FINAL REPORT

TOXICOLOGICAL EVALUATION OF FOUR WOOD TREATING PRODUCTS

Basileum, Meganium, Radaleum and Tailileum

Prepared for National Portable Storage Association

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EXECUTIVE SUMMARY

Shipping containers are being used as modular units for building homes, office spaces and garages, however, there have been questions raised regarding the potential toxicity associated with the pesticides used in the flooring of the containers. The National Portable Storage Association (NPSA) contracted this review to evaluate the toxicity of four commonly used wood treatment products approved for glueline treatments of veneer-based plywood including Basileum (active pesticide ingredient - Phoxim), Meganium 2000/2003 (active pesticide ingredient – Chlorfenapyr), Radaleum (active pesticide ingredient - Cypermethrin) and Tailileum (active pesticide ingredient – Imidacloprid).

Based upon a review of the peer-reviewed toxicological literature which is summarized in this report, it is not expected that any potential exposure to these pesticides present in the flooring of the storage containers would pose an immediate or long-term health concern. The active ingredients in these products are approved for use in consumer products, as food-crop and ornamental-crop insecticides, and for veterinary applications on livestock and pets for control of parasites. These pesticides have been evaluated by the World Health Organization (WHO), Food and Agricultural Organization of the United Nations (FAO) and the United States Environmental Protection Agency (USEPA). Allowable Daily Intakes (ADIs) have been calculated for each of them. The ADI represents the amount of pesticide that a person can be exposed to daily for a lifetime without experiencing adverse health effects. Human health risk assessments have shown that exposure to these pesticides, either through ingestion of food with pesticide residues or through contact during application or surfaces with applied pesticide residues do not pose a concern for human health.

The active ingredients were classified as to their toxicity based upon the International Building Code definition of toxicity. Table ES-1 presents a summary of the toxicity classification of the active ingredients.

Pesticide (Active	Oral ¹	Dermal ²	Inhalation ³
Ingredient)			
Basileum	LD50 - <u>≥</u> 1400	LD50 >5000 mg/kg	LC50 - 2 - 4.6
(Phoxim)	mg/kg in rats.	in rats (not rabbits as specified in IBC	mg/L in rats for 4 hours ⁴
		definition).	liours
Toxic (Yes/No)	No	No	Yes
Meganium	LD50 – 1152	LD50 - >2000	LC50 - 0.83 mg/L
(Chlorfenapyr)	mg/kg in female rats; 441 mg/kg in male rats	mg/kg in rabbits	in rats for 4 hours ⁴
Toxic (Yes/No)	Yes (males)	No	Yes
Radaleum	LD50 - 247	LD50 >2460 mg/kg	LC50 - >2.5 mg/L
(Cypermethrin)	(males) and 309	in rabbits (abraded	for 4 hours ⁴
	(females) mg/kg in rats	skin)	
Toxic (Yes/No)	Yes	No	No
Tailileum	LD50 – 424 mg/kg	LD50 >5000 mg/kg	LC50 - >5.17 mg/L
(Imidacloprid)	in male rats; 450	in rats (not rabbits	for 4 hours ⁴
	mg/kg in female	as specified in IBC	
	rats	definition)	
Toxic (Yes/No)	Yes	No	No

Table ES-1: Summary of Active Ingredient Toxicity Classification

1. A chemical that has a median lethal dose (LD50) of more than 50 milligrams per kilogram, but not more than 500 milligrams per kilogram of body weight when administered orally to albino rats weighing between 200 and 300 grams each.

- 2. A chemical that has a median lethal dose (LD50) of more than 200 milligrams per kilogram, but not more than 1,000 milligrams per kilogram of body weight when administered by continuous contact for 24 hours (or less if death occurs within 24 hours) with the bare skin of albino rabbits weighing between 2 and 3 kilograms each.
- 3. A chemical that has a median lethal concentration (LC50) in air of more than 200 parts per million, but not more than 2,000 parts per million by volume of gas or vapor, or more than 2 milligrams per liter but not more than 20 milligrams per liter of mist, fume or dust, when administered by continuous inhalation for 1 hour (or less if death occurs within 1 hour) to albino rats weighing between 200 and 300 grams each.
- 4. Not 1 hour as specified in IBC definition, general rule multiply 4hr LC50 by 4 for dusts/mists to get 1 hour LC50.

Based upon this classification scheme, Radaleum and Tailileum are considered toxic by the oral route of exposure, Basileum is considered toxic by the inhalation route of exposure, and Meganium is considered toxic by the oral and inhalation route of exposure. None are considered toxic by the dermal route of exposure. However, it is important to note that many common household chemicals would be considered toxic under the IBC definition. For example, nicotine has an LD50 of 9 mg/kg (Fishel et al 2013) and would be classified as extremely toxic under the IBC, while aspirin has an oral LD50 of 200 mg/kg (Deichmann (ed). 1969), and caffeine has an oral LD50 of 192 mg/kg (Lewis (ed) 2004), both of which would be considered toxic under the IBC definition and are more toxic (i.e. lower LD/LC50 values) than Meganium, Radaleum and Tailileum.

