## Appendix E

## Expected Aggregate Risks from Long Range Atmospheric Transport of Genetically Acting Carcinogens Emitted in California

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### Introduction

Traditional air dispersion analysis is limited to distances no more than 50 km from the source. This is not a problem when the social policy question to be addressed by risk analysis is, "What risk does a particular pesticide use impose on the most exposed members of the population, and does that exceed an 'acceptable' level?" The greatest exposure is always found within this distance.

However well established in past regulatory practice, though, this kind of "acceptable risk" framework does not comprise the only policy issue relevant to the pesticide approval questions faced by California pesticide regulators. What on the federal level is abbreviated as FIFRA basically calls for some sort of societal balancing of anticipated benefits vs risks[1].

So to be approved, or to escape cancellation, a pesticide use should not impose overall health harm that is "unreasonable" in relation to expected benefits. A natural framework to interpret this type of balancing is cost benefit analysis—where societal aggregate economic benefits are juxtaposed with societal aggregate harm—both expressed as arithmetic mean "expected value" estimates, averaging across the uncertainties involved in each type of assessment and the variability in risks across the exposed people.

In following this interpretation of the mandate for balance, we argue that it makes sense for regulators to make (and disclose) assessments of the population aggregate cancer risks that are likely to be produced from permitted emissions of substances with low dose linear dose response relationships, in addition to maximal individual risks. To do this requires not only estimates of how much exposure there is expected to be within 50 km of the emission source, but all downwind locations—even those that produce less than the "acceptable risk" criteria of one extra cancer per million or per hundred thousand that have become customary risk management standards in different contexts.

As will be seen below, such estimates of aggregated small risks from long range atmospheric transport can be made without introducing undue added uncertainties. To see this, we can do a first-cut "back of the envelope" calculation here that illustrates in approximate form the quantitative components of more advanced analyses that will be undertaken in subsequent sections of this appendix.

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[1] FIFRA requires that in order to qualify for registration, a pesticide must not be expected to cause "unreasonable adverse effects on man or the environment". Balancing considerations are required in arriving at this kind of judgment. The statute elaborates this by referring to "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide."

## Preliminary Back-of-the-Envelope Calculation of Intake Fraction and Downwind Cancer Cases

### Intake Fraction

Upon leaving the traditional 50 km distance from the source we can assume that molecules of the fumigant will continue to be transported across the U.S. by prevailing westerly winds at an average speed of about 5.9 meters/second (Table 1). At this rate, taking the distance from Los Angeles to New York City less 50 km (3883 km) as the distance to the eastern seaboard, the fumigant molecules would be expected to traverse the country in about 7.6 days. During this time, there will be some depletion of the fumigant molecules at rates determined by reactions with reactive oxygen species and sunlight, in addition to not yet quantified losses from rainout and dry deposition processes.[2] The Hazardous Substances Data Bank lists the atmospheric degradation rates of the three fumigants as:

- Chloropircrin—123 days (from reactions with hydroxyl radicals). Only about 4% loss expected via this process during transit across the U.S.

- Telone—2 days from reactions with hydroxyl radicals) and 7 to 12 hours (from reactions with sunlight). Total half life from losses via these two processes are expected to be about 8.3 hours during daylight and 2 days during nighttime hours. At these rates, total expected loss would be well over 99.9% during transit across the U.S. assuming 12 hours of daylight and 12 hours of darkness each day. On this schedule the average concentration during transit would be expected to be about 11.4% of the initial concentration.

- Metam Sodium—nonvolatile, therefore particle attached material will be removed by dry or wet deposition, not quantified. For the degradation product, methyl isocyanate, the atmospheric half-life is 118 days from reactions with hydroxyl radicals. Similar to chloropicrin, at this loss rate, only about 4% would be expected to be destroyed during transit across the U.S.

