Biomonitoring Subcommittee
Biomarker Seminar

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What Does a Clinician Face?

• A farm worker comes in complaining of nausea, headache, weakness- got sick this morning while at work
  
  – Differential diagnosis:
    • Viral illness
    • Food poisoning
    • Hangover
    • Heat exhaustion
    • Medication reaction
    • Malaria
    • Pesticide poisoning
    • Green tobacco illness (if tobacco worker)
    • Pregnancy (if female)
Organophosphate Metabolites
(Found in children’s urine)
No easily accessible tests for most pesticides

Chlorpyrifos
- 3,5,6 Trichloropyridinol
- Diethylphosphate
- Diethylthiophosphate

Parathion
- Paranitrophenol
- Dimethylphosphate
- Dimethylthiophosphate

Methyl parathion
- Dimethyldithiophosphate

Malathion
The Importance of a Diagnosis: An Accurate Diagnosis Will Dictate More than Decontamination

- An accurate diagnosis leads to care and prevention
  - For the worker
    - Appropriate emergency treatment
    - A reliable report to the Worker Compensation System leading to adequate ongoing care
    - Removing worker from further exposure and worse illness
    - Correcting workplace hygiene failures
    - Education about how to avoid future overexposures
    - Notifying occupational health systems for future prevention
  - For the Public
    - Appropriate treatment for non workers
    - Protection of the public through reports to a surveillance system
    - Reports to EPA through 6(a)2
An Accurate Diagnosis Determines Whether EPA Knows There Is a Problem with a Chemical

- Reports from Clinicians
  - Clinicians don’t know how to diagnose pesticide illness, don’t have the tools
  - No tools = no training - medical schools rarely teach about pesticides
- Surveillance data
  - State systems
  - NIOSH SENSOR system
    - Both dependent on clinician reporting
- Poison Control Data
  - Reports biased toward children and exposures not poisonings
- 6(a)2 reports from Registrants
  - Dependent on clinician reports
Diagnosis: The Weak Link in the Reporting and Care system
We Need Diagnostic/Biomonitoring Tests to Prevent Future Illness

• **The promise of biomonitoring**
  – The availability and application of biomonitoring or diagnostic tests permits the early identification of exposure induced illness before it becomes severe
    – This applies both to individuals and populations
  – In Short:
    • Identify individual illness in the preclinical state
    • Identify population illness in the pre-epidemic phase
Population and Exposure Data, a Critical Component of the National Research Council
Toxicity Testing in the 21st Century

FIGURE S-1 The committee’s vision for toxicity testing is a process that includes chemical characterization, toxicity testing, and dose-response and extrapolation modeling. At each step, population-based and human exposure data are considered, as is the question of what data are needed for decision-making.
What the GAO Found: EPA Made Limited use of Biomonitoring Data in Risk Assessments

GAO recommends that EPA develop a comprehensive research strategy to improve its ability to use biomonitoring in its risk assessments; establish an interagency task force to coordinate federal biomonitoring research; and determine the extent of its legal authority to obtain biomonitoring data under TSCA, asking Congress for more authority if necessary. EPA agreed with the first two recommendations and did not disagree with the third, but provided substantive comments on its implementation.

GAO addressed TSCA but
The GAO did not address the EPA’s authority to require biomonitoring data under FIFRA

FIFRA gives broad authority to the Administrator to require different kinds of data from a registrant
Diagnosis with NEW Chemicals
What will Poisonings Look Like?

• We don’t know what human overexposure looks like
  – Most information comes from ingestions in children or suicides
  – These are extreme and contaminated models
    • Dosages are very high
    • Children are different
    • Suicidal patients are not workers

• Frontline providers need these tools to deal with Old and New chemicals
Why do we Need Diagnostic Tests and Specific Biomarkers

• To improve clinical decision making
  – To initiate antidote use (if available)
  – To get workers the care they deserve (Worker Comp)
  – To make the workplace safer
  – To improve training of clinicians in the diagnosis of overexposures
• To improve EPA’s decision making
  – To enhance decisions regarding pesticides 6(a)2 and other surveillance systems
  – To protect human populations
  – To protect other exposed workers
• To monitor new chemicals and limit harm early
• To validate new toxicity testing paradigm
  – Part of the NRC vision for 21st cent Toxicity Testing
• To improve the science around the health effects of pesticides
  – Exposure assessment is the weakest link in environmental and occupational epidemiology
• Can EPA Do it? Under FIFRA they can.
### What pesticide biomarkers and diagnostic tools are currently available?

<table>
<thead>
<tr>
<th>Analytical Capability</th>
<th>Pesticide Class with Biomarkers/Diagnostic Tools</th>
<th>Examples of Current Monitoring Programs</th>
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</thead>
</table>
| •Measure pesticide compounds and their metabolites in human biological samples using high-throughput analytical methods | •Organophosphates, Pyrethroids, N-Methyl Carbamates, Organochlorines Herbicides, Fungicides, Repellants | •CDC’s National Biomonitoring Program  
•National Children Study |
| •Measure cholinesterase (ChE) inhibition to assess exposure pesticide overexposure | •Organophosphates  
•N-Methyl Carbamates | •State Agricultural Worker Cholinesterase Monitoring Programs  
•California  
•Washington  
•North Carolina  
•Florida |

### What are the near-term priorities (1-5 years) of the 21st Century Workgroup regarding pesticide biomarkers and diagnostic tools?

<table>
<thead>
<tr>
<th>Near-Term Priority</th>
<th>Promising Biomarker/ Analytical Method</th>
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<tbody>
<tr>
<td>•Identify biomarkers of exposure that have greater specificity to individual pesticides</td>
<td>•Analytical methods to detect parent compounds in blood, rather than non-specific urinary metabolites.</td>
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<td>•Develop analytical tools that are cost-effective, produce results rapidly, and can be routinely used in clinical and field settings</td>
<td>•ELISA Immunoassays (e.g. UC-Davis Laboratory of Pesticides &amp; Biotechnology)</td>
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### What are the long-term priorities (5-10 years) of the 21st Century Workgroup regarding pesticide biomarkers and diagnostic tools?

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<td>•Develop new biomarkers of effect that have greater relevance to human health effects</td>
<td>•Toxicogenomic-based analytical methods (e.g. transcriptomics, proteomics, and metabalomics) may be used to identify biomarkers of micro-level changes in biological pathways, gene expression, and protein characteristics</td>
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<tr>
<td>•Develop medical diagnostic tools that can be used to verify that individuals have been poisoned or overexposed to pesticides</td>
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