Potential routes of exposure to these pesticides from the use of storage containers as modular units for homes or office spaces include inhalation through volatilization or dust during renovation activities, dermal contact with the pesticide in the flooring or through ingestion or inhalation of dust that contains the pesticide.

As discussed in the report, all of these pesticides are of very low volatility and therefore would not be expected to volatilize into the airspace at a level that would be of a health concern, therefore inhalation due to volatilization is not of concern.

Direct contact with the floor would generally be non-existent to minimal. An owner has the option to use the container flooring as a subfloor and install another floor covering on top of it, or if the container flooring is in good condition, to sand and polyurethane the treated wood. In all cases, direct contact would be eliminated as the flooring would either be underneath another material or would be sealed with the polyurethane.

During renovation activities, such as sanding the plywood floors, inhalation of wood dust impregnated with the pesticide could be of concern, however, the use of personal protective equipment such as long sleeves and pants and respiratory protection through the use of a dust mask would ameliorate such exposures. It would also be expected that subsequent to sanding, all surfaces would be cleaned, which would remove the impregnated wood dust from further potential exposure by occupants.

Therefore, based on this information, it is concluded that there is minimal to no health risk due to the pesticide-impregnated flooring used in storage containers. Additionally, it is TRC's best professional judgement that actual testing of the storage containers is unnecessary.

1.0 BACKGROUND

There is an aftermarket for surplus shipping containers which are being used as modular units for building homes, office spaces, garages, etc. A simple internet search reveals dozens of website dedicated to pictures, plans and businesses that provide pre-fabricated or custom-built container buildings. However, there are also a number of sites that discuss the potential toxicity associated with shipping container homes, including the pesticides used in the container floors.

Shipping containers are generally eight feet wide, eight to nine-and-a-half feet tall, and between 20 and 40 feet long. They are made of slow-rusting, corrugated steel, accessed via large doors at one or both ends, and possess load-bearing walls that allow them to be efficiently stacked. The floor of a shipping container is typically comprised of thick marine plywood which has been treated with pesticides in accordance with International Shipping Regulations. The Australian Government, Department of Agriculture and Water Resources (AU DAWR) provides a listing of timber permanent preservative formulations that are approved for use as biosecurity treatments as well as the minimum preservative retention for each formulation (AU DAWR 2015). The pesticide treatment prevents transfer of harmful insects from country to country and protects the contents from infestation and damage as well as protects the integrity of the flooring.

The National Portable Storage Association (NPSA) contracted this review to evaluate the exposure to four commonly used wood treatment products and the potential associated toxicity related to this alternative use of the containers. Four commonly used timber preservative formulations approved for glueline treatments of veneer-based products include Basileum (active pesticide ingredient - Phoxim), Meganium 2000/2003 (active pesticide ingredient – Chlorfenapyr), Radaleum (active pesticide ingredient - Cypermethrin) and Tailileum (active pesticide ingredient – Imidacloprid). Per the AU DAWR, plywood and laminated veneer lumber must be comprised of individual veneers up to 2.5 mm thick, the pesticides are applied as a glueline treatment during the lamination process and the preservative should penetrate the full thickness of each veneer.

This report provides a review of the peer-reviewed toxicological literature regarding the active ingredients of these four pesticides (technical grade).¹

The active ingredients were classified as to their acute toxicity based upon the International Building Code (IBC) definition of toxic. A common way to document toxicity is by the Lethal Dose 50% (LD50) or Lethal Concentration 50% (LC50) values. LD50 is the amount of chemical required to provide a "lethal dose" to 50% of the test population, while LC50 is the amount of chemical required to provide a "lethal concentration" to 50% of the population. LD50 is used for oral and dermal exposures and is measured in mg of chemical administered per kg of body weight, while LC50 is used for inhalation exposures and is measured in ppm (mg/cubic meter of air) or milligram per

¹ Note, the review of governing Agency summary documents did not include review of primary sources used in the summary documents.

liter of air (mg/L). An oral LD50 of 500 means that 500 mg of chemical was needed to obtain lethality in a 1 kg subject (e.g. a rabbit). The lower the LD50 value, the less chemical that is required to reach lethality. A chemical with an LD50 of 10 mg/kg is more acutely toxic than one with an LD50 of 100 mg/kg (Fishel et al 2013).

According to the IBC a chemical meeting any of the following categories is considered toxic:

- 1. A chemical that has a median lethal dose (LD50) of more than 50 milligrams per kilogram, but not more than 500 milligrams per kilogram of body weight when administered orally to albino rats weighing between 200 and 300 grams each.
- 2. A chemical that has a median lethal dose (LD50) of more than 200 milligrams per kilogram, but not more than 1,000 milligrams per kilogram of body weight when administered by continuous contact for 24 hours (or less if death occurs within 24 hours) with the bare skin of albino rabbits weighing between 2 and 3 kilograms each.
- 3. A chemical that has a median lethal concentration (LC50) in air of more than 200 parts per million, but not more than 2,000 parts per million by volume of gas or vapor, or more than 2 milligrams per liter but not more than 20 milligrams per liter of mist, fume or dust, when administered by continuous inhalation for 1 hour (or less if death occurs within 1 hour) to albino rats weighing between 200 and 300 grams each.

