M E M O R A N D U M

TO: Jagjinder Sahota, MS, Chief
Worker Health and Safety Branch
Department of Pesticide Regulation

VIA: Shelley DuTeaux, PhD, MPH, Chief
Human Health Assessment Branch
Department of Pesticide Regulation

Shelley DuTeaux

FROM: Eric Kwok, PhD, DABT, Senior Toxicologist
Exposure Assessment Section
Human Health Assessment Branch
Department of Pesticide Regulation

Eric Kwok

Ian Reeve, PhD, Staff Toxicologist (Specialist)
Exposure Assessment Section
Human Health Assessment Branch
Department of Pesticide Regulation

Ian Reeve

DATE: September 8, 2021

SUBJECT: Revised Memorandum on Recalculation of Short-Term Handler and Reentry Worker Exposure Estimates for Propargite and Calculation of the Corresponding Margins of Exposure for Purposes of Mitigation (Memo Revised to Incorporate 3 CCR 6793 Personal Protective Equipment (PPE) Requirements into Handler Exposure Estimates)

---

This memorandum supersedes the October 5, 2020 memorandum titled, "Recalculation of Short-Term Handler and Reentry Worker Exposure to Propargite and Calculation of the Corresponding Margins of Exposure for Purposes of Mitigation." The revision incorporates protection factors (Thongsinthusak, Ross, & Meinders, 1993) for applicable 3 CCR 6793 (Minimal Exposure Pesticide Safety Requirements) PPE into the handler exposure estimate calculations.

The exposure assessment document (EAD) and risk characterization document (RCD) for propargite were published in 2013 and 2014, respectively (Dong, 2013; Lewis, 2014). In the ensuing years, there have been label changes for the registered products which affect the application rates and crops in California. Therefore, at the request of DPR's Worker Health and Safety Branch, all handler and reentry worker exposures have been recalculated based on the latest policies of Human Health Assessment (HHA) Branch, current product labels, and regulatory requirements. The values included in this memorandum represent updated margins of exposure (MOEs) based on the toxicological points of departure in the 2014 RCD. All short-term MOEs for the propargite exposure scenarios identified on the most current labels were updated for handlers. In addition, the short-term MOEs associated for each crop on current labels were updated for reentry workers. The MOEs herein supersede the MOEs for systemic and localized dermal effects in applicators, mixer/loaders, human flaggers, and fieldworkers in the previous memo and those originally published in Tables 26 – 33 of the 2014 RCD.

The MOE is a quantitative tool used by HHA to determine the potential risk arising from exposure to a pesticidal active ingredient. An MOE is defined as the ratio of the point of departure (POD) to the anticipated human exposure. The resulting value is compared to the acceptable or target MOE. Values at or above the target MOE are generally considered as having no health concern. Short-term risk estimates for both dermal and inhalation exposures (detailed below) were calculated for product label handler and reentry worker scenarios.

Human exposure to propargite occurs via both inhalation and dermal routes. To assess occupational risk, inhalation and dermal exposures were combined to reflect reasonable worse-case scenarios as workers may be exposed by both routes simultaneously. To characterize the systemic effects of propargite via inhalation, PODs from inhalation exposures are needed. However, as explained in the 2014 RCD, suitable animal inhalation studies are not available to derive the POD values. In addition, due to the highly corrosive nature of propargite, any inhalation study longer than an acute duration is not recommended (U.S. EPA, 2019). When suitable inhalation data are not available, it is HHA's practice to conduct a route-to-route extrapolation from oral studies to evaluate risks of inhalation exposure. For assessing the human health risk associated with short-term inhalation exposure to propargite, an acute inhalation POD of 0.8 mg/kg/day was derived from an acute oral POD of 0.8 mg/kg/day (i.e., oral-to-inhalation extrapolation assuming 100% inhalation absorption) (Lewis, 2014; Lewis, 2020; Frank, 2008). The RCD also lists an acute dermal POD of 17 mg/kg (Lewis, 2014; Lewis, 2020). However, for assessing the potential occupational health risks associated with combined exposures, the inhalation and dermal PODs need to be based on a common toxicological endpoint. In the absence of a common endpoint, the POD associated with the most sensitive endpoint is selected. In the case of propargite, the most sensitive endpoint (i.e., developmental toxicity observed in a rabbit oral study) was also used to derive the acute dermal POD by employing oral-to-dermal extrapolation assuming 17% dermal absorption in humans. For characterizing the localized (irritation) effects of propargite, an acute dermal POD of 0.7 $mg/cm^2$ was used (Lewis, 2014; Lewis, 2020). The target MOE for systemic effects based on the acute oral POD is 100. The target MOE for localized dermal effects is 30. All toxicity endpoints, critical PODs, and associated uncertainty factors for propargite are summarized in (Lewis, 2020) (see Appendix I).

Short term absorbed daily doses (STADDs) were updated from the 2013 EAD (Dong, 2013). The handler exposure estimates were calculated using currently registered propargite product labels, the Pesticide Handler Exposure Database (PHED) (Beauvais, Powell, & Zhao, 2007), and Title 3 (Food and Agriculture) of the California Code of Regulations (CCRs).

Numerous CCRs apply to handlers of propargite. While the product labels allow for the use of an open mixing/loading system for most use sites or crops listed on the labels, 3 CCR 6746(c) requires the use of a closed mixing/loading system in all cases for products containing propargite. The regulation states, "Employees who mix liquid pesticide products, excluding adjuvants, bearing the statement 'May be fatal if absorbed through skin' or 'Corrosive, causes skin damage' or other comparable language shall use a closed mixing system that is capable of enclosing the pesticide while removing the contents from its original container, preventing the pesticide from contacting handlers…"

The product labels for propargite contain "comparable" language:

- Comite: "Corrosive. Causes irreversible eye damage. Causes skin burns…Harmful if absorbed through skin."
- Decimite and Endomite: "Corrosive. Causes skin burns and irreversible eye damage. Harmful if… absorbed through skin."
- Mitomax 6EC: "Corrosive. Causes irreversible eye damage… Harmful if… absorbed through skin."
- Omite-6E: "Corrosive. Causes skin burns… Causes substantial but temporary eye injury. Harmful if absorbed through skin."
- Victimite: "Corrosive. Causes skin burns and irreversible eye damage… Harmful if… absorbed through skin."

