Proposed Re-evaluation Decision PRVD2020-04

Ziram and Its Associated End-use Products, Used as a Preservative in Adhesives

Consultation Document

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Proposed Re-evaluation Decision

Under the authority of the *Pest Control Products Act*, all registered pesticides must be regularly re-evaluated by Health Canada's Pest Management Regulatory Agency (PMRA) to ensure that they continue to meet current health and environmental safety standards and continue to have value. The re-evaluation considers data and information from pesticide manufacturers, published scientific reports, and other regulatory agencies. Health Canada applies internationally accepted risk assessment methods as well as current risk management approaches and policies.

This document forms part of a re-evaluation assessment of several active ingredients used as preservatives in paints, coatings and related uses. As per Re-evaluation Note REV2018-02, *Approach for the Re-Evaluation of Pesticides Used as Preservatives in Paints, Coatings and Related Uses*, the paint-related uses of sodium omadine, chlorothalonil, dazomet, folpet and ziram were evaluated separately from other uses and relied on data provided by the registrants and the Antimicrobial Exposure Assessment Task Force II (AEATF II). This approach was adopted in order to obtain and review paint-related studies, have risk assessments more reflective of current and realistic exposure scenarios and to allow for a consistent approach to the risk assessment and risk management for these uses. Paint studies/data were also used as surrogates for the assessment of building materials and adhesives.

This document presents the proposed regulatory decision for the re-evaluation of ziram, used as a preservative in adhesives, including the proposed risk mitigation measures to further protect human health, as well as the science evaluation on which the proposed decision was based. All products registered in Canada containing ziram for use as a preservative in adhesives are subject to this proposed re-evaluation decision. This document is subject to a 90-day public consultation period, during which the public, including the pesticide manufacturers and stakeholders, may submit written comments and additional information to Health Canada. The final re-evaluation decision will be published taking into consideration the comments and information received.

Ziram is an "in-can" material preservative used to control bacterial and fungal degradation of dry starch and synthetic latex adhesives. The only other registered use of ziram, as a protectant fungicide in agriculture, was evaluated separately (Re-evaluation Decision RVD 2018-39, *Ziram and Its Associated End-use Products for Agricultural Uses*); all registered agricultural uses in Canada were cancelled. Therefore, all remaining registered products in Canada are solely for use as material preservatives in adhesives (Appendix I).

Outcome of Science Evaluation

With respect to human health, when using ziram as a material preservative risks of concern were identified for occupational workers (mixing/loading the end-use product and handling the impregnated dry starch and latex adhesives) and residential handlers; risks were not shown to be acceptable when used according to label directions. Therefore, cancellation of material preservative uses of ziram in adhesives is proposed.

Proposed Regulatory Decision for Ziram

Under the authority of the *Pest Control Products Act* and based on the evaluation of currently available scientific information, the registration of products containing ziram for use as a material preservative in Canada is proposed for cancellation. In accordance with PRVD2016-06 and RVD2018-39, all agricultural uses of ziram have been cancelled and all maximum residue limits (MRLs) will be revoked (Proposed Maximum Residue Limit PMRL2019-08, *Ferbam, Thiram and Ziram*). Therefore, cancellation of the material preservative use will also result in cancellation of all remaining registered ziram products.

International Context

Ziram is currently acceptable for use in other Organisation for Economic Co-operation and Development (OECD) member countries, including the United States, the European Union (agricultural use only) and Australia. No decision by an OECD-member country to prohibit all uses of this active for health or environmental reasons has been identified.

Next Steps

The public, including the registrants and stakeholders, are encouraged to submit additional information that could be used to refine the risk assessment during the 90-day public consultation period[1] upon publication of this proposed re-evaluation decision.

All comments received during the 90-day public consultation period will be taken into consideration in preparation of the re-evaluation decision document,[2] which could result in revised risk mitigation measures. The re-evaluation decision document will include the final re-evaluation decision, the reasons for it and a summary of comments received on the proposed re-evaluation decision with Health Canada's responses.

