue profiles in food were due to higher than expected persistence of the chemical in California soils and not from illegal applications.
- DDT use in California was restricted in 1963. The last year that significant amounts were used was 1970, when 1.2 million pounds were applied in the state.
- A 2002 risk assessment by Agency for Toxic Substances and Disease Registry (ATSDR) showed that diet was the primary route of exposure to DDT for the general public. Consumption of meat, fish, and poultry were the main contributors. Among other food categories, leafy vegetables and root vegetables contained higher residues than fruits, legumes, and garden vegetables. Chronic dietary exposure was over 10-fold lower than the cRfD of 0.5 ug/kg/day for every subpopulation evaluated, indicating that there was no health concern from DDT residues in the diet. Both infants and children up to 2 years of age were the highest exposed subpopulations, with exposures of approximately 0.044 ug/kg/day.
- DDT has moderate acute toxicity based on its oral LD50 values in laboratory animals. While available studies evaluated its neurotoxicity, liver and reproductive toxicity, there are significant gaps in the database, particularly for neurodevelopmental toxicity and for studies specifically on p,p-DDE, the most commonly detected DDT-related chemical in the California Pesticide Residue Monitoring Program (CPRMP).
- US EPA established a chronic oral RfD of 0.5 ug/kg/day DDTr based on liver lesions in rats in a feeding study, and an oral cancer slope factor of 0.34 $(mg/kg/day)^{-1}$ based on liver tumor data from six studies in mice and rats. ATSDR recommended an acute RfD of 0.5 ug/kg DDTr based on neurotoxicity in neonatal mice after a single dose.
- Our analysis shows that the current levels of DDTr being detected by CPRMP are unlikely to pose an acute health concern. For example, using the aRfD of 0.0017 mg/kg/day, the acute threshold residues for cilantro and spinach are:
    - Cilantro, 170 ppm (highest detect = 0.05 ppm)
    - Spinach, 0.34 ppm (highest detect = 0.051 ppm).
- For 2006-2015, the highest number of detections for the CPRMP was in spinach, kale, and cilantro. The single highest residue was 0.09 ppm DDE on Swiss chard (see Table 1).

No detected residues exceeded the FDA action levels or action levels HHAB is proposing in this document.

- For 2005-2014, the highest percent of detects for PDP (in commodities likely to be sampled by CPRMP) were in kale, spinach, cilantro, and carrots. The single highest residue was 0.187 ppm in cilantro (see Table 2). No residues exceeded FDA action levels or action levels HHAB is proposing in this document.

HHAB recommends the use action levels for similar crops to evaluate DDTr detected residues in commodities that are not covered by existing FDA action levels. Some of these proposed action levels are shown in Table 1. For example, HHAB proposes that an action level of 0.5 ppm should be used to evaluate residues on cilantro since FDA has assigned an action level of 0.5 ppm to other commodities in crop group 4, such as spinach, lettuce, and endive. The newly proposed crop groupings should be used to compare commodities. Until new federal regulations for crop groups are promulgated, these new crop group assignments can be found in the federal docket: http://www.regulations.gov/#!docketDetail;dct=FR%252BPR%252BN%252BO%252BSR;rpp=10;po=0;D=EPA-HQ-OPP-2006-0766

Table 1: Summary of CPRMP DDTr Detects (2006-2015) and Existing and Proposed Action Levels (a).