2.0 TOXICOLGICAL REVIEW

2.1 <u>Basileum</u>

The active ingredient in the wood treatment preservative Basileum is Phoxim (CAS #14816-18-3) which is an organophosphorus insecticide. It is used as a foliage and soil-applied insecticide (non-food crop), a seed dressing and is used for application on livestock against mites and ectoparasites (FAO/WHO, 1983). It is also used in consumer pesticide products such as crack and crevice ant control (liquid and powder) and in ant bait traps (Hahn et al. 2010). It has been banned for use on crops in the European Union since 2007. It is sold primarily in Europe under the following Trade Names: Baythion[®], Sebacil[®], Baymite[®], Byemite[®], and Sarnacuran[®].

2.1.1 Physical Chemical Parameters

The physical/chemical properties of Phoxim are presented in the table below. It is a light yellow oil, which is not very soluble in water. Based upon the vapor pressure and Henry's Law Constant, this chemical is of low volatility. Therefore, it would not be expected to volatilize from the treated storage container flooring.

Molecular weight	298.3 g/mol (1)	
Appearance	Light yellow oil (2)	
Melting Point	$5-6^{0}C(1)$	
Vapor Pressure	~7.5E-04 mmHg @ 20°C (1)	
Henry's Law Constant	2.02E-07 atm-m ³ /mole	
Water solubility	1.5 mg/L @20°C (1)	

(1) Gangolli, 1999

(2) JEFCA 2000.

2.1.2 Toxicity

Organophosphorus insecticides exert their acute effects in both insects and mammals by inhibiting acetylcholinesterase in the nervous system, which results in the toxic accumulation of the neurotransmitter acetylcholine. This results in over-stimulation of the parasympathetic nervous system and the neuromuscular system. Phoxim is toxic to insects but not very toxic to mammals. Phoxim is rapidly metabolized in mammals to non-toxic products (JEFCA 2000).

2.1.2.1 Animal Studies

Oral Exposure

Single-dose studies of toxicity in animals have shown Phoxim to be of low or moderate toxicity by the oral route of exposure in mammalian species (JEFCA 2000). The oral LD50 in rats was found to be equal to or greater than 1400 mg/kg (JEFCA 2000) and therefore is not considered toxic by the IBC.

Chronic (long-term), repeat dose studies of toxicity in animals have shown some liver effects, decreases in organ weights, and decreased plasma, and erythrocyte acetylcholinesterase activity when they were fed Phoxim at high doses. Phoxim did not cause cancer in animal tests (JEFCA 2000).

Inhalation Exposure

Exposure of multiple test species to aerosolized Phoxim for four hours, have shown it to be of moderate toxicity by the inhalation route of exposure. After inhalation, no signs of acetylcholinesterase inhibition were observed, even at the highest doses. Only non-specific effects were seen on the nervous system (JEFCA 2000). The inhalation LC50 in rats exposed to Phoxim for 4 hours was found to range from 2 - 4.6 mg/L (JEFCA 2000) and therefore is considered toxic by the IBC.

No other information was found regarding chronic or developmental studies by the inhalation route of exposure.

Dermal Exposure

Single-dose studies of toxicity in animals have shown Phoxim to be of low toxicity by the dermal route of exposure in mammalian species. There was no sign of adverse effects observed after dermal application (JEFCA 2000). The dermal LD50 in rats (not rabbits as specified by the IBC) was found to be greater than 5000 mg/kg (JEFCA 2000) and therefore is not considered toxic by the IBC.

Irritation and Sensitization

Phoxim was shown to cause only a slight irritation on rabbit's skin, and mild to moderate eye irritation without effects on the iris or cornea. It showed a 60% positive response in a Magnussen-Kligman maximization test with guinea pigs, but showed no sensitization in an open epicutaneous test, also with guinea pigs. The Magnussen-Kligman test uses an adjuvant which is a substance that will enhance the sensitizing effect during the test. The open epicutaneous test was conducted without an adjuvant (JEFCA 2000).

Genotoxicity and Carcinogenicity

Phoxim was tested for its ability to cause genetic mutations. All tests were negative with the exception of one study that found alterations in human lymphocytes *in vitro*, however, this was at a dose toxic to the cells. Therefore, it was concluded that Phoxim was not genotoxic and unlikely to have carcinogenic potential in humans (JEFCA 2000).

Reproductive and Developmental Toxicity

Phoxim was tested in animals to determine whether it was toxic to reproduction or to the developing fetus. Phoxim had a slight effect on reproduction by slightly reducing the number of rat pups in the second litter of the third generation that survived after four weeks of lactation from dams receiving Phoxim at the highest dose tested in their feed. Phoxim was not embryotoxic, fetotoxic or teratogenic in a developmental study with rats.

In a rabbit study, Phoxim caused embryotoxicity (increased resorptions) and fetotoxicity (reduced body weights) from dams fed the highest dose of Phoxim. This dose was also maternally toxic (decreased food consumption and body weight gain). It was not teratogenic (JEFCA 2000).