Additional Scientific Information

No additional scientific data are being requested. However, during the consultation period, the registrants and other stakeholders may consider submitting the following information that may address uncertainties in the available information database of ziram and support refined risk assessment. In addition, stakeholders may consider providing information on risk management options for ziram (for example, additional PPE, engineering controls).

The evaluation of any additional data would be based on the scientific merit and relevance to the risk assessment. While additional data may reduce uncertainty in the risk assessment, continued registration of any uses would be based on the acceptability of risk assessed using a science-based approach.

1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

Additional detailed use description information and other data/information that may allow further refinement of the risk assessment:

- Actual daily amounts of ziram-treated adhesives handled by professional secondary handlers
- Chemical-specific dermal absorption studies conducted with adhesive formulations

Science Evaluation

1.0 Introduction

Ziram is used as an "in-can" material preservative of adhesives. The use of ziram as a protectant fungicide in agriculture was evaluated separately (Proposed Re-evaluation Decision PRVD2016-06, *Ziram* and Re-evaluation Decision RVD2018-39, *Ziram and Its Associated End-use Products for Agricultural Uses*). Only human health (exposure) and value assessments related to the use of ziram as a material preservative are presented herein; these assessments replace those previously presented in PRVD2016-06 for this specific use. Environmental exposure from this use is expected to be minimal.

Appendix I lists all ziram products that are registered for use as a material preservative under the authority of the *Pest Control Products Act*.

2.0 Human Health Assessment

2.1 Toxicology Summary

See PRVD2016-06 and RVD2018-39.

2.2 Dietary Exposure and Risk Assessment

No dietary exposure is anticipated from the material preservative use of ziram in dry starch and latex adhesive products.

2.3 Exposure from Drinking Water

Residues of ziram in potential drinking water sources are not anticipated as a result of the preservative uses.

2.4 Residential and Occupational Exposure and Risk Assessment

Residential and occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating uncertainty factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required.

2.4.1 Toxicology Reference Values for Occupational and Residential Risk Assessment

See PRVD2016-06 and RVD2018-39.

Dermal Absorption

During the consultation period for PRVD2016-06, a human in vitro study (PMRA# 2647410) was submitted and reviewed together with a rat in vivo dermal absorption study (PMRA# 1210449), previously submitted to the Agency.

Human in vitro study

Dermal absorption of [^{14}C]-ziram from a Ziram 76 wettable granular formulation was evaluated in vitro with automated flow-through diffusion cells using non-viable human skin samples. Authors tested skin samples for adequate barrier integrity; however, did not exclude those cells that exceeded the acceptable threshold from the study. Nominal doses of approximately 15 and 6400 µg/cm^2 of [^{14}C]-ziram in a formulation blank were applied and 6-7 cells per dose group were analysed. [^{14}C]-ziram was analyzed in the receptor cell at regular time intervals over 24 hours and skin was washed at 6 hours. After the last receptor fluid sample was collected, the skin membrane surface and the diffusion cell were thoroughly rinsed and the wash matrices were analyzed for radioactivity. Each skin membrane was stripped to remove the stratum corneum. Recovery of the applied dose (mass balance) was deemed acceptable and average recovery ranged from 90-94% for the two dose groups, including all cells. Some cells had recoveries that were outside of the acceptable range in the low dose group. Results including, excluding, and extrapolating for the cells with low recoveries were reported in the study review.

The majority of the administered dose was recovered from the skin wash in both dose groups. Approximately 0.1% and 7% of the applied dose was removed by the tape strips for the high and low dose groups, respectively, with 0.15% or less remaining in the skin. The average amount of the applied dose in the low dose group is primarily being driven by one cell (cell 8) where the skin wash appears to have been incomplete, since the sum of the top two tape strips and the skin wash for this cell is similar to that reported for the skin wash in the other cells. Estimates of dermal absorption were based on the sum of residues retained in the skin (exposed and unexposed skin) + receptor fluid (including compartment rinse and wash) + tape strips.