Commodities w/DDTr detects, 2006-2015	# detects	range (ppm)	FDA ACTION LEVEL	CURRENT CROP GROUP	DEEM4 CROP GROUP	PROPOSED CALIF ACTION LEVEL	SIMILAR CROPS W/FDA ACTION LEVELS
SPINACH	126	0.010 - 0.051	0.5	4A	4A	n/a	n/a
KALE	52	0.010 - 0.040	0.5	5B	4B	n/a	n/a
CILANTRO (CHINESE PARSLEY, CORIANDER LEAVES)	31	0.010 - 0.050	0.5	19A	4A	0.5	Spinach, lettuce, endive = 0.5
LETTUCE; HEAD, LEAF, ROMAINE	23	0.010 - 0.040	0.5	4A	4A	n/a	n/a
SQUASH; ALL, SUMMER, WINTER	23	0.010 - 0.030	0.1	9B	9B	n/a	n/a
CARROTS (ALL OR UNSPEC)	16	0.010 - 0.057	3	1AB	1AB	n/a	n/a
RADISH	15	0.010 - 0.043	0.2	1AB	1AB	n/a	n/a
BOK CHOY (WONG BOK)	12	0.010 - 0.070	0.5	5B	5	n/a	n/a
COLLARDS	7	0.010 - 0.050	0.5	5B	4B	n/a	n/a
POTATO (WHITE, IRISH, RED, RUSSET)	6	0.010 - 0.080	1	1C	1C	n/a	n/a
RADISH TOPS	4	0.010 - 0.042	0.2	2	4B	n/a	n/a
BEANS (GREEN, STRING)	3	0.010 - 0.023	0.2	6B	6B	n/a	n/a
SWISS CHARD (SPINACH BEET)	3	0.011 - 0.090	0.5	4B	4A	n/a	n/a
YAMS, TRUE (LISBON & WHITE YAM)	3	0.010	n/a	1CD	1CD	1	Sweet potato = 1
BEAN, BROAD (FAVA, HORSE BEAN) (ALL/UNSPEC)	1	0.020	0.2	6B	6B	n/a	n/a
BEETS, GENERAL	1	0.012	0.2	1	1	n/a	n/a
BEETS, TABLE, RED, OR GARDEN (ROOT CROP)	1	0.013	0.2	1AB	1AB	n/a	n/a
BROCCOLI	1	0.010	0.5	5	5	n/a	n/a
BROCCOLI RAAB (RAPA, ITALIAN TURNIP, RAPINI)	1	0.010	n/a	5B	4B	0.5	Brassica (cole) leafy vegetables (except broccoli raab, Chinese mustard cabbage, and rape greens) = 0.5
BURDOCK (ROOT CROP) (GOBO, HARLOCK, CLOTBUR)	1	0.020	n/a	1AB	1AB	0.2	Beet, parsnip, radish = 0.2
CELERY, GENERAL	1	0.010	0.5	4B	22B	n/a	n/a
CHINESE BROCCOLI (WHITE FLOWERING) (GAI LON)	1	0.015	0.5	5A	4B	n/a	n/a
CUCUMBER (PICKLING, CHINESE, ETC.)	1	0.070	0.1	9B	9B	n/a	n/a
MUSTARD GREENS, (LEAFY VEGETABLE)	1	0.013	0.5	5B	4B	n/a	n/a
ONIONS (GREEN)	1	0.060	n/a	3B	3B	0.2	Onion, dry bulb = 0.2
PARSNIP	1	0.010	0.2	1AB	1AB	n/a	n/a
PEACH	1	0.050	0.2	12	12B	n/a	n/a
SESAME (SEED & POD VEGETABLE)	1	0.010	n/a	20A	20A	0.1	Cottonseed = 0.1
TARO (DASHEEN) (ROOT CROP) (WETLAND, UPLAND, ETC.)	1	0.010	n/a	1CD	1CD	0.2	Beet, parsnip, radish = 0.2
TURNIP TOPS (FORAGE - FODDER)	1	0.021	0.2	2	4B	n/a	n/a

(a) Yellow shading indicates commodities without FDA action levels.