Omite 30-WS contains similar language. However, unlike the previously mentioned products, which are liquid concentrates, Omite 30-WS comes in a wettable powder formulation enclosed in a water soluble bag (i.e., a closed mixing/loading system). According to 3 CCR 6746(e), when using a closed mixing/loading system, "PPE requirements may be reduced or modified as provided in section 6738.4."

- 3 CCR 6738.4(c): "Protective eyewear, coveralls, chemical-resistant gloves, and a chemical-resistant apron may be worn instead of personal protective equipment required by pesticide product labeling when using a closed system to handle pesticide products with the signal word 'DANGER' or 'WARNING.'"

According to 3 CCR 6790 propargite is one of four Minimal Exposure Pesticides. Therefore, 3 CCR 6793(c) and (d)(1) apply and these regulations add chemical-resistant footwear to the list of PPE required by 3 CCR 6738.4(c).

Title 3 CCRs 6793, and 6738.1 apply to the applicator handling propargite. Both regulations require the handler to wear a coverall. In addition, according to 3 CCR 6793(d) and (d)(4), except for “applicators using equipment with vehicle-mounted spray nozzles directed downward and located below the level of the employee,” which would include the aerial and ground boom application methods, the handler must wear full-body chemical-resistant clothing which, according to 3 CCR 6738.1(g), must cover the torso, head, arms, and legs. 3 CCR 6793(e), (e)(1), and (e)(1)(C), require respiratory protection for applicators using hand application methods or ground application methods, except for, “applicators using equipment with vehicle-mounted spray nozzles directed downward and located below the level of the employee” (e.g., ground boom).

There are also CCR requirements which apply to the flagger handling propargite. 3 CCR 6738.1(e) and 6793(c) require the handler to use coveralls while 3 CCR 6793(d) requires the handler to wear full-body chemical-resistant protective clothing.

Three handwand exposure scenarios (i.e., high-pressure and low-pressure handwand mixer/loader/applicator (M/L/A), and backpack M/L/A) were assessed for propargite. However, these PHED data subsets incorporate open pour liquid mixing/loading. Based on 3 CCR 6746(c), use of open pour mixing/loading would not be allowed for products containing propargite. However, due to a lack of data and the lack of language on the product labels prohibiting the use of handwand application methods, these PHED data subsets were utilized to estimate exposure. The exposure estimates for these scenarios, due to the use of open pour mixing/loading, would likely be greater than the corresponding estimates for scenarios using closed mixing/loading systems. Based on the applicable CCRs, the handler in this exposure scenario is assumed to wear full-body chemical-resistant clothing, coveralls, chemical-resistant gloves, protective eyewear, chemical resistant shoes, and a respirator.

Although not required by the aforementioned CCRs, work clothing, in the form of a long-sleeved shirt and long pants, could potentially be worn by the handler underneath the required PPE. Several product labels require the handler to wear a long-sleeved shirt and long pants underneath a coverall. The protection factor used for the long-sleeved shirt and long pants, which is defined as covering everything but the head, neck, hands, and feet, is 90% (Thongsinthusak et al., 1993). Certain handlers (i.e., airblast applicator, applicators using hand-wand methods, and flaggers), are required by 3 CCR 6793 to wear full-body chemical-resistant protective clothing over a coverall. When calculating exposure estimates, it was assumed that these handlers did not wear a long-sleeved shirt and long pants underneath the coverall. According to 3 CCR 6000, “’Coverall’ means a one- or two-piece garment of closely woven fabric or equivalent that covers the entire body, except the head, hands, and feet, and must be provided by the employer as personal protective equipment. Coverall differs from, and should not be confused with, work clothing that can be required to be provided by the employee". In scenarios where full-body chemical-resistant clothing is not required but a coverall is required, the worker was assumed to wear a long-sleeved shirt and long pants underneath the coverall.

Each handler exposure estimate consists of the 90% upper confidence limit on the 95$^{th}$ percentile of the PHED data and incorporates the product label maximum application rate and protection factors for work clothing, if applicable, and the required PPE (Beauvais et al., 2007; Frank, 2007; Thongsinthusak et al., 1993). Also incorporated into the estimate are the number of acres treated per day (U.S. EPA, 2001), the absorption rate (dermal absorption is 17% (Dong, 2013) and inhalation absorption is 100% (Frank, 2008)), and the default body weight of 70 kg for the worker (U.S. EPA, 1997). A combined dermal and inhalation STADD was calculated for each worker scenario. Systemic toxicity endpoint MOEs were then calculated using the combined STADD and the systemic oral POD of 0.8 mg/kg/day. Table 1 lists the highest STADD value and associated systemic toxicity endpoint MOE for each handler exposure scenario. MOEs below the target value of 100 indicate a concern.

Table 1. Highest Handler Short-Term Absorbed Daily Dosages (STADDs) and Corresponding Margins of Exposure (MOEs) for Systemic Toxicity

| **Exposure Scenario** [a] | **STADD** [b] **(mg/kg/day)** | **MOE** [c] **(target = 100)** |
|---|---|---|
| Ground Application Method Mixer/Loader (closed system, liquids, w/gloves) | 0.039 | 21 |
| Ground Application Method Mixer/Loader (wettable powder, water soluble pouch, w/gloves) | 0.019 | 43 |
| Ground Boom Applicator (open cab) | 0.068 | 12 |
| Aerial Application Method Mixer/Loader (closed system, liquid, w/gloves) | 0.232 | 3 |
| Aerial Application Method Mixer/Loader (wettable powder, water soluble pouch, w/gloves) | 0.066 | 12 |
| Aerial Applicator (liquid, open cockpit) | 0.632 | 1 |
| Airblast Application Method Mixer/Loader (closed system, liquids) | 0.010 | 82 |
| Airblast Application Method Mixer/Loader (water soluble bags containing wettable powder, with gloves) | 0.008 | 106 |

| | | |
|---|---|---|
| Airblast Applicator, open cab (w/gloves) | 0.472 | 2 |
| Flagger (liquids) | 0.150 | 5 |
| High-Pressure Handwand M/L/A (open pour liquid M/L) [d] | 1.743 | 0.5 |
| Low-Pressure Handwand M/L/A (open pour liquid M/L) [d] | 0.021 | 38 |
| Backpack M/L/A (open pour liquid M/L) [d] | 0.072 | 11 |

[a] The Pesticide Handler Exposure Database (PHED) exposure data for the hands, arms, legs, and torso were obtained from patch dosimeters located underneath the long-sleeved shirt, long pants, and gloves worn by the handler. Exposures were adjusted for the use of additional required personal protective equipment.