2.1.2.2 Human Studies

No studies were found regarding the toxicity of Phoxim to humans. The World Health Organization (WHO) in conjunction with the Food and Agricultural Organization of the United Nations (FAO) (JEFCA 2000) has developed an "Allowable Daily Intake" (ADI) based upon animal toxicity studies. The ADI of 0-4 micrograms per kilogram body weight per day (μ g/kg/day), is the total amount of Phoxim that can be ingested daily over a lifetime without an appreciable health risk. Current USEPA guidance (USEPA 2014a) recommends an average bodyweight of 80 kg for an adult and 15 kg for a child, age 0-6 years old for use in human health risk assessments. Therefore, the calculated ADIs are 320 and 60 μ g/day, respectively.

Schenk et al. (1997) evaluated human exposure to airborne pesticides measured in homes treated with wood preservatives. Phoxim was detected in an air sample collected in a home approximately four years after exposure at a concentration of 0.021 ug/cubic meter of air (m³). The calculated intake per day (assuming an adult is exposed for 24 hours/day and 100% of inhaled pesticide) was 0.42 ug/day at the measured air concentration. When compared to the calculated ADIs for an adult and child, it is significantly less than the allowable limit and therefore would not be associated with any health effects.

Hahn et al. (2010) evaluated consumer exposure to biocides to identify relevant sources of exposure and the possibility of health effects. Using worst-case exposure scenarios during the active use of ant insecticides containing Phoxim, it was determined that there was a potential for dermal sensitizing (allergic reactions) effects. However, it should be noted that only one study showed that Phoxim caused sensitization in a guinea pig model, the second study showed that it did not, therefore, this is a very conservative conclusion.

2.2 <u>Meganium 2000/2003</u>

The active ingredient in the wood treatment preservative Meganium 2000/2003 is Chlorfenapyr (CAS #122453-73-0), which is a "pro-insecticide", meaning that it is metabolized in the organism into an active insecticide. In the United States, Chlorfenapyr is registered for use on greenhouse food and non-food crops, and as an insecticide/termiticide for use on indoor and outdoor residential sites, food/feed handling areas, indoor and outdoor commercial sites (including sewers), and indoor medical sites (USEPA 2014b). In the U.S. it is sold as Phantom[®] Termiticide – Insecticide, Phantom[®] II bedbug spray and Pylon[®]. It is a broad spectrum insecticide and acaricide which acts through ingestion and contact. It is active against leafminers, thrips, mites and other pests as well as termites, cockroaches, ants, bedbugs, flies, spiders, centipedes and other pests (FAO 2014). The European Commission has approved Chlorfenapyr as an active ingredient in wood preservatives (EC 2012).

2.2.1 Physical Chemical Parameters

The physical/chemical properties of Chlorfenapyr are presented in the table below. It is a white to pale yellow solid, which is not very soluble in water. Based upon the vapor pressure and Henry's Law Constant, this chemical is of low volatility. Therefore, it would not be expected to readily volatilize from the treated storage container flooring.

Molecular weight	407.6 g/mol (1)
Appearance	White to pale yellow solid (2)
Melting Point	$101.4 - 102.3^{\circ}C(2)$
Vapor Pressure	4.89E-14 mmHg (1)
Henry's Law Constant	$5.73E-9 \text{ atm-m}^3/\text{mol}(3)$
Water solubility	0.11 g/L at 20°C (2)

(1) EC 2012 (2) FAO 2014

(3) PPDB 2017a

2.2.2 Toxicity

Chlorfenapyr works by disrupting the production of adenosine triphosphate (ATP), which transports chemical energy within cells which is then used as fuel during cellular processes. Disruption in the production of ATP causes cell death and ultimately mortality (USEPA 2014b).

2.2.2.1 Animal Studies

Oral Exposure

Single-dose lethality studies of acute toxicity in animals have shown Chlorfenapyr to be of low to moderate toxicity by the oral route of exposure in rat and mice test species, respectively (EC 2012, JMPR 2012). The oral LD50 of Chlorfenapyr in female rats is 1152 mg/kg and 441 mg/kg in male rats (EC 2012) and therefore is considered toxic by the IBC based upon the male rat data.

Repeat-dose studies of toxicity in animals have shown decreased food intake, decreased body weight and increased liver and spleen weights when they were fed Chlorfenapyr at high doses. Studies of neurotoxicity in rats showed reversible changes in the myelin sheath (a membrane wrapped around the nerve fibers) in the brain and spinal cord. Chlorfenapyr was not carcinogenic when tested in rats and mice (EC 2012, JMPR 2012).

Inhalation Exposure

In a whole-body exposure of rats to aerosolized Chlorfenapyr for four hours, Chlorfenapyr was shown to be of moderate toxicity (EC 2012, JMPR 2012). The inhalation LC50 in rats exposed to Phoxim for 4 hours was found to be 0.83 mg/L in male rats (EC 2012) and therefore is considered toxic by the IBC.