Therefore it can be seen that the atmospheric behavior of the three fumigants produces considerable quantitative differences in the expected potential for exposure of distant down-wind

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[2] Dry deposition for gases is complex and has been the subject of extensive analyses in the literature. Early calculations suggest it may be significant in relation to the loss rates of chloropicrin and MITC quoted here. One helpful publication by the California Air Resources Board recommends a deposition velocity of 6 cm/second for reactive and soluble gasses, with lower and upper confidence limits of 3-10 cm/second. (California Air Resources Board, "Lake Tahoe Air Deposition Study." Final Report, September 2006, Chapter 4., Atmospheric Processes Research Section Research Division Air Resources Board California Environmental Protection Agency , p. 4-33.) If this velocity is divided by the assumed afternoon mean mixing height of 1593 meters, it suggests a loss rate of about 3.8E-5 per second, or 3.2 per day—very much larger than the other loss rates in transit. A smaller central estimate figure of about 0.3 cm/second is implied for gases such as ozone and sulfur dioxide is implied by Ma and Daggupaty (Ma, J, Daggupaty, S.M. 2000, Effective Dry Deposition Velocities for Gases and Particles over Heterogeneous Terrain, J. Applied Meteorology 39: 1379- 1390.) Even at this lesser rate, simply dividing by the national mean afternoon mixing height yields (0.003 m/second/1593 meters = 1.9E-6 loss rate from the atmosphere per second, or 0.16 loss rate per day, for a half life of ln(2)/0.16 = 4.3 days. This, of course, would still be much faster than the losses for chloropicrin and telone from sunlight and reactions with hydroxyl radicals.

residents of the U.S. Other factors in the "back of the envelope calculation of exposures from long range transport are:

- A "mixing height" averaging about 1593 meters (averaging afternoon estimates)

Table 1
Annual Average Mixing Heights and Wind Speeds for 62 Weather Stations in the Continental U.S.

| Station No. | Station | Time (m = morning; a = afternoon) | Mixing Height (m) | Wind Speed (m/sec) |
|---|---|---|---|---|
| 1 | Albany, New York | m | 348 | 3 |
| | | a | 2300 | 5.6 |
| 2 | Albuquerque, New Mexico | m | 331 | 4.8 |
| | | a | 2434 | 5.8 |
| 3 | Amarillo, Texas | m | 328 | 7.3 |
| | | a | 1973 | 8.4 |
| 4 | Athens, Georgia | m | 374 | 4.9 |
| | | a | 1542 | 6.2 |
| 5 | Bismark, North Dakota | m | 359 | 5.6 |
| | | a | 1488 | 8.1 |
| 6 | Boise, Idaho | m | 326 | 4.2 |
| | | a | 1758 | 5.7 |
| 7 | Brownsville, Texas | m | 635 | 7.2 |
| | | a | 1284 | 8.7 |
| 8 | Buffalo, New York | m | 631 | 6.1 |
| | | a | 1275 | 7.6 |
| 9 | Burrwood, Louisiana | m | 932 | 6.2 |
| | | a | 956 | 5.9 |
| 10 | Cape Hatteras, North Carolina | m | 789 | 7.6 |
| | | a | 924 | 7.8 |
| 11 | Caribou, Maine | m | 579 | 6.4 |
| | | a | 1379 | 8.3 |
| 12 | Charleston, South Carolina | m | 371 | 5.1 |
| | | a | 1330 | 6.7 |
| 13 | Columbia, Missouri | m | 401 | 6.2 |
| | | a | 1397 | 7.2 |
| 14 | Dayton, Ohio | m | 476 | 5.7 |
| | | a | 1384 | 7 |

| | | | | |
|---|---|---|---|---|
| 15 | Denver, Colorado | m | 268 | 4.2 |
| | | a | 2543 | 6.3 |
| 16 | Dodge City, Kansas | m | 308 | 7.5 |
| | | a | 1540 | 8.8 |
| 17 | El Paso, Texas | m | 571 | 4.5 |
| | | a | 2638 | 6.1 |
| 18 | Ely, Nevada | m | 238 | 4.7 |
| | | a | 2396 | 6.5 |
| 19 | Flint, Michigan | m | 506 | 5.6 |
| | | a | 1368 | 7.4 |
| 20 | Glasgow, Montana | m | 310 | 5.7 |
| | | a | 1564 | 7.5 |
| 21 | Grand Junction, Colorado | m | 384 | 4.3 |
| | | a | 2600 | 5.2 |
| 22 | Great Falls, Montana | m | 524 | 7.3 |
| | | a | 2047 | 9 |
| 23 | Green Bay, Wisconsin | m | 506 | 5.8 |
| | | a | 1243 | 7.6 |