[b] The STADD value for each exposure scenario was generated using the associated PHED data subset short-term exposure rate in µg/lb of AI handled (Beauvais et al, 2007), the maximum product label application rate, the absorption factor (17% for dermal and 100% for inhalation), (Dong, 2013; Frank, 2008), the number of acres treated/day (U.S. EPA, 2001), and the body weight (70 kg) (U.S. EPA, 1997). Each STADD value was rounded to 3 decimal places:

Formulae:

STADD (dermal route of exposure) = [(PHED short-term dermal [non-hand] exposure rate (adjusted for use of required PPE) in µg/lb of AI handled + PHED short-term hand [with gloves] dermal exposure rate in µg/lb of AI handled) x (dermal absorption factor) x (number of acres treated/day) x (maximum product label application rate in lbs of AI/acre)]/(70 kg body weight)

STADD (inhalation route of exposure) = [(PHED short-term inhalation exposure rate in µg/lb of AI handled) x (inhalation absorption factor) x (number of acres treated/day) x (maximum product label application rate in lbs of AI/acre)]/(70 kg body weight)

STADD = STADD (dermal route of exposure) + STADD (inhalation route of exposure)

Sample Calculation (Ground Application Method Mixer/Loader [closed system, liquids, w/gloves])

STADD (dermal route of exposure) = [(9.28148 µg/lb AI handled + 19.27068 µg/lb AI handled) x 0.172 x (200 acres treated/day) x (2.53125 lbs of AI/acre)]/70 kg body weight = 35.51685 µg/kg/day or 0.03551685 mg/kg/day

STADD (inhalation route of exposure) = (0.43712 µg/lb AI handled) x 1 x (200 acres treated/day) x (2.53125 lbs of AI/acre)/70 kg body weight = 3.16131 µg/kg/day or 0.00316131 mg/kg/day

STADD = 0.03551685 mg/kg/day + 0.00316131 mg/kg/day = 0.039 mg/kg/day

[c] MOE = Acute oral systemic point of departure (0.8 mg/kg/day) ÷ STADD (mg/kg/day); target MOE = 100 (Lewis, 2020).

[d] The mixing/loading method for this scenario is open pour of liquid. 3 CCR 6746(c) requires that all methods using propargite utilize a closed mixing/loading system. However, due to a lack of data this PHED scenario was used. These data likely overestimate exposures.

As mentioned earlier, workers wearing full-body chemical-resistant clothing over a coverall are assumed to not wear a long-sleeved shirt and long pants underneath the coverall. Moreover, workers not wearing full-body chemical-resistant clothing over a coverall are assumed to wear a long-sleeved shirt and long pants underneath the coverall. Table 2 shows the percent reduction in the STADD produced by the long-sleeved shirt and long pants in each handler exposure scenario. The handlers wearing the full-body chemical-resistant clothing over a coverall are the airblast applicator (open cab, with gloves), flagger (liquids), high-pressure handwand mixer/loader/applicator (M/L/A) (open pour liquid M/L), low-pressure handwand M/L/A (open pour liquid M/L), and backpack M/L/A (open pour liquid M/L). The impact of the long-sleeved shirt and long pants on the STADD varies amongst scenarios depending on the bodily distribution and levels of pesticide deposition. For example, if the bulk of exposure occurs on areas covered by the long-sleeved shirt and long pants (i.e., everything but the head, neck, hands, and feet) (Thongsinthusak et al., 1993), and the pesticide amounts are enough to penetrate the external layer(s) (i.e., coverall or full-body chemical-resistant clothing over coverall), then the additional layer of work clothing is effective at reducing exposure. In most cases, the reduction created by the additional work clothing layer is insufficient to result in an acceptable MOE.

Table 2. Long-Sleeved Shirt and Long Pants: Impact on Handler Short-Term Absorbed Daily Dosage (STADD)

| **Exposure Scenario** [a] | **(+) Long-Sleeved Shirt and Long Pants** | | **(-) Long-Sleeved Shirt and Long Pants** | | **% Reduction in STADD via Use of Long-Sleeved Shirt and Long Pants** [d] |
|---|---|---|---|---|---|
| | **STADD** [b] **(mg/kg/day)** | **MOE** [c] **(target = 100)** | **STADD** [b] **(mg/kg/day)** | **MOE** [c] **(target = 100)** | |
| Ground Application Method Mixer/Loader (closed system, liquids, w/gloves) | 0.039 | 21 | 0.064 | 13 | 39 |
| Ground Application Method Mixer/Loader (wettable powder, water soluble pouch, w/gloves) | 0.019 | 43 | 0.044 | 18 | 57 |
| Ground Boom Applicator (open cab) | 0.068 | 12 | 0.122 | 7 | 44 |
| Aerial Application Method Mixer/Loader (closed system, liquid, w/gloves) | 0.232 | 3 | 0.384 | 2 | 40 |
| Aerial Application Method Mixer/Loader (wettable powder, water soluble pouch, w/gloves) | 0.066 | 12 | 0.155 | 5 | 57 |
| Aerial Applicator (liquid, open cockpit) | 0.632 | 1 | 1.735 | 1 | 64 |
| Airblast Application Method Mixer/Loader (closed system, liquids) | 0.010 | 82 | 0.016 | 50 | 38 |
| Airblast Application Method Mixer/Loader (water soluble bags containing wettable powder, with gloves) | 0.008 | 106 | 0.018 | 45 | 56 |
| Airblast Applicator, open cab (w/gloves) | 0.465 | 2 | 0.472 | 2 | 1 |
| Flagger (liquids) | 0.140 | 6 | 0.150 | 5 | 7 |
| High-Pressure Handwand M/L/A (open pour liquid M/L) [e] | 1.305 | 0.6 | 1.743 | 0.5 | 25 |
| Low-Pressure Handwand M/L/A (open pour liquid M/L) [e] | 0.020 | 41 | 0.021 | 38 | 7 |
| Backpack M/L/A (open pour liquid M/L) [e] | 0.020 | 41 | 0.072 | 11 | 72 |

