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M E M O R A N D U M

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FROM: Tom Thongsinthusak, Staff Toxicologist
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SUBJECT: Inhalation Exposure of Chlorothalonil

Exposure assessors of the Worker Health and Safety Branch routinely estimate dermal and inhalation exposures for pesticides that are in the risk assessment process. The chlorothalonil document, HS-1475 (Thongsinthusak *et al*., 1996), also contains dermal and inhalation exposures estimated for different activities. Both types of exposure estimates were obtained from field studies using chlorothalonil or from surrogate studies using other pesticides. This memorandum addresses some questions about the range of particle sizes of chlorothalonil aerosols and the proportion of different aerosol fractions.

This is the first time we are making an effort to address those questions on inhalation exposure. In order to come up with reasonable answers, I have reviewed submitted documents, published articles, and other pertinent information concerning definitions of terms used for inhalation exposure, production of aerosols from simulated studies, production of fine particles during transportation and handling of dispersible granules, and ranges of droplet sizes in pesticide application.

I have used several terms to describe inhalation exposure and aerosol particles. The following definitions were adopted from those described by Vincent (1995).

1) Aerosol: A scientific term which applies to any disperse system of liquid or solid particles suspended in a gas - usually air. Typical aerosols are classified as dust (solid particles with sizes ranging from sub-micrometer (μm) to over 100 μm), spray (large liquid droplets with sizes upwards of a few μm), mist (finer liquid droplets with sizes up to a few μm), fume (small

solid particles with sizes usually less than 1 μm), bioaerosol (solid or liquid particles with sizes from a few nanometers and upwards), and smoke (solid or liquid particles of biologically viable organism with sizes ranging from sub-micrometer to greater than 100 μm). Aerosols applicable to chlorothalonil application should be under dust and spray.

2) Inhalable aerosol: The entry by inhalation of particles from ambient air into the respiratory tract. The particle sizes range up to about 400 μm.
3) Extrathoracic deposition: Particles which are deposited in the nose, mouth, and throat.
4) Thoracic deposition: The sum of the tracheobronchial (particle sizes are approximately 7 - 40 μm) and alveolar deposition (particle size are approximately up to 8 μm).
5) Respirable fraction: Fine alveolar penetration fraction with aerodynamic diameter up to about 8 μm.
6) Volume median diameters (VMD): The particle size diameter at 50% of accumulated volume.

Background information:

A. <u>Simulated aerosol generation during mixing/loading and application of Bravo® 500 suspension concentrate (SC).</u>

A study was conducted to simulate aerosol generation during mixing/loading of neat Bravo® 500 SC and production of aerosols from atomizing diluted Bravo® 500 SC through two types of hydraulic nozzles - a hollow cone (TeeJet TXVS-3) and a flat fan tip (TeeJet XR 8003VS) (Wolf *et al*., 1998). Procedures and conditions used in those studies were:

1) The operator accidentally spilling undiluted Bravo® 500 SC onto a dry, 18-gallon metal drum (0.35 meters (m) diameter, 0.67 m length), rotating at 5 revolutions per minute (RPM). A stream of Bravo® 500 SC (0.34 L/min) was released from a height of 0.75 m onto its rotating surface. The drum surface was clean and dry at the end of each minute (min). The operation was repeated for 15 minutes.
2) The operator accidentally spilling undiluted Bravo® 500 SC onto a power take-off (PTO) shaft. This study used an electric motor with a 0.025 m diameter shaft spinning at 1,250 RPM. Bravo® 500 SC was released at a

height of 0.75 m above the rotating shaft at a rate of 0.34 L/min. The sampling time was 15 minutes.

3) The operator pouring undiluted Bravo® 500 SC into a tank containing only water. A 25-liter plastic bucket was filled with tap water and a stream of Bravo® 500 SC was poured into the water at a rate of 0.34 L/min for 15 minutes. Water in the bucket was not agitated.
4) Bravo® 500 SC was diluted at a rate of 15 mL per liter of water. The diluted Bravo® 500 was atomized through two types of hydraulic spray nozzles, a hollow cone nozzle at 380 kPa and a flat fan nozzle at 275 kPa. Flow rates for the hollow cone and flat fan were 0.22 and 1.14 L/min, respectively.
5) A cleanup lasting about 45 minutes was performed at the end of a day's experiments. Pressurized water from a garden hose was used to wash down chlorothalonil-contaminated apparatus, plumbing and work areas.