Table 2: Total DDTr Residues (ppm) on PDP Commodities Likely to be Sampled by CPRMP (2005-2014 data).							
YEAR	COMMOD_NAME	SampCt	HitsCnt	PctHit	MinConcen	MaxConcen	Actual or Proposed Action Level (a)
2006, 2007, 2008	KALE	215	77	35.81%	0.007	0.046	0.5
2006, 2008, 2009	SPINACH	1025	313	30.54%	0.003	0.052	0.5
2009-2010	CILANTRO	739	220	29.77%	0.002	0.187	0.5
2006, 2007, 2013, 2014	CARROTS	2907	798	27.45%	0.002	0.127	3
2006, 2007, 2008	COLLARD GREENS	214	38	17.76%	0.007	0.025	0.5
2007, 2008, 2013, 2014	CELERY	2896	369	12.74%	0.002	0.014	0.5
2005, 2009, 2010, 2011	LETTUCE INCL ORGANIC	2616	110	4.20%	0.003	0.034	0.5
2008, 2009	GREEN ONIONS	744	24	3.23%	0.003	0.003	0.2
2006, 2007, 2008, 2012, 2013, 2014	SUMMER SQUASH	2908	63	2.17%	0.003	0.030	0.1
2008, 2009	POTATOES	1488	32	2.15%	0.007	0.042	1
2005, 2006, 2011, 2012, 2013	WINTER SQUASH	2215	40	1.81%	0.003	0.014	0.1
2010, 2011, 2012	SWEET BELL PEPPERS	1671	28	1.68%	0.001	0.004	0.1
2009, 2010	CUCUMBERS	1488	16	1.08%	0.002	0.014	0.1
2006, 2007, 2008, 2013, 2014	BROCCOLI	2894	20	0.69%	0.002	0.003	0.5
2005, 2007, 2008, 2013, 2014	GREEN BEANS	1742	11	0.63%	0.003	0.009	0.2
2008, 2009, 2010	SWEET POTATOES	1476	4	0.27%	0.007	0.007	1
2011, 2012	SNAP PEAS	1487	2	0.13%	0.002	0.003	0.2
2005, 2006, 2010, 2014	WATERMELON	1493	1	0.07%	0.007	0.007	0.1
2008, 2009, 2010	ASPARAGUS	1466	1	0.07%	0.007	0.007	0.5
2005, 2006, 2011, 2012, 2013	CAULIFLOWER	2754	1	0.04%	0.003	0.003	0.5
2007, 2008, 2013, 2014	NECTARINES	2459	1	0.04%	0.003	0.003	0.2
2006, 2007, 2008, 2013, 2014	PEACHES	2253	1	0.04%	0.007	0.007	0.2
2006, 2007, 2008, 2012, 2013, 2014	BANANAS	2500	0	0.00%	n/a	n/a	n/a
2005, 2006, 2011, 2012, 2013	PLUMS	2435	0	0.00%	n/a	n/a	0.2
2005, 2009, 2010, 2014	APPLES	2408	0	0.00%	n/a	n/a	0.1
2005, 2006, 2009, 2010	ORANGES	2229	0	0.00%	n/a	n/a	0.1
2005, 2009, 2010	GRAPES	2228	0	0.00%	n/a	n/a	0.05
2007, 2008, 2014	BLUEBERRIES	2125	0	0.00%	n/a	n/a	0.1
2005, 2009, 2010	PEARS	2040	0	0.00%	n/a	n/a	0.1
2005, 2010, 2011, 2012	CANTALOUPE	1978	0	0.00%	n/a	n/a	0.1
2008, 2009, 2014	STRAWBERRIES	1661	0	0.00%	n/a	n/a	0.1
2007, 2008, 2014	TOMATOES	1658	0	0.00%	n/a	n/a	0.05
2011, 2012	CHERRY TOMATOES	1482	0	0.00%	n/a	n/a	0.05
2005, 2006	EGGPLANT	1476	0	0.00%	n/a	n/a	0.1
2011, 2012, 2013	MUSHROOMS	1462	0	0.00%	n/a	n/a	0.5
2008, 2009, 2010, 2014	SWEET CORN	1435	0	0.00%	n/a	n/a	0.1
2011, 2012	TANGERINES	1426	0	0.00%	n/a	n/a	0.1
2011, 2012	PAPAYA	750	0	0.00%	n/a	n/a	0.2
2011, 2012	ONION	744	0	0.00%	n/a	n/a	0.2
2010, 2011	HOT PEPPERS	739	0	0.00%	n/a	n/a	0.1
2013	RASPBERRIES	652	0	0.00%	n/a	n/a	0.1
2007, 2014	CHERRIES	647	0	0.00%	n/a	n/a	0.2
2012	AVOCADO	372	0	0.00%	n/a	n/a	0.2
2010	MANGOES	372	0	0.00%	n/a	n/a	0.2
2006	CRANBERRIES	316	0	0.00%	n/a	n/a	0.1
(a) Yellow shading indicates proposed Calif action level.							