| Station No. | Station | Time (m = morning; a = afternoon) | Mixing Height (m) | Wind Speed (m/sec) |
|---|---|---|---|---|
| 24 | Greensboro, North Carolina | m | 440 | 4.8 |
| | | a | 1450 | 6.3 |
| 25 | Huntington, West Virginia | m | 524 | 4.2 |
| | | a | 1511 | 5.5 |
| 26 | International Falls, Minnesota | m | 402 | 5.3 |
| | | a | 1299 | 7.2 |
| 27 | Jackson, Mississippi | m | 425 | 4.1 |
| | | a | 1453 | 5.4 |
| 28 | Jacksonville, Florida | m | 480 | 5.2 |
| | | a | 1455 | 6.7 |
| 29 | Lake Charles, Louisiana | m | 417 | 5.3 |
| | | a | 1188 | 6.4 |
| 30 | Portland, Maine | m | 578 | 5.9 |
| | | a | 1260 | 7.8 |
| 31 | Rapid City, South Dakota | m | 368 | 5.8 |
| | | a | 1810 | 7.9 |
| 32 | St. Cloud, Minnesota | m | 411 | 5.5 |
| | | a | 1173 | 7.5 |
| 33 | Salem, Oregon | m | 471 | 2.9 |
| | | a | 1354 | 4.6 |

| Station No. | Station | Time (m = morning; a = afternoon) | Mixing Height (m) | Wind Speed (m/sec) |
|---|---|---|---|---|
| 34 | Salt Lake City, Utah | m | 300 | 4.7 |
| | | a | 2322 | 5.7 |
| 35 | San Antonio, Texas | m | 694 | 5.9 |
| | | a | 1589 | 6.5 |
| 36 | San Diego, California | m | 625 | 2.2 |
| | | a | 877 | 4.5 |
| 37 | Santa Monica, California | m | 542 | 2.5 |
| | | a | 814 | 5.1 |
| 38 | Sault Ste Marie, Michigan | m | 508 | 5.4 |
| | | a | 1125 | 7.3 |
| 39 | Seattle, Washington | m | 705 | 5.2 |
| | | a | 1175 | 5.4 |
| 40 | Shreveport, Louisiana | m | 497 | 5.7 |
| | | a | 1452 | 6 |
| 41 | Spokane, Washington | m | 335 | 5.1 |
| | | a | 1597 | 5.7 |
| 42 | Tampa, Florida | m | 519 | 5.4 |
| | | a | 1394 | 6.4 |
| 43 | Topeka, Kansas | m | 436 | 6.4 |
| | | a | 1299 | 8.1 |
| 44 | Tucson, Arizona | m | 276 | 4.3 |
| | | a | 2327 | 5.6 |
| 45 | Lander, Wyoming | m | 348 | 3 |
| | | a | 2300 | 5.6 |
| 46 | Las Vegas, Nevada | m | 331 | 4.8 |
| | | a | 2434 | 5.8 |
| 47 | Little Rock, Arkansas | m | 450 | 4.6 |
| | | a | 1491 | 5.9 |
| 48 | Medford, Oregon | m | 375 | 1.7 |
| | | a | 1738 | 3.9 |
| 49 | Miami, Florida | m | 923 | 5.3 |
| | | a | 1351 | 6.5 |
| 50 | Midland, Texas | m | 436 | 6.6 |
| | | a | 2089 | 7.5 |
| 51 | Montgomery, Alabama | m | 420 | 4.1 |
| | | a | 1471 | 5.4 |
| 52 | Nantucket, Massachusetts | m | 707 | 7.9 |
| | | a | 804 | 8.6 |
| 53 | Nashville, Tennessee | m | 492 | 4.4 |
| | | a | 1563 | 6 |
| 54 | New York, New York | m | 839 | 7.4 |

| | | | | |
|---|---|---|---|---|
| | | a | 1286 | 8.2 |
| 55 | North Platte, Nebraska | m | 329 | 5.7 |
| | | a | 1509 | 8.1 |
| 56 | Oakland, California | m | 563 | 3.4 |
| | | a | 811 | 5.5 |
| 57 | Oklahoma City, Oklahoma | m | 377 | 7.8 |
| | | a | 1382 | 8.4 |
| 58 | Peoria, Illinois | m | 362 | 5.4 |
| | | a | 1168 | 7.2 |
| 59 | Pittsburgh, Pennsylvania | m | 510 | 4.9 |
| | | a | 1512 | 7.1 |
| 60 | Washington, D.C. | m | 528 | 4.9 |
| | | a | 1570 | 6.8 |
| 61 | Winnemucca, Nevada | m | 280 | 3.4 |
| | | a | 2407 | 5.8 |
| 62 | Winslow, Arizona | m | 234 | 3.3 |
| | | a | 2613 | 6.7 |

| Station No. | Station | Time (m = morning; a = afternoon) | Mixing Height (m) | Wind Speed (m/sec) |
|---|---|---|---|---|
| | | | mean | stderr |
| 62 site average | | m | 467 | 20 |
| 62 site average | | a | 1593 | 63 |

- North-south distance for California—1040 miles, or about 1674 kilometers (1.674E6 meters).