The use of Bravo® 500 SC in this study is ideal because this formulation is also sold in California. This formulation is essentially the same as Bravo Weather Stik™ Agricultural Fungicide. Bravo Weather Stik™ was the top seller in California in 1995, accounting for 68% of the total chlorothalonil sold (DPR, 1995). The suspension concentrate or flowable formulation normally contains particle sizes ranging from 2 to 8 μm with an average particle size of 4 μm (Halliday, 1983). These particles are definitely respirable according to the definition.

Aerosols produced from scenarios 1 to 4 were directed to a cascade impacter (CI) by a box fan. The cleanup air space was sampled for aerosols without using a box fan. The box fan and the CI were placed 0.8 to 1.2 m from the point of impact or atomization depending on types of simulation. The air velocity at the point of atomization was between 0.76 and 1.61 m/s or 1.7 and 3.6 miles/hr, respectively. The slides of CI collected aerosols that had mean diameters of >13, 13.0, 4.0, and 1.7 μm. The air sampling rate was 17.5 L/min for all scenarios. Chlorothalonil on slides, except for chlorothalonil with mean diameters >13 μm, was analyzed by gas chromatography equipped with flame ionization or electron capture detector. Results for aerosols with diameters of 13.0, 4.0, and 1.7 μm are shown in Table 1.

Table 1. Mean chlorothalonil concentration (as aerosols) resulting from simulated mixing/loading and application scenarios.

Target or scenario	Measured airborne chlorothalonil aerosols (ng/L)*	Respired by male workers (mg/8-hr day)**
Detection threshold	1.7	0.014
Average background	2.2	0.015
Rotating drum	2.1	0.014
Spinning shaft of motor	3.6	0.024
Water in bucket	5.3	0.036
Cleanup after the study	20.6	0.138
Hollow cone nozzle	354	2.379
Flat fan nozzle	96	0.645

* aerosols with mean diameters of 13, 4.0, and 1.7 μm.

** based on inhalation rate of 14 L/min for light activity. This rate was used in the HS-1475 document. An inhalation rate of 29 L/min was used in the submitted report. These inhalation exposure estimates are used for comparison with those in HS-1475 only.

Accidental spills during the simulated mixing/loading operation generated low levels of aerosol. The report did not indicate whether the background level of chlorothalonil aerosols was from contamination or airborne chlorothanil drifted from other applications. I think that a background level should be much higher during actual aerial or air blast applications. Mixer/loaders would also be exposed to background chlorothalonil drifted from application sites. The simulation process excluded a drift factor.

I calculated potential inhalation exposures based on measured chlorothalonil aerosols and an inhalation rate used in HS-1475, which is 14 L/min for light work. Results are shown in the third column. The potential inhalation exposure was 2.38 mg/8-hour day when a hollow cone nozzle was used. I assume that air blast application would yield more fine aerosols because of a wind shear factor and the distance that aerosols can travel. Inhalation exposures for applicators during air blast and ground boom applications shown in HS-1475 were 0.45 and 0.129 mg/person/day, respectively. These inhalation exposures included total inhaled

aerosols. Likewise, inhalation exposures for pilots/mixers and mixer/loaders during aerial application were 0.027 and 0.084 mg/person/day, respectively. The simulation study mentioned above may not be representative to what actually occurred during aerial or ground application with respect to airborne contamination. It is clearly shown that a hollow cone nozzle can produce a great number of fine aerosols. But, a proportion of these fine to coarse aerosols was not known because results of analysis for aerosols that had mean diameters of >13 μm were not available.

The following reports show results of field studies and recommended sizes of spray droplets in pest controls. Reichard *et al*. (1978) reported that all nozzles used in the study delivered the greatest proportions of droplets in either the smallest (7.5-22.5 μm) or next to the smallest (22.5-37.5 μm) size classes. In addition, spray droplet distributions, which passed through foliage, contained a greater proportion of small droplets than those which did not pass through foliage. The VMD of spray droplets ranged from 123.8 to 258.2 μm depending on types of nozzles and the distance from the source of atomization. Particle sizes of up to 20 μm accounted for about 0.1% of cumulative volume. Grover and Reed (1990) plotted accumulated volume percentages versus the particle size diameters, which were generated from several flat spray tips and an operating pressure of 275 kPa. The particle size diameters ranged approximately from 180 to 650 μm. The particle size diameter at the VMD is about 380 μm. A guidance document published in Australia indicated an optimum range of spray droplets from 12 to 100 μm for many insecticides and fungicides, and from 175 to 275 μm for herbicides (Findlay, 1995). These studies indicated that minute particle sizes accounted for only a small fraction of cumulative aerosol volume.