PART 2. TOXICOLOGY SUMMARY FOR DDT/DDE: ESTABLISHING ACUTE NO-OBSERVED-EFFECT LEVEL (NOEL) AND REFERENCE DOSE (RfD) FOR EVALUATION OF ILLEGAL DDT RESIDUES ON FRESH PRODUCE

HHAB reviewed the toxicology database for DDT and its metabolites and established a critical acute NOEL of 0.17 mg/kg/day. This NOEL is based on a decreased density of muscarinic receptors in the brain and increased spontaneous activity in mice that received a single oral dose of 0.5 mg/kg/day DDT at postnatal day 10. We recommend that for DDT cases submitted by the Enforcement Branch to HHAB for risk assessment, the **acute Reference Dose (RfD) of 0.0017 mg/kg/day** is used to evaluate risk.

Toxicological Summary of DDT/DDE

Background

DDT (1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane) is an organochlorine pesticide that was once used widely in the US for insect control (ATSDR 2002). DDT does not occur naturally in the environment. It was first synthesized in 1874 and its insecticidal properties were discovered in 1939. Concerns based on adverse effects in birds (egg shell thinning) and humans led to its cancellation in the US in 1972 except in cases of public health emergency. The Stockholm Convention on persistent organic pollutants (POPs) includes a limited exemption for the use of DDT to control mosquitoes, such as use in certain areas of tropics and subtropics to control malaria and other insect-transmitted diseases. In 2006, the World Health Organization (WHO) supported the indoor use of DDT in African countries where malaria remains a major health problem. Although the use of DDT apart from disease vector control was banned in the US in the 1970s, human exposure to DDT and its metabolites of 1,1-dichloro-2,2-bis(p-chlorophenyl) ethylene (DDE) and 1-chloro-4[2,2-dichloro-1-(4-chlorophenyl)ethyl]benzene (DDD) still occurs due to environmental bioaccumulation and biomagnification of these persistent lipophilic compounds.

A comprehensive toxicological profile for DDT/DDE/DDD was prepared in 2002 by ATSDR, and later updated in 2008 (ATSDR 2002, 2008). In 2011, WHO published a human health risk assessment focusing on DDT use in indoor residual spraying (WHO 2011). A risk assessment document was published by the Michigan Department of Community Health in October 2012 for establishing a fish consumption screening value (MDCH 2012). The International Agency for Research on Cancer (IARC) announced in 2015 that it will release an IARC Monograph (Volume 113) on the carcinogenicity of DDT in the near future (Loomis et al. 2015).

Summary of Toxicology

Technical grade DDT is a mixture of *p,p'*-DDT (85%), *o,p'*-DDT (15%), and *o,o'*-DDT (trace amounts), and may also contain DDE and DDD (Figure 1). The main metabolites of *p,p'*-DDT are *p,p'*-DDE and *p,p'*-DDD. The most prevalent DDT metabolite in the environment is *p,p'*-DDE. The best known effect of DDT is impairment of nerve impulse conduction. The main targets of DDT and its metabolites (DDE/DDD) are the nervous system, liver, and reproductive system. Neurological effects are mediated through disruption of ion channels and neurotransmitters. Hepatic effects are attributed to oxidative stress and disruption of mitochondrial membranes. Reproductive and developmental effects are possibly mediated through estrogenic and antiandrogenic (androgen receptor antagonist) mechanisms. DDT and its metabolites may also alter serum levels of endogenous steroids and hormones through induction of P450 isozymes such as CYP2B1 and CYP3A2 (Harada et al. 2016). The evidence for carcinogenicity in humans is inconclusive, but is considered sufficient in experimental animals. Possible mechanisms for carcinogenic effects include immune-suppression, oxidative stress, promotion of pre-existing abnormal cells or cytotoxicity leading to reactive hyperplasia and