A repeat exposure study to Chlorfenapyr dust aerosol in rats resulted in the premature death of male animals at the highest concentration tested. The study continued with the lower exposure groups. No exposure-related changes in motor activity were noted. There were slight increases in white blood cell counts and a slight disturbance of coagulation was noted in the second highest concentration tested (JPMR 2012).

Dermal Exposure

A single-dose lethality study of acute toxicity in animals showed Chlorfenapyr to be of low toxicity by the dermal route of exposure in rabbits. There was no sign of adverse effects observed after dermal application (EC 2012, JMPR 2012). The dermal LD50 in rabbits was found to be greater than 2000 mg/kg (EC 2012) and therefore is not considered toxic by the IBC.

A repeat dose study in rabbits resulted in decreased red blood cell counts in the highest dose tested and increased serum cholesterol and increased liver weights at the two highest doses tested (JMPR 2012).

Irritation and Sensitization

Chlorfenapyr was shown to be non-irritating to rabbit's skin, and to cause slight eye irritation without effects on the iris or cornea. It was not a sensitizer in the guinea pig maximization test (EC 2012, JMPR 2012).

Genotoxicity and Carcinogenicity

Chlorfenapyr was tested for its ability to cause genetic mutations. All tests were negative. Therefore it was concluded that based on the lack of genotoxicity and absence

of carcinogenicity in the mouse and rat, Chlorfenapyr is unlikely to have carcinogenic potential in humans (EC 2012, JMPR 2012).

Reproductive and Developmental Toxicity

Chlorfenapyr was tested in animals to determine whether it was toxic to reproduction or to the developing fetus. Chlorfenapyr showed no developmental toxicity or teratogenicity and had no effect on fertility or reproduction at the highest doses tested (EC 2012, JMPR 2012).

2.2.2.2 Human Studies

There have been no reports of adverse health effects from Chlorfenapyr exposure in manufacturing plant personnel (JMPR 2012). There are case reports of suicide attempts through the ingestion of Chlorfenapyr (Tharaknath et al. 2013). An ADI for Chlorfenapyr of 0 to 30 ug/kg body weight per day was established by the FAO/WHO Meeting on Pesticide Residues (JMPR 2012). Based on current USEPA recommended bodyweights for an adult and child, the calculated ADIs are 2400 and 350 µg/day, respectively.

2.3 <u>Radaleum</u>

The active ingredient in the wood treatment preservative Radaleum is Cypermethrin (CAS #52315-07-8). Cypermethrin is a synthetic pyrethroid insecticide and is registered in the United States for both agricultural (crops such as cotton, pecans and broccoli and the treatment of livestock) and non-agricultural uses (commercial, industrial and residential pest control). It is used indoors primarily against cockroaches, ants, and fleas; outdoors, it is used primarily for outdoor structures, perimeter and turf for control of subterranean termites and other pests (USEPA 2008). It is sold in the US under the trade names Cyper[®], Demon[®], Fendona[®], Martins Viper[®], Cynoff[®], and ExciteR[®].

2.3.1 Physical Chemical Parameters

The physical/chemical properties of Cypermethrin are presented in the table below. It is a colorless liquid or a white crystalline powder, which is not very soluble in water. Based upon the vapor pressure and Henry's Law Constant, this chemical is of low volatility. Therefore, it would not be expected to readily volatilize from the treated storage container flooring.

Molecular weight	416.3 g/mol (1)
Appearance	Colorless liquid, white, crystalline powder (2, 3)
Melting Point	60-80 [°] C (2)
Vapor Pressure	3.1E-9 mmHg at 20°C (1)
Henry's Law Constant	$1.97E-7 \text{ atm-m}^3/\text{mol}(2)$
Water solubility	0.076 mg/L at 25°C (1)
(1) EPA 2008	

(2) PPDB 2017b

(3) Sigma Aldrich SDS

2.3.2 Toxicity

Cypermethrin works non-systemically by contact or through ingestion possibly through its blocking action on the way that nerves and the brain function (ATSDR 2003). Cypermethrin is a Type II pyrethroid, and includes a cyano group and is characterized by their elicitation of salivation and sinuous writhing as a symptom of poisoning in laboratory rodents (ATSDR 2003).

2.3.2.1 Animal Studies

Oral Exposure

Single-dose lethality studies of acute toxicity in animals have shown Cypermethrin to be highly toxic in mice to slightly toxic in rabbits by the oral route of exposure (Gupta, 1990, EPA 2006, WHO 2014). Clinical signs are typical of Type II pyrethroids including sedation, ataxia, splayed gait, tip-toe walking with occasional tremors and convulsions (JECFA 1996). The oral LD50 in rats was found to be 247 (males) to 309 (females) mg/kg (EPA 2006) and therefore is considered toxic by the IBC.

Repeat-dose studies of toxicity in animals have shown clinical signs of neurotoxicity in mammals but generally did not produce neuropathologic lesions. Neuromuscular effects such as gait abnormalities, tremors, decreased motor activity and convulsions occurred across species, sexes and routes of administration. The clinical signs occurred following acute exposures, but were transient in nature. They primarily occurred in oral studies in the dog and rat (USEPA 2006). Long-term studies in mice, rats and dogs were conducted to evaluate the potential for carcinogenicity. In mice, there was an increase in the incidence of benign lung tumors in females at the highest dose, however, the incidence was within historical controls. There were no increases in compound-related tumors in the rat and dog studies (JECFA 1996).

