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SUBJECT: 2009 REQUEST TO DEVELOP ANALYTICAL METHODS FOR AZOXYSTROBIN, CHLOROTHALONIL, DICHLORAN, IPRODIONE, AND VINCLOZOLIN AND SIGNIFICANT DEGRADATES IN WELL WATER

In order to gather evidence that current regulatory measures are protective of California ground water, EM is seeking to develop analytical methods that include multiple active ingredients (AIs) and their environmentally relevant transformation products. Currently, EM is investigating developing an analytical method for iprodione, iprodione's transformation products and similar AIs (in chemistry and use) that can be analyzed in a single sample.

Characteristics of Pesticides that Impact Ground Water

Usually, the ground water matrix differs from the surface water matrix for analytical method development. Unlike surface water, recharge water percolates from the soil surface to the water table with the soil acting as a porous-media filter. The mineral particles of the soil, with a net negative charge, immobilize neutral or cationic organic residues derived from plant matter, hydrocarbons or pesticides. The subset of pesticides that reach ground water are mobile, negatively-charged polar molecules.

Additionally, pesticides that may be selected for analytical method development are prioritized by resistance to degradation (persistence). When such pesticides are transformed in the environment, the transformation products of the pesticides that are also persistent and should be included in the analytical method. The US EPA defines major transformation products as those that make up 10 percent or more of the mass of parent pesticide application during the laboratory studies, or transformation products that are of concern due to their particular ecological or toxicological significance.

Ground Water Analytical Method Development

In order to develop a method for AIs and relevant transformation products, a Method Detection Limit (MDL) must be established. The MDL is the lowest concentration of the analyte that a method can detect reliably. To determine the MDL, 7 well water samples are spiked at 0.100 µg and processed through the entire method along with a blank. The standard deviation is derived

from the spiked sample recoveries for each analyte using the following equation: MDL = tS, where t is the Student t test value for the 99% confidence level with n-1 degrees of freedom and S denotes the standard deviation obtained from *n* replicate analyses. For the *n*=7 replicates used to determine the MDL, t=3.143. The Reporting Limit (RL) refers to a level where reliable quantitative results may be obtained, and is traditionally set by EM for ground water analysis at 0.05 ppb, between 1-5 times the MDL.

An additional consideration for method development is the need for unequivocal detection (*see* Fatah, 2009), i.e. detection without opportunity for ambiguity that may result from interference or coelution. For multiple herbicides, if the analytical method is developed using the liquid chromatography/mass spectrometer (LC/MS), the lab has techniques to deal with coelution. The method distinguishes elution of similar compounds based on two retention times, one in the LC stage, and another in the MS stage. Each active ingredient or transformation product has characteristic fragments, based on size and charge, that help in its determination. For example, in the case of tebuthiuron, two transformation products with similar charge and retention times were not distinguishable based on either LC or MS. The lab modified the mobile phase used during liquid elution by altering the solvent to water ratio to increase peak separation in order to produce unequivocal detection of the two transformation products.

Active Ingredients and Transformation Products to Include in 2009 Method Development Request

Priority AIs for method development.

EM prioritized AIs on the 6800 GWPL using a combined ranking scheme based on fate and transport modeling and pesticide use reporting. Of the AIs that were high priority, iprodione was selected as the primary candidate for analytical method development, with dicloran, azoxystrobin and ethofumesate identified as lower ranked priorities. Ethofumesate is not analytically compatible with iprodione, however EM believes the following active ingredients could be included in the 2009 analytical method request:[1]

Azoxystrobin
Chlorothalonil
Dicloran[2]
Iprodione
Vinclozolin

[1] Listed in alphabetical order in this memo for ease of reference.
[2] Dicloran has no significant transformation products.

Vinclozolin has about a tenth of the use of iprodione, however EXTOXNET states, "In soils that had been treated consistently with iprodione for 10 or more years, slow or little breakdown of the compound vinclozolin occurred, while in soil that had been treated with vinclozolin rapid degradation of vinclozolin and iprodione occurred." Although vinclozolin is currently only registered for turf, historically its use on crops was similar to iprodione use. Because of degradation interactions and common breakdown products, iprodione and vinclozolin should be included in the same analytical method.

Environmentally relevant transformation products for method development.

Rather than prioritizing potential analytes by toxicity, EM experience has shown it is more valuable to prioritize method development and monitoring based on persistence and mobility. Additionally, in the data EM reviewed, few documents discuss of the toxicity of transformation products that can be expected from contact with the soil column. Toxicity discussions are geared toward establishing food tolerances of AIs and metabolites, i.e. biotic breakdown products found in plants and animals, rather than toward toxicity of degradates that were identified in soil metabolism and half-life studies. Therefore, transformation products for ground water method development were selected on the following basis:

1. Transformation products formed that were greater than or equal to 10 percent of the applied parent in laboratory soil metabolism or dissipation studies; and/or
2. Transformation products that have particular ecological or toxicological significance; and/or
3. Transformation products that appear to be persistent in the environment.

General information regarding transformation product toxicity is included in the discussion if such information is available.