[a] The Pesticide Handler Exposure Database (PHED) exposure data for the hands, arms, legs, and torso were obtained from patch dosimeters located underneath the long-sleeved shirt, long pants, and gloves worn by the handler. Exposures were adjusted for the use of additional required personal protective equipment and, depending on the handler exposure scenario, the long-sleeved shirt and long pants.
[b] The STADD value for each exposure scenario was generated using the associated PHED data subset short-term exposure rate in µg/lb of AI handled (Beauvais et al, 2007), the maximum product label application rate, the absorption factor (17% for dermal and 100% for inhalation), (Dong, 2013; Frank, 2008), the number of acres treated/day (U.S. EPA, 2001), and the body weight (70 kg) (U.S. EPA, 1997). Each STADD value was rounded to 3 decimal places:

Formulae
STADD (dermal route of exposure) = [(PHED short-term dermal [non-hand] exposure rate (adjusted for use of required PPE) in µg/lb of AI handled + PHED short-term hand [with gloves] dermal exposure rate in µg/lb of AI handled) x (dermal absorption factor) x (number of acres treated/day) x (maximum product label application rate in lbs of AI/acre)]/(70 kg body weight)

STADD (inhalation route of exposure) = [(PHED short-term inhalation exposure rate in µg/lb of AI handled) x (inhalation absorption factor) x (number of acres treated/day) x (maximum product label application rate in lbs of AI/acre)]/(70 kg body weight)

STADD = STADD (dermal route of exposure) + STADD (inhalation route of exposure)

Sample Calculation (Ground Application Method Mixer/Loader [closed system, liquids, w/gloves])
STADD (dermal route of exposure) = [(9.28148 µg/lb AI handled + 19.27068 µg/lb AI handled) x 0.172 x (200 acres treated/day) x (2.53125 lbs of AI/acre)]/70 kg body weight = 35.51685 µg/kg/day or 0.03551685 mg/kg/day

STADD (inhalation route of exposure) = (0.43712 µg/lb AI handled) x 1 x (200 acres treated/day) x (2.53125 lbs of AI/acre)/70 kg body weight = 3.16131 µg/kg/day or 0.00316131 mg/kg/day

STADD = 0.03551685 mg/kg/day + 0.00316131 mg/kg/day = 0.039 mg/kg/day

[c] MOE = Acute oral systemic point of departure (0.8 mg/kg/day) ÷ STADD (mg/kg/day); target MOE = 100 (Lewis, 2020).

[d] Percent Reduction in STADD

$$= 100\% \text{ x} \left( \frac{\text{STADD without long sleeved shirt and long pants} - \text{STADD with long sleeved shirt and long pants}}{\text{STADD without long sleeved shirt and long pants}} \right)$$

[e] The mixing/loading method for this scenario is open pour of liquid. 3 CCR 6746(c) requires that all methods using propargite utilize a closed mixing/loading system. However, due to a lack of data this PHED scenario was used. These data likely overestimate exposures.

In addition to systemic toxicity, propargite has a dermal irritation toxicity endpoint with a POD of 0.7 mg/cm$^2$. The exposure estimates generated for calculating the MOEs utilized the body part (i.e., head, neck, chest, back, upper arms, lower arms, thighs, lower legs, feet, and hands), surface pesticide amounts used to calculate the STADDs and the corresponding body part surface areas (Beauvais et al., 2007; Beauvais, 2007). As with the STADDs, the body part surface concentration calculations incorporated protection factors for the required PPE and, depending on the handler scenario, long-sleeved shirt and long pants. The dermal toxicity endpoint MOEs below 30 are presented in Table 3. MOEs below this target value indicate a concern.

Table 3. Handler Body Parts with Associated Dermal Toxicity Estimated Margins of Exposure (MOEs) < 30

| **Exposure Scenario** | **Patch Location** [a] | **MOE** [b] **(target = 30)** |
|---|---|---|
| Airblast Applicator, open cab (w/gloves) | head (all) | 5 |
| Aerial Application Method Mixer/Loader (closed system, liquids, w/gloves) | hand (w/gloves) | 11 |
| Aerial Applicator (liquid, open cockpit) | head (all) | 19 |
| | hand (w/gloves) | 6 |
| Flagger (liquids) | hand (w/gloves) | 28 |
| High-Pressure Handwand Mixer/Loader/Applicator (open pour, liquid Mixer/Loader) [c] | head (all) | 6 |
| | hand (w/gloves) | 2 |

[a] The Pesticide Handler Exposure Database (PHED) (Beauvais et al., 2007) exposure data for the arms, legs, torso, and hands were obtained from dosimeters located underneath the long-sleeved shirt, long pants, and gloves worn by the handler. Exposures were adjusted for the use of additional required personal protective equipment and, depending on the handler exposure scenario, long-sleeved shirt and long pants.
[b] Margin of Exposure (MOE) = Acute local dermal point of departure (0.7 mg/cm$^2$) ÷ surface concentration in mg/cm$^2$; target MOE = 30 (Lewis, 2020).
[c] The mixing/loading method for this scenario is open pour of liquid. 3 CCR 6746(c) requires that all methods using propargite utilize a closed mixing/loading system. However, due to a lack of data, this PHED (Beauvais et al., 2007) scenario was used. These data likely overestimate actual exposures.

Table 4 lists the reentry worker exposure scenario and associated STADD and MOE for each crop group represented on the product labels. The STADD and associated MOE either represent the highest exposure case or the only case present on the product labels. Exposure estimates were calculated for workers entering the treated field immediately after the REI or PHI. Crop-specific REIs are listed on the product label and in 3 CCR 6772. This regulation requires that the REI used for a given crop be the longer of the two provided. Reentry worker exposures were estimated according to this requirement.