Calculated dermal absorption values were 5% for the low dose group and 0.2% for the high dose group. These values are considered to be conservative estimates as all residues in the skin were considered to be absorbed, and skin membranes that failed the skin barrier test were included in the calculations.

Rat in vivo study

Dermal absorption of [^{14}C]-ziram was evaluated *in vivo* in male Charles River rats. Nominal doses of 68, 688, and 6880 µg/cm^2 [^{14}C]-ziram in a Ziram 87.3 wettable powder formulation blank were applied to the backs of rats. Rats were sacrificed using 4 rats per dose level at time points of 0.5, 1, 2, 4, 10, and 24 hours. A skin wash occurred following sacrifice. Following each sacrifice event, urine, faeces, cage wash/wipe, blood, skin test site, carcass, stripping skin wash, dose enclosure, and cell cover were collected and analyzed for recovery via liquid scintillation counting (LSC).

Average recovery of the applied dose for the high dose group was acceptable and ranged from 97 to 104%. However, average recovery of the applied dose for the low and medium doses were unacceptable and ranged from 71 to 89 %. Unrecovered radioactivity was included in the calculated absorbed dose, as expired air was not monitored in this study and is a major route of excretion for ziram. The majority of the administered dose was recovered from the skin wash for all dose groups. The amount of the applied dose retained at the application site ranged from 0.6 to 10%. Estimates of dermal absorption were based on the sum of residues retained at the skin test site + urine (including cage wash and rinse) + faeces + carcass + blood + unrecovered administered dose.

For the 10 and 24 hour exposure/sacrifice groups, mean dermal absorption (including the amount of applied dose not recovered) ranged from 29 to 30%, 27 to 31%, and 2% for the low, medium, and high dose groups, respectively. These values are considered to be conservative as all of the residues at the skin site were assumed to become bioavailable and the unrecovered radioactivity was included in the dermal absorption value.

Major limitations were identified for this study, such as unacceptable mass balance for the low and medium dose groups, variability in the dose solutions, and radioactivity in the expired air was not measured. Despite these limitations, this study is considered to be acceptable to estimate the dermal absorption of ziram for human health risk assessment.

Based on the data available, a dermal absorption value of 2% was selected for mixers/loaders of the commercial class dust product during the manufacture of adhesive products. A dermal absorption value of 30% was selected for all other scenarios related to material preservative uses. These values are not expected to underestimate exposure, as there are conservatisms with the values selected.

2.4.2 Residential Exposure and Risk Assessment

Residential risk assessment involves estimating risks to the general population, including youth and children, during or after pesticide application.

A residential applicator assessment for the ziram preservative itself was not required, since there are no registered domestic-class pesticide products for adhesive-related material preservatives. Residential handling of adhesives preserved with ziram is considered as a postapplication scenario.

The following postapplication scenarios were assessed:

- Individuals applying dry starch and synthetic latex adhesives preserved with ziram; and
- Dermal contact with surfaces to which dry starch and synthetic latex adhesives preserved with ziram were applied.

2.4.2.1 Residential Postapplication Exposure and Risk Assessment

Residential postapplication exposure occurs when an individual is exposed through dermal, inhalation and/or incidental oral (non-dietary ingestion) routes as a result of handling a product that has been treated with a pesticide, or being in a residential environment that has been previously treated with a pesticide.

Dry starch and synthetic latex adhesive products

To estimate exposure to residential handlers applying dry starch and synthetic latex adhesives preserved with ziram, the following relevant assumptions and algorithms were used in conducting the risk assessment:

There is potential for short-term exposure for residential handlers (≥16 years old) applying products preserved with ziram, via the dermal and inhalation routes. In the absence of use description information, the default amount of paint handled per day from the USEPA 2012 Residential SOP (PMRA# 2409268) by a residential painter (7.58 L) was used as a surrogate for the amount of adhesive handled. Likewise, in the absence of a scenario-specific exposure study, the brush and roller study (2018; PMRA# 2849401) submitted by the Antimicrobial Exposure Assessment Task Force (AEATF) II was used as a surrogate for applying dry starch and synthetic latex adhesives.