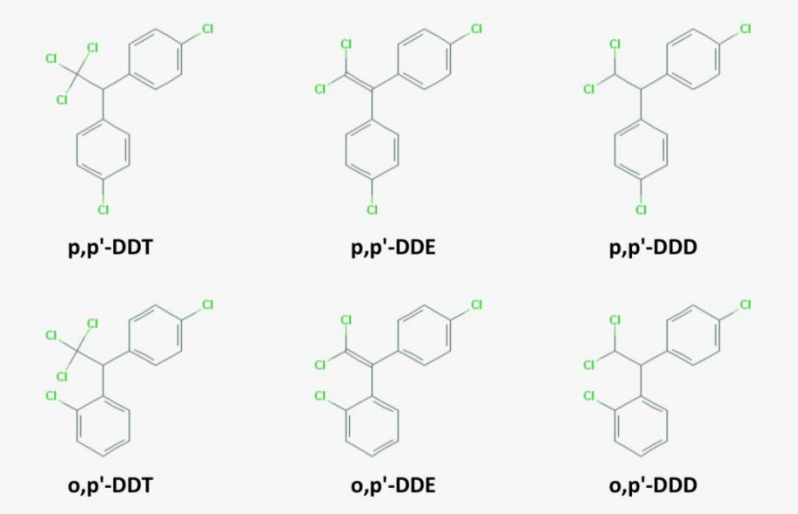

Figure 1: DDT and its isomers (chemical structures copied from Pubchem)

tumor promotion. Of all the DDT-related compounds, the *o,p'*-DDT isomer has the strongest estrogen-like properties, the *p,p'*-DDE has the antiandrogenic properties, and the *o,p'*-DDD is cytotoxic to the adrenal gland.

Acute toxicity: The DDT acute oral lethal dose LD_{50} for rats ranged from 113 to 800 mg/kg. The LD_{50} values in newborn, preweanling, weanling, and adult rats were > 4,000, 438, 355, and

195 mg/kg/day, respectively. DDT poisoning in young and adult rats was characterized by hyperexcitability, intense tremoring and respiratory failure, however, additional toxic responses such as seizures and hyperthermia were only observed in adult rats, which may account for the increased susceptibility of mature rats (Henderson and Woolley 1970). The LD_{50} for mice ranged from 237 to 300 mg/kg for a single exposure dose, and was 85.7 mg/kg/day for a 6-day feeding period. The LD_{50} values for guinea pigs and rabbits after a single oral exposure to DDT were 400 and 300 mg/kg/day, respectively. Acute and short-term toxicity studies for DDT in laboratory animals are summarized in Table 3. The critical endpoint used for deriving the critical NOEL is bolded in the table.

Chronic Toxicity: Liver is the most sensitive target organ following chronic (>1 year) exposure in mouse, rat, hamster, dog, and monkey. Reduced liver weight, liver necrosis, amyloidosis, fatty metamorphosis, focal hepato-cellular necrosis, and severe liver damage occurred in animals exposed to 3.7-160 mg/kg/day DDT. Other effects included reduced body weight, chronic inflammation of kidney, and tremors. Increased mortality has also been reported in monkey (6.9 mg/kg/day), rat (19 mg/kg/day), and mouse (15 mg/kg/day).

Reproductive and Developmental Toxicity: Laboratory animal studies showed that *o,p'*-DDT induced delayed vaginal opening and increased uterine and ovarian weights, and *p,p'*-DDE caused reduced anogenital distance, retention of thoracic nipples in male pups, delayed puberty, and reduced accessory sex organ weights in adult males. Neonatal exposure to a single dose of DDT at 0.5 mg/kg in mice at 10 days of age led to hyperactivity in adults. In human studies, associations have been reported between high blood levels of DDE and shortened duration of lactation and height abnormalities in children.