Inhalation Exposure

In a whole-body exposure of rats to aerosolized Cypermethrin for four hours, Cypermethrin was shown to be of low toxicity (JECFA 1996, EPA 2006). Rats tolerated inhalation for 4 hours of the maximum concentration of dust that could be produced. The LC50 was not calculated but determined to be higher than 2.5 mg/L (EPA 2006) and is therefore considered not toxic by the IBC.

Dermal Exposure

A single-dose lethality study in animals showed Cypermethrin to be of low toxicity by the dermal route of exposure in rabbits (JECFA 1996, EPA 2006). The dermal LD50 in rabbits was found to be greater than 2460 mg/kg (abraded skin) (EPA 2006) and therefore is considered not toxic by the IBC.

A repeat-dose study in rabbits showed slight to severe skin irritation after exposure to Cypermethrin on abraded skin for 6 h/day, 5 days/week for 3 weeks. Decreased food intake and body weights were observed at the highest dose (JECFA 1996).

Irritation and Sensitization

Cypermethrin was shown to be non-irritating to rabbit's skin, and to cause slight eye irritation without effects on the iris or cornea. It was not a sensitizer in the guinea pig maximization test (JECFA 1996).

Genotoxicity and Carcinogenicity

Cypermethrin was tested for its ability to cause genetic mutations. All tests were negative. Therefore, it was concluded that based on the lack of genotoxicity and absence of carcinogenicity in the mouse and rat, Cypermethrin is unlikely to have carcinogenic potential in humans (JECFA 1996).

Reproductive and Developmental Toxicity

Cypermethrin was tested in animals to determine whether it was toxic to reproduction or to the developing fetus. Cypermethrin showed no developmental toxicity or teratogenicity and had no effect on fertility or reproduction at the highest doses tested (JECFA 1996).

2.3.2.2 Human Studies

Cypermethrin has a relatively low toxicity to humans. The signs and symptoms of acute exposure from pyrethroids are similar to the animal models. Occupationally exposed individuals had abnormal skin sensations (burning, itching or tingling), dizziness, headache, nausea, anorexia, fatigue, coughing and difficulty breathing have been commonly reported (USEPA 2008, JEFCA 1996). Accidental ingestions or suicide attempts caused increased vomiting, chest tightness, paresthesia (tingling/numbness sensation), palpitations and blurred vision in exposed individuals (JECFA 1996). Reports have suggested that Cypermethrin can cause asthma or asthma-like symptoms in susceptible individuals (USEPA 2008).

Inhalation

There have been two reported cases of death from Cypermethrin as a result of a severe allergic reaction consistent with a reactive airway response. Both deaths were the result of using a dog shampoo on their pet. The shampoos contained 0.06% to 0.2% Cypermethrin. No information regarding contribution from inhalation or dermal exposure routes were addressed in the case reports (ATSDR 2003). No other reports were located addressing death in humans following exposure to Cypermethrin.

An ADI for Cypermethrin of 0 to 50 ug/kg body weight per day was established by the FAO/WHO Meeting on Pesticide Residues (JECFA 1996). Based on current USEPA recommended bodyweights for an adult and child, the calculated ADIs are 4000 and 750 μ g/day, respectively.

The USEPA conducted a human health risk assessment for Cypermethrin as part of its Reregistration Eligibility Decision for Cypermethrin (USEPA 2008). As part of the evaluation, USEPA considered residential exposures and evaluated acute residential handler exposures through inhalation as well as exposure to toddlers through inhalation

and ingestion from hand-to-mouth, object-to-mouth and incidental soil exposure. Residential handler inhalation risks were below USEPA's level of concern for nonoccupational handler scenarios. Since dermal toxicity is not a concern, dermal risks were not evaluated. Additionally, USEPA did not anticipate long-term adult exposures would occur to Cypermethrin, therefore, they were not addressed. Residential toddler risk was below a level of concern. Long-term inhalation risk to Cypermethrin is considered negligible, since the vapor pressure is very low.

2.4 <u>Tailileum</u>

The active ingredient in the wood treatment preservative Tailileum is Imidacloprid (CAS #138261-41-3). Imidacloprid has been registered for use in products in the United States since 1994 (Gervais, et al. 2010). Imidacloprid is currently registered for the following uses: Indoor and outdoor ornamental plantings, ornamental lawns and turf, pre- and post-construction termiticide applications, spot-on treatments for dogs and cats, and crack and crevice treatments. Additionally, it is registered for use on mattresses for bed bug control (USEPA 2010). It is sold in the US under the following Trade Names: Bayer Advanced[®] Complete Insect Killer, Merit[®] Insecticide Granules, Maxforce[®], Invict[®], Dominion[®], Advantage[®] flea treatment for cats and dogs.