Given these dimensions, the vision is that fumigant molecules entering into long range transport will be dispersed in a volume of about 1.67E6 meters (north to south distance of the California borders) X 1593 meters high X 24 hours/day * 60 minutes/hour * 60 seconds/minute * 5.9 meters/second west to east (the latter from the prevailing westerly wind speed) = 1.36E15 cubic meters. For our back-of-the envelope calculation of population aggregate exposure/emissions we need only compare this volume with the volume of air breathed in per day for all of the down-wind people. The population of the 48 contiguous states in 2012 was approximately 307 million. At a recommended long term adult breathing rate of about 16 cubic meters per day, the total potential inhalation intake (if there were no loss during transit across the country) comes to about 307 E8 X 16 m3/day = 4.9 billion cubic meters. Therefore, the fraction of long range transported outdoor air potentially inhaled by US residents between California and the Eastern seaboard is approximately 4.9E9/1.36E15 = 3.6E-6. [3] For long-lasting chloropicrin and Methyl Isocyanate, this could be somewhat increased by inhalation during subsequent passages around the earth, but decreased by dry deposition and rainout losses not yet included quantitatively in the mechanisms of transport loss listed above. In a more refined calculation, adjustments should also be made for the weighted differences in breathing rates of the full spectrum of age groups in the population.

### Fraction of Fumigants Use that Winds up as Emissions, and Expected Resulting Cancer Cases

The remaining piece to the picture is to estimate fumigant emissions from available data on the volume of fumigant use in California. Of that used, what fraction should be estimated to reach the atmosphere, and what fraction is destroyed by microbial action and chemical reactions in the soil? A brief literature search has turned up several papers that seem to give ranges on the order of 50% emissions,[4] although at least two report that the use of tarps can hold emissions to under 10%[5] and as low as 1-2% for "Totally Impermeable Film" (TIF).[6] Using 50% of total California fumigant use as our starting point, Table 2 shows expected emissions of the various fumigants for the most recent year, tentative amounts likely to be inhaled, and potential aggregate cancer cases given the official cancer "slope factors" in units of cancer transformations per lifetime exposure in mg/kg-day.[7] The final risk calculations, therefore represent

Additional cancer cases per year of fumigant use =

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[3] If the mean of morning and afternoon mixing heights (1030 meters) were used instead of the afternoon average of 1593 meters, the fraction inhaled would rise to 5.6 E-6.

[4] Yates et al., citing several earlier references, give a range of 20%-90%. Yates, SR, Gan, J, Papiernik, SK, Dungan, R, Wang, D (2002) Reducing fumigant emissions aftyer soil application. Pathophysiology 92: 1344-1348; Noling JW (2015) Reducing Fumigant Application Rates and Soil Emissions with Plastic Mulch Technology[1] University of Florida IFAS Extension Paper #ENY046, available at https://edis.ifas.ufl.edu/in403

[5] Papiernik, SK, Yates, SR, Dungan, RS, Lesch, SM, Zheng, W, Guo, M (2004). Effect of surface tarp on emissions and distribution of drip-applied fumigants. Environ. Sci. Technol. 38 (16): 4254-4262.

[6] Gao, S, Sosnoskie, LM, Cabrera, JA, Qin, R, Hanson, BD, Gerik, JS, Wang, D, Browne, GT, Thomas, JE. (2015). Fumigation efficacy and emission reduction using low-permeability film in orchard soil fumigation. Pest Manag Sci. doi 10.1002/ps.3993.