Azoxystrobin transformation products:

1. Methyl(Z)-2{2-[6-(2-cyanophenoxy)pyrimidin-4-yloxy]phenyl}-3-methoxyacrylate (R-230310).
2. (E)-2-[6(2-cyanophenoxy)pyrimidin-4-yloxy]phenyl}-3-methoxyacrylic acid (R-234886).

R-230310 is the geometrical isomer of azoxystrobin. No information regarding the half-life or mobility of R-230310 is currently available.

R-234886 makes up 28.8% of the applied mass in laboratory studies, and is a persistent transformation product of azoxystrobin. In a 1995 California terrestrial field dissipation study Zeneca found R-234886 at the 0-6” depth after 377 days (Registrant Data, Record No. 146894).

In an uncited study quoted by US EPA, R-234886 was found after 371 days in the 6-18" soil depth of another terrestrial field study.

Chlorothalonil transformation products:

1. 4-hydroxy-2,5,6-trichloroisophtalonitrile (SDS-3701)
2. 2-amido-3,5,6-trichlo-4-cyanobenzenesulphonic acid (R-417888)
3. 3-carbamyl-2,4,5-trichlorobenzoic acid (SDS-46851)

The three chlorothalonil transformation products all exceed 10% of the applied mass of the parent; furthermore, the transformation products are more mobile and persistent than chlorothalonil. Toxicological research regarding SDS-3701 is included in the April 1999 EPA RED for chlorothalonil because residues for SDS-3701 have been found in food products, finding that SDS-3701 is moderately toxic. Syngenta Crop Protection's "ENVIROfacts" notes that R-417888 and SDS-26851 have been detected in ground water but claim that the molecules are not biologically active and therefore pose no risk. The EU Footprint Database, however, notes moderate R-417888 toxicity for both mammals and fish, as well as low mammalian toxicity and moderate fish toxicity for SDS-46851.

SDS-3701 makes up 32% of the applied mass in laboratory studies. The EU Footprint database lists SDS-3701 soil half-life as 387 days (with an EU dossier range of 20-343 days) in the environment, with a half-life of 130.6 days under laboratory conditions at 20° C. The Koc of SDS-3701 is moderately low at 380 ml/g, although the EU dossier contains a range for Koc values of 95-1100 mg/L.

R-417888 makes up 20% of the applied mass in laboratory studies. The EU Footprint database lists a half-life of 121.1 days under laboratory conditions at 20° C. The Koc of SDS-417888 is very low at 10 ml/g, and the EU dossier range for Koc values is 6-17 mg/L.

SDS-46851 makes up 13.2% of the applied mass in laboratory studies. The EU Footprint database lists a half-life of 103 days under laboratory conditions at 20° C. The Koc of SDS-417888 is very low at 77 ml/g, but no range for Koc values is listed.

Iprodione transformation products:

1. 3,5-dichloroaniline (RP-32596);
2. 3-(1-methylethyl)-N-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidine carboxamide (RP-30228);

RP-32596, also known as 3,5-dichloroaniline (3,5-DCA), is described as a "toxicant of concern" by the EPA because it is both carcinogenic and toxic to the liver and kidneys. Because 3,5-DCA is also the final breakdown product of vinclozolin, in order to correctly identify the parent compound both iprodione and vinclozolin must be included in the analytical method.

RP-30228 is the stereoisomer of iprodione, and forms spontaneously in neutral and alkaline environments. RP-30228 is more persistent than iprodione (recorded half-lives 215 and 319 days versus recorded half-lives 41.8 and 126 days, respectively), but has a higher Koc (6608 - 58120 versus 373-700, respectively). Importantly, RP-30228 makes up about 30% of the initial degradation products after iprodione application

Vinclozolin transformation products:

1. 3,5-dichloroaniline (same as iprodione transformation product RP-32596).

Confounding Analytical Method Combination Factors

It is possible that other AIs could be detected along with the fungicides discussed above. However, some products that could be added to the multiple analyte screen are already included in other multiple analyte screens or should be. For instance, the herbicides alachlor, metalochlor and s-metalochlor may be analytes that could be combined in the iprodione multiple analyte screen. However, there is an existing method for these AIs that include the environmentally relevant transformation products of those analytes.

It is also possible that linuron could be added to iprodione screen, however there are several reasons to exclude linuron. First, it is reasonable to combine AIs that have major transformation products in common to derive their provenance. Linuron's major transformation product is 3,4-dichloroanaline (3,4-DCA), which is also a transformation product of diuron and propanil. Diuron is included in the triazine screen (which does not include diuron's transformation products). Propanil should be folded into the triazine screen because it is currently in an inefficient single-analyte method. The triazine screen currently includes one AIs that is no longer registered (cyanazine) and another in which use has declined dramatically (metribuzin).

Availability of Standards:

Standards are readily available for azoxystrobin, chlorothalonil, dicloran, iprodione, and vinclozolin. Transformation products with established residue tolerances must be provided to the lab per EPA's Test Residue Guidelines, OPPTS 860.1650, Submittal of Analytical Reference

Standards. Of the environmentally relevant transformation products listed above, food tolerances have been established for the following:

- Azoxystrobin: R-230310
- Chlorothalonil: SDS-3701
- Iprodione: RP-32596 and RP-30228

If not readily available, the registrant or other companies specializing in boutique chemical manufacture may be able to synthesize the standards for transformation products that do not have food residue tolerances.

References

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