The brush and roller study was designed to quantify dermal and inhalation exposures to both occupational and residential painters while applying paint, containing an antimicrobial, using a brush or roller. The study monitored 18 test subjects using a brush and/or roller in six identical rooms in a warehouse space. The surrogate non-volatile active ingredient used in this study was 1,2-benzisothiazolin-3-one (BIT). The total amount of paint handled (8.520 to 9.940 kg), the time spent while painting (48 to 172 min), and the surface area painted (25 to 82.5 m^2), were all measured. Dermal exposures were measured using inner and outer cotton whole body dosimeters, painter's hat, hand washes (all subjects did not wear gloves) and face and neck wipes. Inhalation exposures were measured using air sampling tubes. Separate dermal unit exposure values were generated for residential painters wearing a short-sleeved shirt and shorts and for occupational workers wearing a long-sleeved shirt, long pants and no gloves. The inhalation unit exposure values for both occupational and residential handlers were generated for each individual performing light activities. The total dermal and inhalation unit exposure values were presented as arithmetic lognormal mean (AMu) of all test subjects.

Using the unit exposure values from this study, assuming the clothing scenario of a residential handler to be shorts and a short-sleeved shirt, the combined (dermal and inhalation) non-cancer risks from applying dry starch and synthetic latex adhesives were not shown to be acceptable. Similarly, the lifetime cancer risks were not shown to be acceptable when amortizing the exposure over the lifetime, assuming residential handlers would use the treated products 4 days per year for 50 years with a life expectancy of 78 years. To mitigate this risk, it is proposed that the use of ziram as a material preservative be cancelled. See Appendix II, Table 1 for more information.

To determine the potential transfer of preservative residues from a surface treated with dry starch and synthetic latex adhesives that contain ziram, paint transferable residue studies (PMRA# 2967976 and 2883917) were submitted by the AEATF II. These studies demonstrated that the transfer of residues onto the skin following contact with a painted surface is minimal. Hence exposure to ziram is expected to be negligible. Based on the findings of these studies, a quantitative residential postapplication risk assessment for contact with a treated surface for preservatives used in dry starch and synthetic latex adhesives was not required.

Bystander Exposure

Bystander exposure is expected to be negligible for the preservative uses of ziram.

2.4.3 Occupational Exposure and Risk Assessment

There is potential for exposure to ziram in occupational scenarios when workers handle the pesticide during the mixing and loading process in industrial (manufacturing) settings and for postapplication exposure to workers handling products treated with ziram.

2.4.3.1 Mixer, Loader and Applicator Exposure and Risk Assessment

There is potential for exposure to workers who mix and load the commercial class dust product when manufacturing dry starch and synthetic latex adhesives. Therefore, the following scenario was assessed:

- Mixing/transfer of solids, open pour

Exposure to ziram from its use in manufacturing is expected to be long-term in duration, via the dermal and inhalation routes.

Chemical-specific exposure data were not available for ziram for this scenario. However, solid pour exposure studies (PMRA# 2834812) were submitted by the AEATF II.

These solid pour studies were designed to determine the dermal and inhalation exposures to occupational workers (primary handlers) when open pouring two solid formulations (powder and granules) containing an antimicrobial.

Four different pouring scenarios were considered in this study. Two scenarios involved pouring powder and granular formulations in an occupational setting and the other two considered pouring powder and granular formulations in a residential setting. Study details are provided for the occupational scenarios only. The surrogate active ingredient used was cyanuric acid (1,3,5-triazine-2,4,6-triol, CAS number 108-80-5). Eighteen occupational workers poured the solid products into an indoor mix tank.

Each subject was randomly assigned two monitoring numbers to account for two consecutive monitoring events, starting with the granules followed by the powder formulation, to minimize the potential for cross contamination. All scenarios included manual pouring and/or scooping from different heights, using various sized containers.