[7] The latter are officially designated as upper confidence limits, but earlier calculations indicate that for genetically acting carcinogens such slope factors are generally not very far from arithmetic mean estimates when a number of uncertainties in the calculations are modeled as lognormal distributions. Hattis, D., and Goble, R., "Expected Values for Projected Cancer Risks from Putative Genetically-Acting Agents," Risk Analysis, Vol. 11, pp. 359-363, 1991. A more refined calculation will reevaluate this assumption given the available data for the specific fumigant carcinogens involved.

$$\frac{\text{Slope factor (per mg/kg-day lifetime) * lbs fumigant use/year * 50\% emissions/lbs used*3E-6 inhaled/emitted*4.54 E5 mg/lb*(1/70 lifetime/year of use and exposure)*3.07E8 exposed people*average fraction remaining after losses in transit across the country}}{\text{365 days/year*70 kg body weight/person}}$$

Table 2
Preliminary Back-of-The-Envelope Calculation of Potential Cancer Cases from 2013 Soil Fumigant Use in California Followed by Long Range Transport Across the U.S.

| | **MITC from Metam Na and K** | **Chloropicrin** | **1,3-Dichloropropene (Telone)** |
|---|---|---|---|
| 2013 use (millions of lbs) | 14.29 | 8.216 | 12.917 |
| Possible emissions (at 50% use) in millions of pounds per year | 7.15 | 4.11 | 6.46 |
| Possible total inhalation( in pounds per year) at 3E-6 | 2.57E+01 | 1.48E+01 | 2.33E+01 |
| Ave fraction remaining after transit losses across US | 0.98 | 0.98 | 0.114 |
| Millions lbs/yr inhalation during long range transport | 2.52E+01 | 1.45E+01 | 2.65E+00 |
| Conversion from lbs to mean mg/kg-day for total US population of 309 million assuming 70 kg body weight and 365 d/year | 1.45E-06 | 8.33E-07 | 1.52E-07 |
| Slope factor (cancer transitions per mg/kg-day lifetime) | 0.185 | 2.2 | 0.2 |
| mg MITC/mg metam sodium ratio | 0.566031893 | 2.2 | 0.2 |
| slope factor after conversion of MITC slope factor to metam Na equivalents | 0.105 | 2.2 | 0.2 |
| mean cancer risk per person per year of fumigant use | 1.52E-07 | 1.83E-06 | 3.05E-08 |
| Expected cancer cases induced/year fumigant use | 47 | 566 | 9 |

## Improvements Needed to Refine the Analysis of Cancer Risks from Long Range Transport

In possible future work we propose to refine the estimates of downwind cancer cases by undertaking the following:

- Add quantitative estimates of dry and wet deposition processes, which will decrease the amounts of each fumigant available for inhalation on long range transport.
- Adjust the inhalation amounts to account for age-related differences in breathing rates, based on the age distribution of the downwind population.[8]
- Exclude from the downwind population a few selected states that are rarely or never downwind of the California emissions (e.g. Washington, Oregon, Idaho, Montana, and North and South Dakota).
- Adjust the long range inhalation expectations for the months in which the emissions occur for each fumigant (with two peaks--in spring and fall, based on the emissions for the two locations assembled so far).
- Explicitly take into account the increased sensitivity of younger age groups for carcinogenesis from genetically acting agents.[9]
- Explicitly model the aggregate effects on cancer risks of general human interindividual variability in metabolic activation, metabolic detoxification and DNA repair processes.[10]
- Explicitly model the uncertainty distribution for human risks from genetically acting agents arising from differences between human and animal sensitivity for carcinogenesis, as represented by interspecies differences in susceptibility to toxicity from a set of anti-cancer agents and other sources of data on these differences.[11,12]

[8] Hattis, D. "Distributional Analyses for Children's Inhalation Risk Assessments." Journal of Toxicology and Environmental Health, 71(3):218-226, 2008.
[9] Hattis, D., Goble, R., and Chu, M. "Age-Related Differences in Susceptibility to Carcinogenesis. II. Approaches for Application and Uncertainty Analyses for Individual Genetically Acting Carcinogens." Environmental Health Perspectives, 113: 509-516, April, 2005.
[10] Hattis, D. and Barlow, K. "Human Interindividual Variability In Cancer Risks--Technical And Management Challenges" Human and Ecological Risk Assessment, Vol. 2, pp. 194-220, 1996
[11] Bussard, M D, Chiu, W, Hart, A, Hattis, D, Herzler, M, Slob, W,Vermeire, T. 2014. Guidance Document on Evaluating and Expressing Uncertainty in Hazard Characterization, IPCS/WHO Harmonization Project Document 11, World Health Organization, 2014.
[12] Hattis, D. and Goble, R. L. "Uncertainties in Risk Assessment for Carcinogenesis: A Road Map Toward Practical Improvements" White paper for the U.S. Environmental Protection Agency, May, 2007.