Table 4. Reentry Worker Short-Term Absorbed Daily Dosages (STADDs) and Estimated Systemic Toxicity Margins of Exposure (MOEs) for each Crop Group Represented on the Product Labels [a]

| Crop Group | Reentry Activity [b] | STADD (mg/kg/day) [c] | MOE (target = 100) [d] |
|---|---|---|---|
| Field/Row (sweet corn) | Scouting | 0.012 | 67 |
| | Irrigation (hand-set) | 0.021 | 39 |
| | Weeding (hand) | 0.001 | 1057 |
| | Detasseling | 0.095 | 8 |
| | Harvesting (hand) | 0.035 | 23 |
| Vegetable, Root (potato) | Scouting | 0.001 | 1020 |
| | Irrigation (hand set) | 0.007 | 113 |
| | Weeding (hand) | 0.000 | 3060 |
| Nut Trees (almond) | Scouting | 0.013 | 64 |
| | Orchard maintenance | 0.002 | 370 |
| | Transplanting | 0.005 | 161 |
| | Poling | 0.002 | 370 |
| | Harvesting (mechanical shaking) | 0.003 | 282 |
| Bunch/Bundle (hop) | Scouting | 0.006 | 138 |
| | Irrigation (hand-set) | 0.017 | 47 |
| | Weeding (hand) | 0.006 | 138 |
| | Stripping | 0.006 | 138 |
| | Transplanting | 0.002 | 385 |
| | Tying and Training | 0.006 | 138 |
| | Harvesting (mechanically assisted) | 0.013 | 63 |
| Fruit Trees (dates) | Scouting | 0.008 | 105 |
| | Hand-weeding | 0.001 | 607 |
| | Hand-pruning | 0.018 | 43 |
| | Dethorning tree | 0.018 | 43 |
| | Transplanting | 0.003 | 264 |
| Vine/Trellis (table grapes) | Scouting | 0.002 | 335 |
| | Tying/Training | 0.021 | 39 |
| | Hand Pruning | 0.002 | 335 |
| | Irrigation (hand-set) | 0.007 | 113 |
| | Hand-weeding | 0.002 | 335 |
| | Transplanting | 0.001 | 931 |
| | Leaf Pulling | 0.021 | 39 |
| | Girdling | 0.072 | 11 |
| | Turning | 0.072 | 11 |

Table 4. Reentry Worker Short-Term Absorbed Daily Dosages (STADDs) and Estimated Systemic Toxicity Margins of Exposure (MOEs) for each Crop Group Represented on the Product Labels [a]

| Crop Group | Reentry Activity [b] | STADD (mg/kg/day) [c] | MOE (target = 100) [d] |
|---|---|---|---|
| | Harvesting (hand) | 0.021 | 39 |
| Berry, low (blueberries, low bush) | Scouting | 0.013 | 63 |
| | Weeding | 0.001 | 985 |
| | Irrigation (hand-set) | 0.022 | 36 |
| | Transplanting | 0.003 | 300 |
| Evergreen Trees (Christmas trees) | Hand-pruning/shaping | 0.016 | 52 |
| | Scouting | 0.016 | 52 |
| | Hand-weeding | 0.003 | 299 |
| | Irrigation (hand-set) | 0.051 | 16 |
| | Transplanting | 0.006 | 130 |
| | Grading/tagging | 0.003 | 299 |
| Flowers, cut (roses, field grown) | Container moving | 0.003 | 246 |
| | Pinching | 0.003 | 246 |
| | Hand-pruning | 0.003 | 246 |
| | Hand-weeding | 0.003 | 246 |
| | Irrigation (hand-set) | 0.027 | 30 |
| | Scouting | 0.003 | 246 |
| | Transplanting | 0.003 | 246 |

[a] The transfer coefficient (TC) and dislodgeable foliar residue (DFR) values for a given activity and representative crop were incorporated into the following formula developed by Zweig *et al*. (1984 and 1985). The ADD is the absorbed daily dosage:

$$\text{ADD } (\mu g / kg / day) = \frac{\text{DA} \times \text{DFR } (\mu g / cm^2) \times \text{TC } (cm^2 / hour) \times \text{ED } (hours / day)}{\text{BW(kg)}}$$

The assumed exposure duration (ED) is 8 hours, the dermal absorption (DA) rate is 17.2%, and the adult bodyweight is 70 kg (U.S. EPA, 1997). Crop groups and TC values were obtained from U.S. EPA's Scientific Advisory Panel for Exposure (ExpoSAC) Policy 3 document (U.S. EPA, 2017). The specific crop in parenthesis underneath the group is the only product label crop in the group or the crop with the highest associated reentry worker exposure estimates. The restricted entry interval (REI) and preharvest interval (PHI) DFR values were estimated using regression analysis of registrant propargite DFR data (Andrews, 2000). DFR values were adjusted to the product label maximum application rate. If the worker enters the treated field post-restricted entry interval (REI), no protective personal equipment is required. Hence, protection factors were not incorporated into the exposure estimates. The Short-Term Absorbed Daily Dosage (STADD) values were rounded to 3 decimal places.
[b] Reentry activity: activities carried out by workers entering the treated field immediately after the REI or PHI (U.S. EPA, 2017).
[c] STADD: Short-Term Absorbed Daily Dosage
[d] MOE (Margin of Exposure)= Acute oral systemic point of departure (0.8 mg/kg/day) ÷ STADD (mg/kg/day); target MOE = 100.

In addition to systemic toxicity, propargite has a dermal irritation toxicity endpoint with a POD of 0.7 $mg/cm^2$. The exposure estimates generated for calculating the MOEs consisted of the estimated body part (e.g., face, neck, front torso, rear torso, legs, arms, and hands), surface pesticide amounts for various reentry activities and crops (Eberhart & Ellisor, 1993; Honeycutt, 1993; Klonne, Artz, & Rotondaro, 1999a; Klonne, 1999b; Klonne, Fuller, & Honeycutt, 1999c; Klonne, Fuller, & Howell, 2000; Klonne, Fuller, & Belcher, 2001; Korpalski, 1993a; Korpalski, 1993b; Leighton, 1999), divided by the default surface area of the body part (Beauvais, 2007). The dermal toxicity endpoint MOEs below 30 are presented in Table 5. MOEs below this target value indicate a concern.