Dermal exposure was measured using inner and outer cotton whole body dosimeters, hand washes and face and neck wipes. All subjects were also given safety glasses and a dust mask. Subjects in the occupational scenario wore chemical-resistant gloves. Inhalation exposures were measured using IOM air sampling tubes (Institute of Occupational Medicine).

Separate dermal unit exposure values were generated for occupational workers wearing different levels of personal protective equipment. The inhalation unit exposure values for occupational handlers were generated for each individual performing light activities. The total dermal and inhalation unit exposure values were presented as the AMu of all test subjects.

The unit exposure values from the solid open pour study were combined with the default amounts of paint (also used as a surrogate for building materials) treated per day by workers in manufacturing facilities to estimate exposures. The amounts of paint treated per day were based on the USEPA Antimicrobial Division Draft Summary of Amounts Handled or Treated for Occupational Handler Scenarios[3], where it was assumed that facilities may treat up to 7571 L (9388 kg) of paint per day.

Calculated MOEs for mixing/transfer of the commercial-class dust product did not reach the target MOE or the lifetime cancer risk of 1×10^{-5}, when used according to the label directions. For risks to be acceptable, the maximum label rate must be reduced, workers must wear additional PPE and not handle more than 2.935 kg a.i./person/day (Appendix III, Table 1). Nevertheless, as postapplication exposures were not shown to be acceptable (see Section 2.4.3.2), it is proposed that the use of ziram as a material preservative be cancelled.

2.4.3.2 Postapplication Worker Exposure and Risk Assessment

There are no available data to quantify potential exposure to workers handling dry starch and synthetic latex adhesives preserved with ziram.

Exposure to ziram in dry starch and synthetic latex adhesives impregnated with ziram is expected to be long-term in duration (that is, >180 days), via the dermal and inhalation routes.

In the absence of use description information, the default amount of paint applied per day by a worker using a brush and roller was used as a surrogate for the amount of adhesive handled per day (23.2 kg/day). Likewise, in the absence of chemical-specific and scenario-specific exposure data, the exposure study submitted by the AEATF II for the application of paint using a paint brush and roller (PMRA# 2849401) was used as a surrogate for the application of adhesives.

Calculated MOEs did not reach the target MOE or the lifetime cancer risk (1×10^{-5}) even at the lowest label rate. Therefore, it is proposed that the use of ziram in dry starch and latex adhesives be cancelled. Appendix III, Table 2 summarizes the non-cancer and cancer risks to professional workers.

[3] PMRA# 3084493. USEPA (2018). Summary of Amounts Handled or Treated for Occupational Handler Scenarios. EPA: Washington, DC.

2.5 Aggregate Exposure and Risk Assessment

Aggregate exposure is the total exposure to a single pesticide that may occur from food, drinking water, residential and other non-occupational sources, and from all known or plausible exposure routes (oral, dermal and inhalation).

In an aggregate risk assessment, the combined potential risk associated with food, drinking water and various residential exposure pathways is assessed. A major consideration is the likelihood of co-occurrence of exposures. Additionally, only exposures from routes that share common toxicological endpoints can be aggregated.

In the case of dry starch and synthetic latex adhesives impregnated with ziram, residential risks of concern were identified; therefore, an aggregate exposure and risk assessment was not conducted.

2.6 Cumulative Assessment

The *Pest Control Products Act* requires that the PMRA consider the cumulative effects of pest control products that have a common mechanism of toxicity.

As the use in dry starch and latex adhesives is proposed for cancellation, a cumulative risk assessment for the material preservative scenario was not required.

2.7 Incident Reports

As of 20 December 2019, no human or domestic animal incidents involving ziram as a material preservative were submitted to the PMRA.

3.0 Value Assessment

Ziram is registered as a material preservative in adhesives. It is incorporated into products during manufacturing, to provide protection from bacterial and fungal degradation.