Results from the study conducted by Wolf *et al*. (1998) clearly indicate that there is substantial inhalation exposure from particle sizes smaller than 13 μm generated from hollow cone nozzles. In contrast, information from other studies revealed that particle sizes of less that 13 μm would constitute only a very small fraction of cumulative aerosol volume. However, I do not know the total volume of aerosols to permit estimation of inhalable or other fraction of aerosols. Moreover, inhalation exposure of chlorothalonil used in HS-1475 does not indicate a proportion of droplet sizes for extrathoracic and thoracic fractions. These fractions were combined to represent inhalation exposure of chlorothalonil. Even if the

proportion of these two fractions are known, our default deposition/absorption of 50% may not be applicable to all fractions. A majority of extrathoracic deposition may be eliminated or swallowed. In contrast, absorption of alveolar fraction may be greater than 50%.

B. Determination of granular integrity based upon surface shipment, controlled mechanical shaking, and internal attrition (Raythatha, 1991a-c).

A chlorothalonil formulation, ASC 66518.X.1207 dispersible granule (chlorothalonil DG), was used in this study. This formulation is representative of commercial quality Bravo® 825 DG (82.5%). Treatment conditions for each study were:

a) Actual surface shipment conditions. Packages of granular chlorothalonil were transported to a location approximately 1,300 miles away by UPS Surface Services and then the packages were transported back to the original location.
b) Controlled mechanical shaking. The bottle containing chlorothalonil the granular product was shaken using a wrist action bottle shaker (350 oscillations/min.) for a total of six hours.
c) Internal attrition. Drums were filled with chlorothalonil DG and were allowed to tumble on a tumbler unit (rotated 61 revolutions/min) for a total of 144 hours. At the conclusion of these treatments, the material was tested for granular size distribution using the U.S. Standard Tyler sieves and Malvern laser light scattering particle size analyzer. Results showed that chlorothalonil DG from the three studies failed to generate granules or fines smaller that 40 μm.

C. Determination of granular integrity after severe ball mill type attrition (Rathatha, 1991d) and intense milling using an air mill (Rathatha, 1991e).

For ball mill type attrition, a cylinder containing stainless steel balls and the chlorothalonil DG was allowed to rotate at 25 revolutions/min for six minutes. For air milling, the chlorothalonil DG was milled one and two times by using a "Micro-jet 8" air mill operated at the inlet pressure of 70 psi and the milling pressure of 55 psi. The end products were analyzed for particle size distribution. Table 2 shows granular size distribution of chlorothalonil DG after mechanical attrition and air milling. Air milling yielded more fine particles than mechanical attrition. Air milling one or two times yielded similar percentages of the same

particle size. More than 63% of particles by weight produced are below 10 µm diameter after air milling. A majority of particles were in the respirable range. The air milling process can be employed to pulverize particles to small size suitable for SC or flowable formulation. A good flowable product is produced if the particle size range is from 2 to 8 µm with an average particle size of 4 µm (Halliday, 1983). Handlers of wettable or flowable products may be exposed to fine particles in the respirable range.

Table 2. Granular size distribution of ASC-66518.x.1207 after mechanical attrition and air milling

	% By weight, below the corresponding granular size		
Granular size (µm)	Mechanical attrition	Air milling (1 time)	Air milling (2 times)
300	88.28	100	100
250	68.07	100	100
150	26.09	100	100
125	19.51	100	100
110	19.28	99.8	99.6
100	18.30	98.8	97.8
80	14.16	94.5	90.4
60	7.88	87.3	78.9
50	5.35	83.6	73.9
40	4.12	80.5	71.4
30	3.14	77.7	70.5
25	2.28	76.2	70.0
20	1.76	ND	ND
15	0.98	ND	ND
10	0.57	63.2	65.6
5	0.10	33.4	40.3
3	0.00	11.6	12.3
2	ND	3.1	2.1

ND = no data

Conclusions:

1. Dispersible granular formulation of chlorothalonil should not produce significant inhalation exposure during handling.
2. Respirable aerosols were generated from a simulation study using hydraulic spray nozzles indicating substantial inhalation exposure can occur to handlers.
3. Results from simulated application studies or other studies mentioned in this memo could not be used to determine inhalation exposure as shown in HS-1475 for extrathoracic and thoracic (tracheobronchial and alveolar) fractions. Furthermore, extrathoracic and thoracic fractions were not reported in field inhalation exposure studies for chlorothalonil and other surrogate pesticides used in HS-1475.
4. Based on available information, inhalation exposure for chlorothalonil as used in HS-1475 cannot be refined to reflect exposure to the upper or lower respiratory tract.

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