Table 5. Product Label Reentry Worker Scenarios with Dermal Toxicity Margins of Exposure (MOEs) < 30 [a]

| Product Label [b] | Crop | Reentry Worker Scenario | Body Part | MOE [c] (target = 30) |
|---|---|---|---|---|
| Comite | jojoba | hand-harvesting | hands | 14 |
| Decimite | jojoba | hand-harvesting | hands | 15 |
| Victimite | jojoba | hand-harvesting | hands | 15 |

[a] Dermal irritation acute adjusted No Observable Effect Level (NOEL) is 0.7 $mg/cm^2$ (Lewis, 2020)
[b] Current CA registered product labels: Comite, Decimite, Omite-30WS, Endomite, Omite-6E, Mitomax 6EC, and Victimite
[c] MOE = Acute local dermal point of departure POD (0.7 $mg/cm^2$) ÷ surface concentration in $mg/cm^2$; target MOE = 30.

**References**

Andrews, C. 2000. HSM-00011: Worker Health and Safety Branch Policy on the Statistical Analysis for Dislodgeable Foliar Residue Data. Department of Pesticide Regulation, California Environmental Protection Agency, 1001 I Street, Box 4015. Sacramento, California 95812.

Beauvais, S., Powell, S., and Zhao, W., 2007. HS-1826: Surrogate Handler Exposure Estimates for Use in Assessments by the California Department of Pesticide Regulation. Department of Pesticide Regulation, California Environmental Protection Agency, 1001 I Street, Box 4015. Sacramento, California 95812.

Beauvais, S. 2007. Exposure Assessment Lecture Series with Body Part Surface Areas Obtained or Derived from U.S. EPA, 1997. *Exposure Factors Handbook.* EPA/600/P-95/002. Office of Health and Environmental Assessment, Washington, DC.

Dong, M. H., 2013. HS-1527: Human Pesticide Exposure Assessment Propargite (A Miticide for the Control of Spider Mites on a Variety of Agricultural Commodities). Worker Health and Safety Branch, Department of Pesticide Regulation, California Environmental Protection Agency, 1001 I Street, Box 4015. Sacramento, California 95812.

Eberhart, D.C., and Ellisor, G.K., 1993. Evaluation of Worker Exposure to Tribufos During Harvesting of Cotton Treated with DEF 6 (Study Number: AR1004). Mobay Corporation (BayerUSA, Inc.) Agricultural Chemicals Division, Box 4913, Kansas City, Mo. 64120. Report Date: March 15, 1993.

Frank, J.P., 2007. HSM-07005: Method for Approximating Confidence Limits for Upper Bound and Mean Exposure Estimates from the Pesticide Handlers Exposure Database (PHED). Department of Pesticide Regulation, California Environmental Protection Agency, 1001 I Street, Box 4015. Sacramento, California 95812.

Frank, J.P., 2008. HSM-08011: Default Inhalation Retention/Absorption Values to be used for Estimating Exposure to Airborne Pesticides. Sacramento, CA: California Department of Pesticide Regulation, California Environmental Protection Agency, 1001 I Street, Box 4015. Sacramento, California 95812.

Honeycutt, R.C., 1993. Worker Reentry Exposure to Profenofos in Cotton Treated with Curacron® 8E (Study Number: AR1006). Ciba Plant Protection, Ciba-Geigy Corporation, P.O. Box 18300, Greensboro, North Carolina 27419. Study Completion Date: May 21, 1993.

Klonne, D.R., Artz, S.C., and Rotondaro, A., 1999a. Determination of Dermal and Inhalation Exposure to Reentry Workers during Scouting in Dry Peas (Study Number: ARF021). Agricultural Reentry Task Force. Report Date: September 8, 1999.

Klonne, D.R., Artz, S.C., Bruce, E.D., and Belcher, T., 1999b. Determination of Dermal and Inhalation Exposure to Reentry Workers during Scouting in Grapes (Study Number: ARF023). Agricultural Reentry Task Force. Report Date: November 4, 1999.

Klonne, D.R., Fuller, R., and Honeycutt, R., 1999c. Determination of Dermal and Inhalation Exposure to Reentry Workers during Scouting in Sweet Corn (Study Number: ARF009). Agricultural Reentry Task Force. Report Date: November 8, 1999.

Klonne, D.R., Fuller, R., and Howell, C., 2000. Determination of Dermal and Inhalation Exposure to Reentry Workers during Hand Line Irrigation in Potato (Study Number: ARF036). Agricultural Reentry Task Force, LLC. Report Date: July 6, 2000.

Klonne, D.R., Fuller, R., Belcher, T.I., 2001. Determination of Dermal and Inhalation Exposure to Reentry Workers During Harvesting in Wine Grapes (Study Number: ARF048). Agricultural Reentry Task Force, LLC. Report Date: March 29, 2001.

Korpalski, S.J., 1993a. COMITE® on Cotton: Weeder Reentry Study (Study Number: AR1018). Uniroyal Chemical Company, Inc., 74 Amity Rd., Bethany, CT 06524-3402. Study Completion Date: February 4, 1993.

Korpalski, S.J., 1993b. COMITE® on Beans: Weeder Reentry Study (Study Number: AR1019). Uniroyal Chemical Company, Inc., 74 Amity Rd., Bethany, CT 06524-3402. Study Completion Date: February 11, 1993.

Leighton, T., 1999. HED's Review of the Reentry Portion of, "LORSBAN 4E and 50W Insecticides: Assessment of Chlorpyrifos Exposure to Applicators, Mixing/loaders, and Re-entry Personnel During and Following Application to Low Crops"; MRID 429745-01. PC Code 059101. DP Barcode D253135. U.S. EPA, Office of Prevention, Pesticides, and Toxic Substances. Washington, D.C. 20460.

Lewis, C. M., 2014. Propargite (Omite) Risk Characterization Document – Occupational and Ambient Exposure. Medical Toxicology Branch. Department of Pesticide Regulation, California Environmental Protection Agency, I Street, Box 4015, Sacramento, California 95812.