This active ingredient is effective at controlling the various micro-organisms responsible for degrading adhesive products, when used as currently directed on the registered product labels.

Protection of these products is important to industry as degradation of the products can lead to a failure of the product to perform its intended purpose, discoloration, odour formation or other complications arising from bacterial or fungal growth.

4.0 Conclusion of Science Evaluation

4.1 Human Health

Based on the evaluation of currently available scientific information, cancellation of the use of ziram as a preservative in dry starch and synthetic latex adhesives is proposed in order to protect professional and residential users (secondary handlers). As there are no other registered uses of ziram, cancellation of the use of ziram will entail cancellation of all remaining registered ziram products.

4.2 Value

Ziram is used to control bacterial and fungal degradation in dry starch and synthetic latex adhesives in order to prevent deleterious effects imposed on the product by the degrading organisms. Alternatives are available for industry to utilize.

List of Abbreviations

µg	microgram
% w/w	percent weight per weight, concentration of solute in solution
AEATF II	Antimicrobial Exposure Assessment Task Force II
a.i.	active ingredient
AMu	arithmetic lognormal mean
BIT	1,2-benzisothiazolin-3-one
bw	body weight
CF	conversion factor
cm	centimetre(s)
g	gram(s)
IOM	Institute of Occupational Medicine
kg	kilogram(s)
L	litre(s)
LADD	lifetime average daily dose
LSC	liquid scintillation counting
m	metre(s)
m^2	square meters
mg	milligram(s)
min	minute(s)
mL	millilitre(s)
MOE	margin of exposure
MRL	maximum residue limit
NOAEL	no observed adverse effect level
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
PRVD	Proposed Re-evaluation Decision
REV	Re-evaluation Note
RVD	Re-evaluation Decision
USEPA	United States Environmental Protection Agency

Appendix I Products Used as Preservatives in Adhesives

Table 1 Ziram Products Used as Preservatives in Adhesives as of 23 December 2019.

Registrant	Registration Number	Product Name	Marketing Class
Taminco US LLC.	28426	Ziram Technical (98.4%)	T
	30858	Vancide MZ-98	C

T = technical grade active ingredient; C = commercial
Note: Discontinued products and products with submissions for discontinuation not included.

Appendix II Non-Occupational (Residential) Risk Assessment

Table 1 Non-Cancer (Short-Term) and Cancer Residential Exposure and Risk Assessment

Scenario	Application rate (g a.i./kg adhesive)[a]	Amount handled per day (g a.i./day)[b]	Unit exposure value[c] (µg/kg a.i.)		Daily exposure[d] (mg/kg bw/day)			Margin of exposure (MOE)[e]			LADD[h] (mg/kg bw/day)	Cancer Risk[i]
			Dermal	Inhalation	Dermal	Inhalation	Combined	Dermal[f]	Inhalation[f]	Combined[g]		
Shorts, short-sleeved shirt, no gloves												
Brush and roller	4.92	46	237445	17.3	0.04	0.00001	0.04	121	500000	121	0.00029	5×10^{-6}
	1.82	17	237445	17.3	0.02	0.000004	0.02	328	1351314	328	0.00011	2×10^{-6}

Shaded cells indicate where the MOE is less than the target MOE (300) or the cancer risk is greater than 1×10^{-6}

[a] Application rate = Product application rate (0.5% [max] or 0.185% [min] w/w) × a.i. guarantee × CF (1000 g/kg)

[b] Amount handled per day = Application rate × amount of adhesives applied/day (7.58 L using brush and roller) × paint density (1.24 kg/L; surrogate for adhesives)

[c] Unit exposure values from AEATF II brush and roller study

[d] Dermal or inhalation daily exposure = [Amount handled per day × Unit exposure value × CF (1 mg/1000 µg) × CF (1 kg/1000 g) × Absorption (30% dermal or 100% inhalation)]/80 kg bw. Combined daily exposure = Dermal exposure + inhalation exposure

[e] MOE = NOAEL/Daily exposure

[f] Dermal and inhalation NOAEL of 5 mg/kg bw/day from rat developmental neurotoxicity study and target MOE of 300.