Genotoxicity and Carcinogenicity: DDT and related compounds are not mutagenic in prokaryotes, but tests in mammalian cells were equivocal for chromosomal aberrations and gene mutations. Studies in mice, rats, and hamsters showed that DDT, DDE and DDD are carcinogenic, primarily to the liver. Oxidative stress was proposed as a key factor in hepatocarcinogenesis by DDT. Genotoxic effects were reported in humans, but these studies were usually confounded by simultaneous exposure to other chemicals. Several epidemiological studies showed associations between DDT exposure and liver and testicular cancers, as well as non-Hodgkin's lymphoma. However, studies both with volunteers that received oral doses of DDT or workers exposed under occupational scenarios (inhalation, oral, and dermal exposures) reported only mild liver alterations of limited clinical significance. DDT was initially classified as "possibly carcinogenic to humans" (Group 2B) by IARC. However, in 2015 IARC reclassified DDT as "probably carcinogenic to humans" (Group 2A) in 2015 a result of the reassessment of carcinogenicity by 26 experts from 13 counties (IARC Monographs, Volume 113, to be released) (Loomis et al. 2015).

DDT residues on commodities not covered by FDA action levels

Dietary exposure via leafy vegetables

Since its cancellation in 1970s, the concentration of DDT in the environment, animals, and humans has decreased significantly. However, DDT/DDE residues persist in the environment and accumulate in fatty tissues. The main exposure route of DDT/DDE for the general public is through the diet. Exposure through air and skin is primarily restricted to workers. Drinking water exposure is minimal due to low water solubility. The main exposure route is through the consumption of foods that contain DDT/DDE residues resulting from bioaccumulation/ biomagnification, illegal use, or legal use from areas of the world where DDT applications are still permitted. The largest dietary fraction of DDT comes from meat, poultry, dairy products, and fish (particularly from sport fish in DDT-contaminated sites), and to a lesser extent from vegetables. Leafy vegetables generally contain more DDT than other vegetables, possibly because DDT evaporates from soil into the air and subsequently deposits on the leaves (ATSDR 2002).

Acute Oral NOEL and Acute Oral Reference Dose (RfD)

The lowest acute lowest observed effect level (LOEL) in the available database is 0.5 mg/kg based on a neurobehavioral endpoint derived from a series of studies performed by the same group of investigators (Table 1). In these studies, DDT was given to mice as a single oral dose by gavage at 10 days of age, a critical time for brain development in mice, and then tested for behavioral changes at 4, 5, and 7 months. Two responses were consistent in all studies: 1) a decrease in the density of muscarinic cholinergic receptors in the cerebral cortex; and, 2) an increase in spontaneous motor activity in adults. ATSDR used the 0.5 mg/kg/day dose to derive an acute minimal risk level (MRL[1]) of $5x10^{-4}$ mg/kg/day. This MRL was estimated using a 1000-fold uncertainty factor (10X LOEL-to-NOEL, 10X interspecies, 10X intraspecies; ATSDR, 2002). Because these studies employed only one dose level (0.5 mg/kg), a dose-response evaluation could not be performed. However, similar findings were made in all 6 studies and all studies had sufficient sample sizes (n = 9-12 from three or four litter per treatment group). In addition, as noted above, the exposure window (postnatal day 10) represents a sensitive developmental stage for neurogenesis in mice. Therefore, the LOEL of 0.5 mg/kg based on a decreased density of muscarinic receptors in the brain and increased spontaneous activity in mice could be used to estimate the critical acute oral NOEL for DDT. ATSDR considered the effect at the LOEL, disruption of a simple and non-associative learning process, to be mild (ATSDR 2002). Therefore the NOEL can be estimated from the LOEL by applying an uncertainty factor

[1] An MRL is defined as an estimate of daily human exposure to a substance that is likely to be without an appreciable risk of adverse effects (noncarcinogenic) over a specified duration of exposure.

of 3. The resulting NOEL is 0.17 mg/kg. The acute RfD[2] is calculated by further applying a default uncertainty factor of 10 for interspecies and a default uncertainty factor of 10 for intraspecies variation. The resultant RfD is 0.0017 mg/kg/day.

Potential method for detecting illegal use of DDT

Soil and biota samples are usually characterized by a high prevalence of DDE relative to DDT (a ratio of DDE-to-DDT of 2 or higher). This is likely the result of DDT's ban in the 1970s. For example, the average residues of DDE and DDT in leafy vegetables sampled in 1979-1980 were 1.7 and 0.2 ppb, respectively, and in 1980-1982 were 2.4 and 0 ppb, respectively. A lower ratio of DDE-to-DDT or high prevalence of DDT detected in vegetables may indicate an illegal use of DDT. However, rigorous experimental data are needed to validate this conclusion. In addition, high levels of DDT relative to DDE are plausible in sites where DDT degradation is slow (Hitch and Day 1992) or in predominantly anaerobic sites where DDT is largely degraded to DDD (Menzie et al. 1992).