Lewis, C.M., 2020. Toxicity Endpoints, Critical Points of Departure, and Targets of Risk for Propargite. Memorandum to Eric Kwok and Ian Reeve, Exposure Assessment Section, Human Health Assessment Branch from Carolyn Lewis, Research Scientist III, Peter Lohstroh, Senior Toxicologist, Toxicology and Dose Response Section, and Svetlana Koshlukova, Senior Toxicologist, Risk Assessment Section, Human Health Assessment Branch, Department of Pesticide Regulation, California Environmental Protection Agency, I Street, Box 4015, Sacramento, California 95812.

Thongsinthusak, T., Ross, J. and Meinders, D., 1993. Guidance for the Preparation of Human Pesticide Exposure Assessments. Report no. HS-1612. Sacramento, CA: Worker Health and Safety Branch, Department of Pesticide Regulation, California Environmental Protection Agency, 1001 I Street, Box 4015, Sacramento, California 95812.

U.S. EPA, 1997. *Exposure Factors Handbook.* EPA/600/P-95/002. Office of Health and Environmental Assessment, Washington, DC.

U.S. EPA, 2001. Standard Values for Daily Acres Treated in Agriculture. Policy Number 009.1, Science Advisory Council for Exposure. Revised September 25.

U.S. EPA, 2017. Science Advisory Council for Exposure (ExpoSAC) Policy 3 (Revised January, 2017), U.S. Environmental Protection Agency, Office of Pesticide Programs, Health Effects Division.

U.S. EPA, 2019. Propargite: Draft Human Health Risk Assessment in Support of Registration Review. U.S. Environmental Protection Agency, Office of Pesticide Programs, Health Effects Division, October 15, 2019. EPA-HQ-OPP-2014-0131-0051.

Zweig, G., Gao, R.-Y., Witt, J.M., Popendorf, W. and Bogen. K., 1984. Dermal exposure to carbaryl by strawberry harvesters. Journal of Agricultural and Food Chemistry 32:1232-1236.

Zweig, G., Leffingwell, J.T. and Popendorf, W., 1985. The relationship between dermal pesticide exposure by fruit harvesters and dislodgeable foliar residues. Journal of Environmental Science and Health B20:27-59.

## Appendix I: Toxicity Endpoints, Critical Points of Departure, and Targets of Risk for Propargite

Department of Pesticide Regulation

Val Dolcini
*Acting Director*

Gavin Newsom
*Governor*

Jared Blumenfeld
*Secretary for Environmental Protection*

M E M O R A N D U M

TO: Eric Kwok, PhD, DABT, Senior Toxicologist
Ian Reeve, Ph.D., Staff Toxicologist (Specialist)
Exposure Assessment Section
Human Health Assessment Branch

THROUGH: Shelley DuTeaux, PhD MPH, Chief
Human Health Assessment Branch

FROM: Carolyn M. Lewis, MS, Research Scientist III
Peter Lohstroh, PhD, Senior Toxicologist
Toxicology and Dose Response Section
Svetlana Koshlukova, PhD, Senior Toxicologist
Risk Assessment Section
Human Health Assessment Branch

DATE: August 13, 2020

SUBJECT: Toxicity Endpoints, Critical Points of Departure, and Targets of Risk for Propargite

---

This memorandum summarizes the toxicity endpoints, critical points of departure (PODs), and targets of risk (expressed as a target Margins of Exposure or MOEs) for propargite established in the 2014 Risk Characterization Document (RCD) (DPR, 2014). This summary is intended to provide the Exposure Assessment Section of the Human Health Assessment (HHA) Branch with guidance to calculate revised MOEs for mitigating agricultural handler and reentry worker exposure.

## Introduction

Propargite is an organosulfur miticide/acaricide whose pesticidal mechanism of action involves the inhibition of magnesium-stimulated ATPase. One of its primary modes toxicity in mammals is local irritation at the site of first contact. In laboratory animals, systemic effects and the target organs varied with the route of exposure. The most sensitive endpoint for all routes and durations of exposure was reduced food consumption and body weight. Based on the weight of evidence, there does not appear to be increased sensitivity to propargite in infants, children or women of childbearing age.

## Critical PODs and Targets of Risk

The toxic endpoints, critical PODs, and targets of risks for propargite are summarized in Table 1.

PODs are doses that will not produce toxicologically significant effects for a corresponding route and duration. All critical PODs for propargite were derived from oral and dermal studies in laboratory animals (rats and rabbits). Oral PODs were used to characterize risk to humans from inhalation exposures. These values were either a no-observed-effect level (NOEL) or an estimated no effect level (ENEL) based on the lowest observed effect level (LOEL).

In the 2014 propargite RCD, the risks from non-oncogenic effects were expressed as MOEs. An MOE was calculated by dividing the critical POD for a specific exposure duration and route by an estimate of human exposure:

MOE = POD (mg/kg/day) / Exposure (mg/kg/day)

Each estimated MOE was then compared with a route and duration-specific target of MOE. The target MOE is the product of uncertainty factors (UFs). When PODs are derived from studies in laboratory animals, the commonly used default UFs are 10x to account for interspecies variability ($UF_A$) and 10x to account for intraspecies (human) sensitivity ($UF_H$). An estimated MOE that is lower than the target MOE indicates a potential health concern.

DPR considered a target MOE of 100, consisting of 10 x for each $UF_A$ and $UF_H$, to be adequate to protect human health from systemic effects of propargite following inhalation or dermal exposures. DPR considered an MOE of 30 to be protective of local effects (e.g. irritation and sensitization) following dermal exposures. In this case, the $UF_A$ was reduced from 10 to 3 based on evidence that rabbits are more sensitive to dermal irritation than humans (Campbell and Bruce, 1981; Phillips *et al.*, 1972; Marzulli and Maibach, 1975; Brown, 1971; Nixon *et al.*, 1975). A full $UF_H$ of 10 was retained to account for inter-individual variability in humans.