2.4.1 Physical Chemical Parameters

The physical/chemical properties of Imidacloprid are presented in the table below. It is a beige powder, which is not very soluble in water. Based upon the vapor pressure and Henry's Law Constant, this chemical is of low volatility. Therefore, it would not be expected to readily volatilize from the treated storage container flooring.

Molecular weight	255.7 g/mol (1)
Appearance	Beige powder (1)
Melting Point	$144^{0}C(1)$
Vapor Pressure	3E-12 mmHg at 20°C (1)
Henry's Law Constant	$1.97\text{E}-15 \text{ atm-m}^3/\text{mol}(1)$
Water solubility	0.0006 mg/L at 20°C (1)

(1) JMPR 2008

2.4.2 Toxicity

Imidacloprid works by disrupting the nerve's ability to send a normal signal, interfering with normal nervous system activity. It is more toxic to insects than mammals and birds because it binds better to the receptors of the insect nerve cells (Gervais et al. 2010).

2.4.2.1 Animal Studies

Oral Exposure

Single-dose lethality studies of acute toxicity in animals have shown Imidacloprid to be of moderate toxicity by the oral route of exposure (USEPA 2010, FAO 2013). Transient signs and symptoms included behavioral and respiratory effects, disturbances of motility, and transient spasms and trembling observed in rats and mice (JMPR 2001). The oral LD50 in rats was found to be 424 (males) and 450 (females) mg/kg (FAO 2013) and therefore is considered toxic by the IBC.

Reduced body weight gain and liver effects were observed in repeat exposure studies in mice, rats and dogs, and slight effects on the thyroid gland were observed during repeat exposure studies dogs (JMPR 2001).

Inhalation Exposure

In a whole-body exposure of rats to Imidacloprid for four hours, Imidacloprid was shown to of low toxicity (USEPA 2010, FAO 2013). Rats tolerated inhalation for 4 hours of the maximum concentration of dust that could be produced. The inhalation LC50 in rats was found to be greater than 5.17 mg/L (FAO 2013) and therefore is not considered toxic by the IBC.

Dermal Exposure

A single-dose lethality study of acute toxicity in animals showed Imidacloprid to be of low toxicity by the dermal route of exposure in rabbits (USEPA 2010, FAO 2013). Very little toxicity was seen after dermal application. The dermal LD50 in rats (not rabbits as specified by the IBC) was found to be greater than 5000 mg/kg (FAO 13) and therefore is not considered toxic by the IBC.

Irritation and Sensitization

Imidacloprid was shown to be non-irritating to rabbit's skin or eyes. It was not a sensitizer in guinea pigs or mice (USEPA 2010, FAO 2013).

Genotoxicity/Carcinogenicity

Imidacloprid was tested for its ability to cause genetic mutations. All tests were negative. Therefore it was concluded that based on the lack of genotoxicity and absence of carcinogenicity animal models, Imidacloprid is unlikely to have carcinogenic potential in humans (USEPA 2010, FAO 2013).

Reproductive/Developmental Toxicity

Imidacloprid was tested in animals to determine whether it was toxic to reproduction or to the developing fetus. Imidacloprid showed no teratogenicity and had no effect on fertility or reproduction at the highest doses tested. In a rat developmental neurotoxicity study, at the highest dose tested, pup effects included decreased body weight, decreased motor activity and a decrease in the width of the caudate/putamen (the structure in the brain which prepares and aids in the movement of the limbs), however, this was at a dose that showed maternal toxicity (USEPA 2010).

2.4.2.2 Human Studies

There are a few case reports in the scientific literature regarding human exposure to Imidacloprid. Most reports are due to suicide attempts or to accidental overexposures. Signs of toxicity in these cases included drowsiness, dizziness, vomiting, disorientation, increased heart and respiratory rate, breathlessness and fever (Kumar et al. 2013).

An ADI for Imidacloprid of 0 to 60 ug/kg body weight per day was established by the FAO/WHO Meeting on Pesticide Residues (JMPR 2001). Based on current USEPA

recommended bodyweights for an adult and child, the calculated ADIs are 4800 and 900 μ g/day, respectively.

The USEPA conducted a human health risk assessment for Imidacloprid in support of its Final Rule for establishing pesticide tolerances for Imidacloprid (USEPA 2010). Since Imidacloprid is approved for indoor crack and crevice control use and bed-bug control, USEPA considered residential exposures through inhalation and dermal contact as well as exposure to toddlers through inhalation, dermal contact and ingestion from hand-to-mouth, object-to-mouth and incidental soil exposure. USEPA concluded "that there is a reasonable certainty that no harm will result to the general population, or to infants and children from aggregate exposure to Imidacloprid residues" (USEPA 2010).