[2] The RfD is an estimate of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious effects during a lifetime.

Table 3: Summary of Acute and Short-term Oral Studies (*p,p'*-Isomers only)

System	Species (isomer)	Exposure duration (route)	NOEL (mg/kg)	LOEL (mg/kg)	Effect	References
Hepatic	Monkey (DDT)	Once (G)	--	150	Increased serum LDH, AP, and transaminases	(Agarwal et al. 1978)
	Rat (DDT)	12-14 d (3 doses) (G)	--	12-40	Increased relative liver weight; necrotic changes; increased liver GSH and AHH enzyme activities	(de Waziers and Azais 1987; Kostka et al. 2000)
	Mouse (DDE)	1 wk (F)	--	42.9	Increased absolute liver weight; increased cytochrome-c reductase and P-450	(Pasha 1982)
Endocrine	Rat (DDT)	Once (G)	25	50	Reduced capacity to concentrate iodine in thyroid	(Goldman 1981)
	Dog (DDT, DDD)	Once, 6d or 15d (C)	--	100-200	Degenerative adrenal changes	(Powers et al. 1974)
Immulogical Lymphoreticular	Rabbit (DDT)	10 d (G)	4.3	--	--	(Shiplov et al. 1972)
Neurological	Human (DDT)	Once (F)	10.3	16	Convulsions	(Hsieh 1954)
	Monkey (DDT)	Once (G)	--	150	Decreased CNS total lipids, phospholipids and cholesterol	(Sanyal et al. 1986)
	Rat (DDT)	Once (G)	25	50-160	Tremors, myoclonus	(HietanenE and Vainio 1976; Hong et al. 1986; Hwang and Van Woert 1978)
	Mouse (DDT)	Once (G)	--	160-200	Tremors, convulsions	(HietanenE and Vainio 1976; Matin et al. 1981)
	Guinea pig (DDT)	Once (G)	--	160	Paralysis of hind legs	(HietanenE and Vainio 1976)
	Hamster (DDT)	Once (G)	160	--	--	(HietanenE and Vainio 1976)
Reproductive	Rat-adult males (DDE)	4 d or 5 d(G)	--	200	Reduced seminal vesicle and ventral prostate weight	(Kelce et al. 1995; Kelce et al. 1997)
	Rabbit (DDT)	Gd 7-9 (3 doses) (G)	--	10-50	Increased resorptions	(Hart et al. 1971; Hart et al. 1972)
Developmental	Rat-pregnant females (DDT)	Gd15-19 (5 doses) (G)	28	--	--	(Gellert and Heinrichs 1975)
	Rat-pregnant females (DDE)	Gd14-18 (5 doses) (G)	10	10-100	Reduced anogenital distance; decreased ventral prostate weight; retained thoracic nipples (male offspring)	(Kelce et al. 1995; Loeffler and Peterson 1999; Wolf et al. 1999; You et al. 1998)
	Mouse-at PND 10 (DDT)	**Once (G)**	**--**	**0.5**	**Decreased muscarinic receptors in cerebral cortex; increased spontaneous activity at 4, 5, and 7 months**	**(Eriksson and Nordberg 1986; Eriksson et al. 1990a; Eriksson et al. 1990b; Eriksson et al. 1992; Johansson et al. 1995, 1996)**
	Rabbit-pregnant females (DDT)	Gd4-7 (4 doses) or Gd 7-9 (3 doses) (G)	--	1-50	Decreased fetal weight on day 28	(Fabro et al. 1984; Hart et al. 1971; Hart et al. 1972)

Modified from Table 3-1 in ATSDR 2002

C, capsule; d, day(s); F, food; G, gavage; Gd, gestation day; PND, postnatal day; wk, week(s)

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