[g] Combined MOE = NOAEL/ (combined daily exposure) and target MOE of 300.

[h] LADD = Combined daily exposure × frequency of exposure (4 days/year) × exposure duration (50 years) / (365 days/year × life expectancy (78 years))

[i] Cancer risk = LADD × q_1* (1.82×10^{-2} (mg/kg bw/day)$^{-1}$)

Appendix III Occupational Risk Assessment

Table 1 Occupational Long-Term (Non-Cancer and Cancer) Exposure and Risk Assessment for Use of Ziram in Manufacturing Facilities Using Solid, Open Pour Scenario

Use	Application rate (g a.i./kg adhesives)[a]	Amount handled per day (g a.i./day)[b]	Unit exposure value[c] (µg/kg a.i.)		Daily exposure[d] (mg/kg bw/day)			Margin of Exposure (MOE)[e]			LADD[i] (mg/kg bw/day)	Cancer Risk[j]
			Dermal	Inhalation	Dermal	Inhalation	Combined	Dermal[f]	Inhalation[f]	Combined[g]		
Single layer, chemical-resistant gloves												
Adhesives	4.92	46188	585	575.71	0.0068	0.3324	0.3392	104	2	2	0.1191	2×10^{-3}
	1.82	17090	585	575.71	0.0025	0.1230	0.1255	280	6	6	0.0440	8×10^{-4}
Chemical-resistant coveralls over single layer, chemical-resistant gloves, respirator												
Adhesives	4.92	46188	198	57.571	0.0023	0.0332	0.0355	306	21	20	0.0125	2×10^{-4}
	1.82	17090	198	57.571	0.0008	0.0123	0.0131	827	57	53	0.0046	8×10^{-5}
	1.82	2935	198	57.571	0.0001	0.0021	0.0022	4819	331	310	0.0008	1×10^{-5}

Shaded cells indicate where the MOE is less than the target MOE (100) or the cancer risk is greater than 1×10^{-5}

[a] Application rate = Product application rate (0.5% [max] or 0.185% [min] w/w) × a.i. guarantee × CF (1000 g/kg)

[b] Amount handled per day = Application rate × maximum amount of adhesives treated per day (7571 L) × paint density (1.24 kg/L; surrogate for adhesives). The amount of 2395 g a.i./day results in MOEs that are not of concern.

[c] Unit exposure values from the AEATF II solid pour study

[d] Dermal or inhalation daily exposure = [Amount handled per day × Unit exposure values × CF (1 mg/1000 µg) × CF (1 kg/1000 g) × Absorption (2% dermal or 100% inhalation)]/80 kg bw. Combined daily exposure = Dermal exposure + inhalation exposure

[e] MOE = NOAEL/Daily exposure

[f] Dermal and inhalation NOAEL of 0.7 mg/kg bw/day from a 2-year rat dietary study and a target MOE of 100.

[g] Combined MOE = NOAEL/ (combined daily exposure) and target MOE of 100.

[h] LADD = Combined daily exposure × frequency of exposure (250 days/year) × exposure duration (40 years) / (365 days/year × life expectancy (78 years))

[i] Cancer risk = LADD × q_1* (1.82×10^{-2} (mg/kg bw/day)$^{-1}$)

Table 2 Professional Handler Long-Term (Non-Cancer and Cancer) Exposure and Risk Assessment

Scenario	Application rate (g a.i./kg adhesives)[a]	Amount handled per day (g a.i./day)[b]	Unit exposure value[c] (µg/kg a.i.)		Daily exposure[d] (mg/kg bw/day)			Margin of Exposure (MOE)[e]			LADD[h] (mg/kg bw/day)	Cancer Risk[i]
			Dermal	Inhalation	Dermal	Inhalation	Combined	Dermal[f]	Inhalation[f]	Combined[g]		
Single layer, no gloves												
Brush and roller	4.92	114	175871	17.3	0.0752	0.00002	0.0753	9	28374	9	0.00661	1×10^{-4}
	1.82	42	175871	17.3	0.0278	0.00001	0.0278	25	76685	25	0.00244	5×10^{-5}