3.0 CONCLUSIONS

Based upon a review of the peer-reviewed toxicological literature which is summarized in this report, it is not expected that any potential exposure to these pesticides present in the flooring of the storage containers would pose an immediate or long-term health concern. These products are approved for use in consumer products, as food-crop and ornamental-crop insecticides, and for veterinary applications on livestock and pets for control of parasites. These pesticides have been evaluated by the World Health Organization (WHO), Food and Agricultural Organization of the United Nations (FAO) and the USEPA. Allowable Daily Intakes (ADIs) have been calculated for each of them. The ADI represents the amount of pesticide that a person can be exposed to daily for a lifetime without experiencing adverse health effects. Human health risk assessments have shown that exposure to these pesticides, either through ingestion of food with pesticide residues or through contact during application or surfaces with applied pesticide residues do not pose a concern for human health.

Table 1 summarizes of the active ingredient toxicity classification based upon the IBC definition of toxicity.

Pesticide (Active	Oral ¹	Dermal ²	Inhalation ³
Ingredient)			
Basileum	LD50 - <u>≥</u> 1400	LD50 >5000 mg/kg	LC50 - 2 - 4.6
(Phoxim)	mg/kg in rats.	in rats (not rabbits	mg/L in rats for 4
		as specified in IBC	hours ⁴
		definition).	
Toxic (Yes/No)	No	No	Yes
Meganium	LD50 – 1152	LD50 - >2000	LC50 - 0.83 mg/L
(Chlorfenapyr)	mg/kg in female	mg/kg in rabbits	in rats for 4 hours ⁴
	rats; 441 mg/kg in		
	male rats		
			.
Toxic (Yes/No)	Yes (males)	No	Yes
Radaleum	LD50 - 247	LD50 >2460 mg/kg	LC50 - >2.5 mg/L
(Cypermethrin)	(males) and 309	in rabbits (abraded	for 4 hours ⁴
	(females) mg/kg in	skin)	
	rats		
	X 7		
Toxic (Yes/No)	Yes	No	No
Tailileum	LD50 – 424 mg/kg	LD50 >5000 mg/kg	LC50 - >5.17 mg/L
(Imidacloprid)	in male rats; 450	in rats (not rabbits	for 4 hours ⁴
	mg/kg in female	as specified in IBC	
	rats	definition)	
Toxic (Yes/No)	Yes	No	No

 Table 1: Summary of Active Ingredient Toxicity Classification

1. A chemical that has a median lethal dose (LD50) of more than 50 milligrams per kilogram, but not more than 500 milligrams per kilogram of body weight when administered orally to albino rats weighing between 200 and 300 grams each.

- 2. A chemical that has a median lethal dose (LD50) of more than 200 milligrams per kilogram, but not more than 1,000 milligrams per kilogram of body weight when administered by continuous contact for 24 hours (or less if death occurs within 24 hours) with the bare skin of albino rabbits weighing between 2 and 3 kilograms each.
- 3. A chemical that has a median lethal concentration (LC50) in air of more than 200 parts per million, but not more than 2,000 parts per million by volume of gas or vapor, or more than 2 milligrams per liter but not more than 20 milligrams per liter of mist, fume or dust, when administered by continuous inhalation for 1 hour (or less if death occurs within 1 hour) to albino rats weighing between 200 and 300 grams each.
- 4. Not 1 hour as specified in IBC definition, general rule multiply 4hr LC50 by 4 for dusts/mists to get 1 hour LC50.

Based upon this classification scheme, Radaleum and Tailileum are considered toxic by the oral route of exposure, Basileum is considered toxic by the inhalation route of exposure. None are considered toxic by the dermal route of exposure. However, it is important to note that many common household chemicals would be considered toxic under the IBC definition. For example, nicotine has an LD50 of 9 mg/kg (Fishel et al 2013) and would be classified as extremely toxic under the IBC, while aspirin has an oral LD50 of 200 mg/kg (Deichmann (ed). 1969), and caffeine has an oral LD50 of 192 mg/kg (Lewis (ed) 2004), both of which would be considered toxic under the IBC definition and are more toxic (i.e. lower LD/LC50 values) than Meganium, Radaleum and Tailileum.

Potential routes of exposure to these pesticides from the use of storage containers as modular units for homes or office spaces include inhalation through volatilization or dust during renovation activities, dermal contact with the pesticide in the flooring or through ingestion or inhalation of dust that contains the pesticide.

As discussed, all of these pesticides are of very low volatility and therefore, would not be expected to volatilize into the airspace at a level that would be of a health concern, therefore, inhalation due to volatilization is not of concern.

Direct contact with the floor would generally be non-existent to minimal. An owner has the option to use the container flooring as a subfloor and install another floor covering on top of it, or if the container flooring is in good condition, to sand and polyurethane the treated wood. In all cases, direct contact would be eliminated as the flooring would either be underneath another material or would be sealed with polyurethane.

During renovation activities, such as sanding the plywood floors, inhalation of wood dust impregnated with the pesticide could be of concern, however, the use of personal protective equipment such as long sleeves and pants and respiratory protection through the use of a dust mask would ameliorate such exposures. It would also be expected that subsequent to sanding, all surfaces would be cleaned, which would remove the impregnated wood dust from further potential exposure by occupants.

Therefore, based on this information, it is concluded that there is minimal to no health risk due to the pesticide-impregnated flooring used in storage containers. Additionally, it is TRC's best professional judgement that actual testing of the storage containers is unnecessary.

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