**Table 1. Critical End Points, PODs, and Targets of Risk from the 2014 Propargite Risk Characterization Document**

| Exposure Scenario | POD [a] mg/kg/day | Adjusted POD | Effects on LOEL [b] | Target MOE [c] | Reference |
|---|---|---|---|---|---|
| **Oral/Inhalation Exposure - Systemic** | | | | | |
| Acute | 2.0 | 0.8 mg/kg/day (absorbed [d]) | Maternal: Anorexia (Day 2) in rabbit does<br>Developmental: Delayed ossification in rabbit fetuses | 100 | Serota *et al.*, 1983 |
| Seasonal | 2.0 | 0.8 mg/kg/day (absorbed [d]) | Maternal: Anorexia, adipsia, reduced body wt. gain, reduced survival in rabbit does<br>Developmental: Delayed ossification in rabbit fetuses | 100 | Serota *et al.*, 1983 |

**Table 1. Critical End Points, PODs, and Targets of Risk from the 2014 Propargite Risk Characterization Document**

| Exposure Scenario | POD [a] mg/kg/day | Adjusted POD | Effects on LOEL [b] | Target MOE [c] | Reference |
|---|---|---|---|---|---|
| Chronic | 3.8 | 1.5 mg/kg/day (absorbed [d]) | ↓ Body weights and food consumption in rats | 100 | Trutter, 1991 |
| **Dermal Exposure - Systemic** | | | | | |
| Acute | 100 | 17 mg/kg (absorbed [e]) | No clinical signs or changes in food consumption and body weights during first week in rabbits | 100 | Bailey, 1987 |
| Seasonal | 1 | 0.17 mg/kg/day (absorbed [e]) | ↓ Body weights, changes in clinical chemistry and hematology values, ↑ relative liver and kidney weights in rabbits | 100 | Bailey, 1987 |
| Chronic | 1 | 0.17 mg/kg/day (absorbed [e]) | ↓ Body weights, changes in clinical chemistry and hematology values, ↑ relative liver and kidney weights in rabbits | 100 | Bailey, 1987 |
| **Dermal Exposure – Local** | | | | | |
| Acute | 0.03 [f] | 0.7 mg/cm$^2$ [g] | Erythema in rabbits after 6-hr exposure | 30 | Goldenthal, 1989 |
| Seasonal/ Chronic | 0.01 [g] | 0.21 mg/cm$^2$ [h] | Erythema, edema, eschar, exfoliation, atonia, desquamation, fissuring, blanching, coriaceousness in rabbits | 30 | Goldenthal, 1989 |

**Table Legend**

***a*** POD = Point of Departures for propargite are either no-observed-effect levels (NOELs) or an estimated no effect level (ENEL).

***b*** LOEL = Lowest-Observed-Effect Level

***c*** MOE = Margin of Exposure = POD / Exposure. The target MOE for systemic effects is the default of 100 assuming humans are 10 times more sensitive than laboratory animals and that there is a 10-fold variation in sensitivity within the human population. For local dermal effects, the target MOE is 30 assuming a default 10-fold variation in sensitivity within humans, a 1X uncertainty factor (UF) for interspecies variation based on evidence that rabbits are more sensitive than humans to dermal irritation and an additional 3X UF based on evidence of dermal sensitization.

***d*** Oral POD converted to absorbed dose to evaluate inhalation exposure assuming 40% oral absorption in rats.

***e*** Dermal POD converted to absorbed dose assuming 17% dermal absorption since dermal exposure expressed as an absorbed dose in rabbits.

***f*** Estimated no effect level (ENEL) by dividing lowest observed effect level (LOEL) of 0.1 mg/kg/day by an UF of 3 due to mild effects at the LOEL.

***g*** ENEL derived by dividing by a default UF of 10 since local effects at LOEL were frank effects.

***h*** Dose in mg/kg/day converted to dermal concentration assuming an average body weight of 2.5 kg and a surface area of 0.12 $cm^2$ for the application site at the LOEL of 0.1 mg/kg/day in rabbits. There was no adjustment for absorption in converting external dermal doses to dermal concentrations in the experimental animals.

## References

**Bailey, D.E., 1987.** 21-Day dermal toxicity study in rabbits. Uniroyal Chemical Co., Inc. DPR Vol. 259-093, Rec. No. 72509.

**Brown, V.K.H., 1971.** A comparison of predictive irritation tests with surfactants on human and animal skin. *J. Soc. Cosmet. Chem.* 22: 411-420.

**Campbell, R.L., and R.D. Bruce, 1981.** I. Direct comparison of rabbit and human primary skin irritation responses to isopropylmyristate. *Toxicol. Appl. Pharmacol.* 59: 555-563.

**Dourson, M., G. Charnley, and R. Scheuplein, 2002.** Differential sensitivity of children and adults to chemical toxicity. II. Risk and regulation. *Regul. Toxicol. Pharmacol.* 35: 448-467.
https://www.sciencedirect.com/science/article/abs/pii/S027323000291559X?via%3Dihub

**DPR, 2014.** Propargite (Omite) Risk Characterization Document - Occupational and Ambient Air Exposures. Department of Pesticide Regulation, California Environmental Protection Agency. Sacramento, CA. 116 pp.
https://www.cdpr.ca.gov/docs/risk/rcd/propargite_2014.pdf

**Goldenthal, E.I., 1989.** 21-Day repeat dose dermal toxicity study in rabbits - Omite® technical. Uniroyal Chemical Co., Inc. DPR Vol. 259-191, Rec. No. 176620.

**Marzulli, F.N., and H.I. Maibach, 1975.** The rabbit as a model for evaluating skin irritatns: A comparison of results obtained on animals and man using repeated skin exposures. *Food Cosmet. Toxicol.* 13: 533-540.

**Nixon, G.A., C.A. Tyson, and W.C. Wertz, 1975.** Interspecies comparisons of skin irritancy. *Toxicol. Appl. Pharmacol.* 31: 481-490.

**Phillips, L., M. Steinberg, H.I. Maibach, and W.A. Akers, 1972.** A comparison of rabbit and human skin response to certain irritants. *Toxicol. Appl. Pharmacol.* 21: 369-382.

**Serota, D.G., G.W. Wolfe, R.S. Durloo, and W.L. Fezio, 1983.** Teratology study in rabbits - Omite Technical (Revised Final Report). Uniroyal Chemical Co., Inc. DPR Vol. 259-042, Rec. No. 35303.

**Trutter, J.A., 1991.** Combined chronic toxicity and oncogenicity study in rats with Omite® technical. Uniroyal Chemical Co., Inc. DPR Vol. 259-128, pts 1-10, Rec. No. 89293.