Shaded cells indicate where the MOE is less than the target MOE (100) or the cancer risk is greater than 1×10^{-5}

[a] Application rate = Product application rate (0.5% [max] or 0.185% [min] w/w) × a.i. guarantee × CF (1000 g/kg)

[b] Amount handled per day = Application rate × maximum amount of adhesives treated per day (18.7 L) × paint density (1.24 kg/L; surrogate for adhesives)

[c] Unit exposure values from the AEATF II brush and roller study

[d] Dermal or inhalation daily exposure = [Amount handled per day × Unit exposure value × CF (1 mg/1000 µg) × CF (1 kg/1000 g) × Absorption (30% dermal or 100% inhalation)]/80 kg bw. Combined daily exposure = Dermal exposure + Inhalation exposure

[e] MOE = NOAEL/Daily exposure

[f] Dermal and inhalation NOAEL of 0.7 mg/kg bw/day from a 2-year rat dietary study and a target MOE of 100.
[g] Combined MOE = NOAEL/ (dermal exposure + inhalation exposure) and target MOE of 100.
[h] LADD = Combined daily exposure × frequency of exposure (250 days/year) × exposure duration (10 years) / (365 days/year × life expectancy (78 years))
[i] Cancer risk = LADD × q_1* (1.82×10^{-2} $(mg/kg\ bw/day)^{-1}$)

Appendix IV Proposed Label Amendments For End-Use Products Containing Ziram

The use of ziram as a material preservative in adhesives is proposed for cancellation.

Therefore, the following products are proposed for cancellation:

- Dust products for dry starch and synthetic latex adhesives
  - Technical Product [Registration Number: 28426]
  - Commercial End-use Product [Registration Number: 30858]

References

A. Information Considered for the Toxicology Assessment

Studies Submitted by the Registrant

PMRA Document Number	Reference
2647410	2006, Ziram (76 WG) In Vitro Dermal Penetration Study at Two Dose Levels Using Human Skin, DACO: 5.8
1210449	1991, Dermal Absorption of 14C- Ziram in Male Rats, DACO: 4.3.8

B. Information Considered for the Occupational and Residential Assessment

Published Information

PMRA Document Number	Reference
2409268	USEPA (2012a). Standard Operating Procedures for Residential Pesticide Exposure Assessment. EPA: Washington, DC. Revised October 2012.

AEATF II Studies

PMRA Document Number	Reference
2834812	A Study for Measurement of Potential Dermal and Inhalation Exposure During Manual Pouring of Two Solid Formulations Containing an Antimicrobial. American Chemistry Council, Antimicrobial Exposure Assessment Task Force II, Washington, DC. (AEATF II) Project ID: AEA07.
2849401	A Study for Measurement of Potential Dermal and Inhalation Exposure During Application of a Latex Paint Containing an Antimicrobial Pesticide Product Using a Brush and Roller for Indoor Surface Painting. Antimicrobial Exposure Assessment Task Force II (AEATF II), Washington, DC. January 31, 2018 Project ID: AEA09.
2967976	Analysis of Propiconazole Used as an In-Can Paint Preservative in Wall Wipe Samples Collected from Dried Paint During An Airless Paint Monitoring Study. American Chemistry Council, Antimicrobial Exposure Assessment Task Force II (AEATF II). (AEATF II) Project ID: AEA10.
2883917	Analysis of 1,2-Benzisothiazolin-3-one (BIT) in Background Wall Wipe Samples from Indoor Wall Surfaces Painted with Latex Paint Using a Brush and Roller (Non-GLP). Antimicrobial Exposure Assessment Taskforce II (AEATF II), Washington, DC. (AEATF II) Project ID: AEA19.